Lecture 10
Part 2

• Definition, concepts, advantages and limitations of
  – Antimicrobial sensitivity testing
  – Pathogen-directed therapy
  – Empirical therapy
  – Prophylaxis therapy

• Monitoring antimicrobial resistance patterns
Advantages and Limitations of Antimicrobial Sensitivity Testing
Testing is conducted in order to determine the best antimicrobial therapy for organisms isolated from clinical specimens.
ANTIMICROBIAL SENSITIVITY TEST

The type & extent of antimicrobial testing conducted depends on:
- The organism isolated
- Source of the culture (body site)
- Available antimicrobial agents
- Typical susceptibility patterns
LIMITATION OF ANTIMICROBIAL SENSITIVITY TESTS

- Sensitivity testing measures antimicrobial activity against bacteria under laboratory conditions (*in-vitro* activity), & not in the patient (*in-vivo* activity)

http://www.chemistryland.com/CHM107Lab/Lab1/PourWaterInTestTube.jpg
LIMITATION OF ANTIMICROBIAL SENSITIVITY TESTS

It cannot be assured, therefore, that an antimicrobial which kills or prevents an organism from growing in-vitro will be a successful treatment.
LIMITATION OF ANTIMICROBIAL SENSITIVITY TESTS

Selecting appropriate antimicrobial treatment also involves considering:

- the patient’s clinical condition
- the type & site of the infection
- any history of drug hypersensitivity

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http://www1.va.gov/optometry/images/patient_education.jpg
LIMITATION OF ANTIMICROBIAL SENSITIVITY TESTS

- It is also necessary to know the activity of the different drugs including their:
  - rates of absorption
  - diffusion in the tissues
LIMITATION OF ANTIMICROBIAL SENSITIVITY TESTS

- metabolism
- excretion,
- possible toxicity
- effects on the patient’s normal microbial flora

ANTIMICROBIAL SUSCEPTIBILITY TESTING

- It has also been used to determine if organisms are related.
- The microbiology laboratory routinely performs susceptibility testing for most bacteria.
If, for example, one finds numerous isolates with the same distinctive susceptibility pattern, it is necessary to determine whether the isolates come from an outbreak.
In many cases, susceptibility patterns are relatively stable & correlate well with the results of other typing systems.
However, selective pressure within an environment (hospital) may cause organisms to rapidly gain or lose resistance determinants.
Hence, it is relatively non-specific & has limited usefulness in determining true relatedness.
INDICATORS FOR ANTIMICROBIAL USE

- Appropriate reasons for antimicrobial use are influenced by:
  - Pathogen-directed therapy
  - Empirical therapy
  - Prophylactic therapy
Advantages and Limitations of Pathogen Directed Therapy
PATHOGEN DIRECTED THERAPY

◆ It describes antimicrobial use when the microbial pathogen has been determined based on the results of traditional culture, serology or newer molecular methods such as PCR to detect distinct nucleic acids of the microbial pathogen.

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http://www.uic.edu/classes/bios/bios100/lecturesf04am/nucleotides.jpg
PATHOGEN DIRECTED THERAPY

- If a culture has been used to recover the offending microbe & that microbe is a bacterium or yeast, antimicrobial susceptibility results can then be made available.

http://depts.washington.edu/nnptc/online_training/std_handbook/gallery/images/yeast.jpg
In pathogen directed therapy, the use of the narrowest spectrum antimicrobial is believed to reduce the emergence of antimicrobial resistance & superinfection.

Minimizing the cost of therapy is also important whenever equivalent alternatives are available.
Although therapy based on a positive nucleic acid amplification (PCR) is considered pathogen directed, susceptibility results are not available to tailor therapy.
To overcome this problem, a culture sometimes is preferred in tandem to confirm the non-culture diagnostic test results & to provide organisms for future susceptibility testing.

An example is the diagnosis of TB

http://health.state.ga.us/programs/tb/images/haltTb001.jpg
In other instances, the non-culture results direct therapy against a pathogen with a predictable susceptibility pattern.
PATHOGEN DIRECTED THERAPY

For example, a nucleic acid amplification test (PCR) with positive results, in the case of STDs caused by Gonorrhea or Chlamydia, routinely triggers therapy that has been recommended by consensus public health guidelines.

PATHOGEN DIRECTED THERAPY

- Likewise, in most hospitals, *C. difficile* colitis is almost never diagnosed on the basis of a positive culture & even when it is, susceptibility testing is rarely performed.

- The therapy chosen to treat *C. difficile* colitis should be based on recommendations from consensus guidelines.
Advantages and Limitations of Empirical Therapy
When no information about a causative pathogen is available (although Gram stain can be highly suggestive), therapy is said to be empirical.
It is usually represented in hospitalized patients, because they are sufficiently ill to warrant treatment before culture & sensitivity results are available.
Appropriate cultures, usually including more than one blood culture, should be collected from hospitalized patients before therapy is initiated.
Advantages and Limitations of Prophylaxis
Antimicrobial use that is designed to prevent infection rather than treat known or suspected infection is deemed prophylactic.
Most common type of prophylaxis is surgical antimicrobial prophylaxis.

It is indicated for surgical procedures in which the risk of wound infection is high enough to show significant benefit of prophylaxis.
For example, operations involving placement of a prosthetic device or operations in patients with severe immunosuppression.
Basic principles of antimicrobial prophylaxis in surgery should be recognized.

The antimicrobial spectrum of the drug chosen should be appropriate for the organisms most likely to cause infection.
The most common target pathogens are *Staphylococcus*, or *Streptococcus sp.*

Even in abdominal surgeries in which other organisms predominate in the bowel flora

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http://www3.niaid.nih.gov/NR/rdonlyres/263D4EDB-3C96-4AC6-8C58-B7AF8F6CF2C5/0/staphylococcus_epidermidis.jpg
Adequate tissue levels of the antimicrobial agent, usually a first generation Cephalosporin, should be present throughout the operative procedure from the time of first incision onward.
The duration of prophylactic antimicrobial use should be as short as necessary to:

- Minimize the emergence of resistant organism
- Reduce the incidence of side effects
- Reduce cost
This translates, in most cases, to a single preoperative dose & occasionally an additional dose or two if surgery duration is prolonged.
PROPHYLAXIS

- In general, any time the skin or mucosa is incised, prophylaxis should be considered.
- Whether the wound is clean, clean-contaminated, or contaminated.
Other unique medical conditions requiring antimicrobial prophylaxis include:

- Prevention of endocarditis in patients with high-risk valvular lesions
- Spontaneous bacterial peritonitis in patients with ascites
- Malaria in patients traveling to endemic areas
PROPHYLAXIS

- Certain types of prophylaxis are given immediately after exposure to high risk pathogens which can cause diseases such as meningococcal meningitis & HIV.

Monitoring Antimicrobial Resistance Patterns
Excessive use of antimicrobial agents must be curtailed to limit the emergence & spread of multiple resistance organisms.
Excessive use of antimicrobial agents is linked not only to the emergence & spread of resistance but also to adverse drug reactions in patients & added costs to healthcare institutions.
Clinicians usually focus their attention on the individual patient & are rarely aware of the ecological effects of antimicrobial agents on the patient, the hospital, the community & the world at large.
Healthcare institutions contain patients at increased risk of infection because the pathogens they harbor are exposed to antimicrobial selective pressure. These patients are also at risk of colonization or infection by antimicrobial-resistant pathogens.
NIH-Supported Sequencing Projects: Pathogens with High Levels of Drug Resistance

- HIV
- *Enterococcus faecalis*
- *Mycobacterium tuberculosis*
- *Neisseria gonorrhoeae*
- *Salmonella typhimurium*
- *Staphylococcus aureus*
- *Streptococcus pneumoniae*
- *Streptococcus pyogenes*
- *Candida albicans*
- *Plasmodium falciparum*
MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

- These patients are in close proximity to one another such that resistance is transmitted easily.
- Strategies, other than simply new drug development, must be stressed to curb antimicrobial resistance.
The surveillance for antimicrobial resistance is an essential first step in identifying priority areas for managing antimicrobial use from an infection control versus a pharmacy or antibiotic cost-containing perspective.
STRATEGY FOR MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

- Surveillance
- Formation of multidisciplinary antimicrobial team
- Drug utilization & clinical practice

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STRATEGY FOR MONITORING ANTIMICROBABIL RESISTANCE PATTERNS

◆ Surveillance
  - Periodic preparation of instructional resistance patterns (Antibiograms)
  - Provides Infection Control Practitioners (ICP) insight into what antimicrobial classes are most used & potentially misused

http://www.carec.org/annrep99/images/Image77.gif
STRATEGY FOR MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

- Surveillance
  - ICPs should also consider tracking the number of patients who are found on routine cultures to be newly colonized or infected with problem areas of resistance such as MRSA, VRE or C. difficile.
STRATEGY FOR MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

◆ Surveillance
  – the spread of these forms of resistance may be expressed as episodes of newly detected colonization or infection per 100 admissions or 1000 patient days.

Stomach and duodenum
(101 – 103 CFU/ml)
Lactobacilli
Streptococci
Yeasts

Jejunum and ileum
(104 – 108 CFU/ml)
Lactobacilli
Coliform bacteria
Streptococci
Bacteroides
Bifidobacteria
Fusobacteria

Colon
(1010 – 1012 CFU/ml)
Bacteroides
Bifidobacteria
Streptococci
Eubacteria
Fusobacteria
Coliform bacteria
Clostridia
Veillonella
Lactobacilli
Proteus
Staphylococci
Pseudomonades
Yeasts
Protozoa

CFU = colony-forming units

http://www.nutrition-partner.com/data/A7B8F05951E0452A9E03FFE84A866D6E.0.png
STRATEGY FOR MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

- **Surveillance**
  - This information is crucial for infection control efforts aimed at controlling resistance & antimicrobial use quality improvement
STRAIGHTY FOR MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

◆ Surveillance
  – Vigilance should be maintained by laboratory & infection control personnel regarding possible emergence of sentinel resistance patterns such as Vancomycin resistance in S. aureus.
STRATEGY FOR MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

◆ Formation of a multidisciplinary team
  – to achieve antimicrobial auditing
◆ Members of the team should include
  – an infectious disease physician
  – clinical / infectious disease pharmacists
  – microbiology laboratory
  – infection control
The mission of the multidisciplinary team usually includes:

- Controlling antimicrobial costs
- Improving patient care
- Reducing resistance
STRATEGY FOR MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

- Multidisciplinary team goals cont’d:
  - More emphasis should be placed on reducing resistance

- In order to achieve this, guidelines of acceptable use are necessary against which to compare actual practices
STRATEGY FOR MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

- Example of Formation of multidisciplinary team
- The community-acquired pneumonia guidelines cosponsored by the American Thoracic Society & Infectious Disease Society of America (IDSA)
- Guidelines for the empirical treatment of febrile neutropenic patients sponsored by the IDSA

http://www.uspharmacist.com/ce/105057/pneumonia.jpg
Another method of achieving the team’s mission includes the appropriateness of dosing, i.e.

- whether surgical antimicrobial prophylaxis is used according to the guidelines
- whether empirical therapy is routinely narrowed to pathogen directed therapy when culture results become available
STRATEGY FOR MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

◆ Drug utilization & clinical practice
  – Success of any program depends on improving practice wherever inappropriate antimicrobial use is found
  – Interventions such as computer-assisted drug protocols & feedbacks of prescribing habits in relation to guidelines have also been adopted

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STRATEGY FOR MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

- Drug utilization & clinical practice
  - Totalitarian approach may also be used to monitor, prevent & control antimicrobial resistance.
  - This method involves restricting access to certain drugs
STRATEGY FOR MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

Drug utilization & clinical practice
- Exclusion from formulary
- Placement on a list of drugs requiring approval before dispensing
- Alternating the use of different classes of antimicrobials to prevent the emergence of resistance (antibiotic cycling)
STRATEGY FOR MONITORING ANTIMICROBIAL RESISTANCE PATTERNS

◆ Drug utilization & clinical practice
  – Promulgation of institutional antimicrobial guidelines as well as educating prescribers such as clinical pharmacists, physicians & nurse practitioners can also be used to monitor, prevent & control antimicrobial resistance.