

University of Minnesota  
College of Pharmacy

PHAR 6124  
Pharmacotherapy IV

Patient-Centered  
Pathophysiologic Approach

Mark Kirstein, Pharm.D.  
Course Director

Spring 2009

# PHARMACOTHERAPY IV: Patient-Centered Pathophysiologic Approach

## Section Directors:

Infectious Diseases:  
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Oncology:  
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Pharmacotherapy IV – SPRING 2008  
Patient-Centered Pathophysiologic Approach  
MoosT 1-450  
T, Th – 10:10-12:05  
Friday – 9:05 – 9:55

This course serves as an introduction to the pathophysiology and pharmacology of infectious diseases, oncologic, and toxicologic disorders.

MEETING PLACE AND TIME

Lectures for this course will be held in MoosT 1-450. Tuesday, Thursday 10:10-12:05 and Friday 9:05-9:55

**Infectious Diseases Schedule**

**2009 INFECTIOUS DISEASES SCHEDULE**

<i>Day (Date)</i>	<i>Time</i>	<i>Topic, Readings</i>	<i>Lecturer</i>
Tuesday (1/20/09)	10:10-12:05	INTRODUCTION/PHARMACODYNAMICS	J. Rotschafer
Thursday (1/22/09)	10:10-11:00	BACTERIOLOGY	M. Ullman
	11:15-12:05	BACTERIAL RESISTANCE I	A. Noreddin
Friday (1/23/09)	09:05-09:55	BACTERIAL RESISTANCE II	J. Rotschafer
Tuesday (1/27/09)	10:10-11:00	AMINOGLYCOSIDE MONITORING	J. Rotschafer
	11:15-12:05	SINGLE DAILY DOSE AMINOGLYCOSIDES	J. Rotschafer
	12:00-12:00	ONLINE QUIZ	
Thursday (1/29/09)	10:10-11:00	AMINOGLYCOSIDE PROBLEM SETS	M. Ullman
	11:15-12:05	VANCOMYCIN	J. Rotschafer
	12:00-12:00	1 <sup>st</sup> AMINOGLYCOSIDE PHARMACOKINETICS QUIZ	
Friday (1/30/09)	09:05-09:55	FLUOROQUINOLONES	A. Noreddin
Tuesday (2/3/09)	10:10-11:00	ANTIFUNGALS	M. Ullman
	11:15-12:05	URINARY TRACT INFECTIONS	J. Rotschafer
	12:00-12:00	ONLINE QUIZ	
Thursday (2/5/09)	10:10-11:00	VACCINES	M. Ullman
	11:15-12:05	MENINGITIS	J. Rotschafer
	12:00-12:00	2 <sup>ND</sup> AMINOGLYCOSIDE PHARMACOKINETICS QUIZ	
Friday (2/6/09)	09:05-09:55	TUBERCULOSIS	A. Noreddin
Tuesday (2/10/09)	10:10-11:00	HIV-I	H. Vezina
	11:15-12:05	HIV-II	H. Vezina

	12:00-12:00	ONLINE QUIZ	
Thursday (2/12/09)	10:10-11:00	SEXUALLY TRANSMITTED DISEASES	M. Peterson
	11:15-12:05	HIV-III	H. Vezina
	12:00-12:00	3 <sup>rd</sup> AMINOGLYCOSIDE PHARMACOKINETICS QUIZ	
Friday (2/13/09)	09:05-09:55	VIRAL INFECTIONS	H. Vezina
Tuesday (2/17/09)	10:10-11:00	OPPORTUNISTIC INFECTIONS	M. Ullman
	11:15-12:05	SKIN AND SOFT TISSUE INFECTIONS	M. Peterson
	12:00-12:00	ONLINE QUIZ	
Thursday (2/19/09)	10:10-11:00	PNEUMONIA	J. Rotschafer
	11:15-12:05	OSTEOMYELITIS	M. Peterson
Friday (2/20/09)	09:05-09:55	ENDOCARDITIS	J. Rotschafer
Tuesday (2/24/09)	10:10-11:00	INTRA-ABDOMINAL INFECTIONS	M. Peterson
	11:15-12:05	BIOTERRORISM	J. Rotschafer
Thursday (2/26/09)	10:10-11:00	PARASITIC INFECTIONS	M. Ullman
	11:15-12:05	REVIEW	M. Ullman
Friday (2/27/09)	09:05-09:55	TOXICOLOGY THROUGH THE AGES	Filandrinos
<b>Tuesday (3/3/09)</b>	<b>10:10-12:05</b>	<b>FINAL EXAM</b>	

TOXICOLOGY SCHEDULE 2009

DAY (DATE)	TIME	TOPIC	LECTURER
Friday (2/27/09)	9:05-9:55	Toxicology Through the Ages	Filandrinos
Tuesday (3/3/09)	10:10-11:00	Infectious Diseases Final Exam	Rotschafer
	11:15-12:05	Infectious Diseases Final Exam	Rotschafer
Thurs. (3/5/09)	10:10-11:00	General Management and Gastric Decontamination	Filandrinos
	11:15-12:05	Laboratory Evaluation of the Poisoned Patient	Sioris
Friday (3/6/09)	9:05-9:55	Drugs of Abuse (Stimulants) <b>Case Study</b>	Gualtieri
Tuesday (3/10/09)	10:10-11:00	Drugs of Abuse (Opiates, hallucinogens, GHB, inhalant abuse)	Gualtieri
	11:15-12:05	Sedative Hypnotics/Alcohol Withdrawal	Gualtieri
Thursday (3/12/09)	10:10-11:00	Acetaminophen Toxicity <b>Case Study</b>	Filandrinos
	11:15-12:05	Snakes and Spiders	Keyler
Friday (3/13/09)	9:05-9:55	Mid-Term	Sioris
Tuesday (3/17/09)	10:10-11:00	SPRING BREAK	
	11:15-12:05	SPRING BREAK	
Thursday (3/19/09)	10:10-11:00	SPRING BREAK	
	11:15-12:05	SPRING BREAK	
Friday (3/20/09)	9:05-9:55	SPRING BREAK	
Tuesday (3/24/09)	10:10-11:00	Calcium Channel Blockers/Beta Blockers <b>Case Study</b>	LeMaster
	11:15-12:05	OTC Drug Products/Vitamins/Dietary Supplements	K. Sioris
Thursday (3/26/09)	10:10-11:00	Salicylates/Non-Steroidals <b>Case Study</b>	Kingston
	11:15-12:05	Toxicology Potpourri	LeMaster
Friday (3/27/09)	9:05-9:55	Antidepressants <b>Case Study</b>	Gualtieri
Tuesday (3/31/09)	10:10-11:00	Ethylene Glycol/Methanol <b>Case Study</b>	Filandrinos
	11:15-12:05	Household Products & Carbon Monoxide <b>Case Study</b>	Sioris
Thursday (4/2/09)	10:10-11:00	Alcohol & Forensic Toxicology	Sioris
	11:15-12:05	Pesticides (Organophosphates & Pyrethrins) <b>Case Study</b>	K. Sioris
Tuesday (4/7/09)	10:10-11:00	Toxicology Final	Sioris

### *Oncology Schedule*

<i>Date</i>	<i>Topic</i>	<i>Lecturer</i>
Friday 4/3/09	Introduction to Oncology	Jacobson
<b>Tuesday 4/7/09</b>	<b>Toxicology Exam</b>	Sioris
Tuesday 4/7/09	Introduction to Oncology	Jacobson
Thursday 4/9/09	Chemotherapeutic agents	Kirstein
Thursday 4/9/09	Chemotherapeutic agents	Kirstein
Friday 4/10/09	Antiemetics	Whalen/Lohr
Tuesday 4/14/09	Antiemetics	Whalen/Lohr
Tuesday 4/14/09	Colorectal Cancer/Pancreatic Cancer	Kirstein
Thursday 4/16/09	<b>Quiz</b> ; Prostate Cancer/Renal Cell	Kirstein
Thursday 4/16/09	Oncology Complications	Lohr
Friday 4/17/09	Oncology Complications	Lohr
Tuesday 4/21/09	Fever and Neutropenia	Jacobson
Tuesday 4/21/09	Breast Cancer	Fahrenbruch
Thursday 4/23/09	Breast Cancer	Fahrenbruch
Thursday 4/23/09	Lung Cancer	Kirstein
<b>Friday 4/24/09</b>	<b>Exam through Fever and Neutropenia</b>	Kirstein
Tuesday 4/28/09	Gynecologic Cancers	Lohr
Tuesday 4/28/09	Cancer Pain	Fahrenbruch
Thursday 4/30/09	Cancer Pain	Fahrenbruch
Thursday 4/30/09	Lymphoma	Long-Boyle
Friday 5/1/09	PHARMACY DAY – NO CLASS	
Tuesday 5/5/09	<b>Quiz</b> Pharmacogenetics	Jacobson
Tuesday 5/5/09	Leukemia	Lohr
Thursday 5/7/09	Leukemia	Lohr
Thursday 5/7/09	Hematopoietic Stem Cell Transplant (HSCT)	Jacobson
Friday 5/8/09	Chemotherapy Orders	Kirstein/Jacobson
<b>Final Exam: Finals Week</b>	<b>Exam (Breast Cancer through HSCT)</b>	Kirstein

### COURSE OBJECTIVES

#### *Infectious Diseases*

The infectious diseases section of the course relates to pharmacotherapeutics and treatment of infectious diseases and aims to integrate material from MedC 6156, and other courses, with infectious disease topics important to the clinical setting. Ideally, at the end of this course the student will be able to: identify likely pathogens responsible for a particular infectious disease process; select the appropriate antibiotic(s) to provide antimicrobial coverage for these possible pathogens; select alternative antibiotics should they become necessary; and identify appropriate actions to monitor for efficacy and toxicity. To accomplish these goals, the student will be required to comprehend common microbiologic laboratory tests used to identify microorganisms.

The student will be expected to know the mechanisms of action, antimicrobial spectrum, mechanisms of bacterial resistance, common adverse reactions, pharmacokinetics, and appropriate dosing of the various antibiotics discussed in the upcoming lectures. The students

will be expected, given a set of serum concentration time data, to calculate an appropriate dose and dosage interval for any one of the available aminoglycosides.

### Toxicology

Upon completion of this section of the course, the student should be able to:

1. Describe the general principles in the management of all drug overdoses and chemical exposures including how to perform each of the following measures:
  - Supportive care/CPR
  - External decontamination (skin/eye)
  - Internal decontamination (oral)
  - Prevention of absorption
  - Enhanced excretion
  
2. Know the appropriate clinical indications, uses, dosages, hazards/side effects and clinical monitoring parameters of the following agents:
  - Emetics
  - Lavage
  - Adsorbents
  - Cathartics
  - Whole Bowel Lavage
  - Forced alkaline/acid diuresis
  - Dialysis/hemoperfusion
  - Antidotes
  
3. Describe the clinical toxicology, i.e. toxic doses, toxic blood levels, mechanism of toxicity, signs and symptoms of toxicity, clinical course, prognosis, incidence, clinical and laboratory monitoring parameters, general and specific treatments necessary to manage the following poisoning emergencies:
  - Acetaminophen
  - Household Products
  - Carbon Monoxide
  - Salicylates
  - Iron
  - Pesticides
  - Sedative Hypnotics
  - Calcium Channel Blockers
  - Beta Blockers
  - Psychotropics
  - Cyclic Antidepressants, SSRIs
  - Serotonin Syndrome, Neuroleptic Malignant Syndrome
  - Drugs of Abuse (e.g. cocaine, amphetamines, ethanol, etc.)
  - Toxic alcohols (methanol, ethylene glycol)
  - Common OTC Drugs

### Hematologic and Oncologic Malignancies

The objectives of the oncology section of the course are to provide information about the pathophysiology of common oncology disorders and to present standard therapies for treating these disorders. Emphasis will be placed on designing appropriate regimens, defining therapeutic goals, monitoring clinical and laboratory parameters, and identifying drug interactions and adverse reactions. The pharmacist helps to manage patients who experience the many complications related to the disease (e.g., pain management, hypercalcemia) and adverse

effects associated with treatment. Hence, the student is expected to devote considerable time, learning about the medication management of these unwanted side effects (e.g., febrile neutropenia, nausea/vomiting, etc.) in the oncologic setting.

#### COURSE PREREQUISITES

Successful completion of Pharmacotherapy I-III.

All students will have completed or be in the process of completing anatomy, physiology, and pharmacology. The student is responsible for this material to the extent necessary as a framework for infectious, oncologic and toxicologic therapeutics. Thus, students are encouraged to review basic anatomy and physiology and specifically encouraged to review the section of the pharmacology textbook relevant to the classes of drugs covered.

#### REQUIRED TEXTBOOKS

1. Pharmacotherapy, 7th ed, 2005, Ed. J.T. DiPiro, et. al. Reading assignments relevant to lecture topics.
2. Schwinghammer Pharmacotherapy Casebook will also be required for the Oncology Section of this course.
3. Electronic and print journal articles as outlined in the course schedules: infectious diseases, toxicology, oncology

In addition, the following references in toxicology are excellent resources for the student as additional recommended readings:

1. Goldfrank, Lewis. Goldfrank's Toxicologic Emergencies, 7th Edition, Appleton & Lange, Norwalk, Conn., 2007.
2. Clinical Management of Poisoning & Drug Overdose, Shannon, Borron, and Burns, Eds, 4<sup>th</sup> edition, WB Saunders Co, Philadelphia, 2007.
3. Poisindex, by Micromedix, Inc. Thompson Reuters, Englewood, Colorado.

#### WORK LOAD

For undergraduate courses, one credit is defined as equivalent to an average of three hours of learning effort per week (over a full semester) necessary for an average student to achieve an average grade in the course. We expect at least that much effort from our professional students. In this 5 credit course, you should expect to spend ten hours or more a week on coursework outside the classroom.

#### OVERALL DIVISION OF POINTS

The weighting of the total points for the class will be done according to the number of lectures devoted to each of the three sections: infectious diseases, toxicology, and oncology.

There will be 600 total points for the class. Infectious diseases will have 240 points, toxicology will have 160 points, and oncology will have 200 points. Each section director will divide the points within their section as they see fit.

A final grade for the course will be obtained by adding up the points gained in each section and dividing by 600, the total possible. For example, if a student received 200 points in infectious diseases, 120 points in toxicology, and 170 points in oncology, s/he would have 490 total points, or 82%, which would correspond to a final grade of B-.

## COURSE STRUCTURE/EXAMINATIONS

### INFECTIOUS DISEASES

The examinations for the infectious disease section of PHAR 6124 consist of 4 quizzes each worth 10 points, an aminoglycoside pharmacokinetic exam worth 20 points (ultimately everyone will need to demonstrate 100% competency to receive a grade in the course), and a 160 point final examination. Quizzes and the aminoglycoside pharmacokinetics exam will be given via WebCT/Vista. If competency is not established on the 1<sup>st</sup> aminoglycoside pharmacokinetic exam, students will be provided with two other opportunities via WebCt/Vista to establish competency.

In addition to passing the kinetics competency tests, each student MUST hand in answers to Problem Set II ([http://www.courses.ahc.umn.edu/pharmacy/6124/tutorials/glycoside\\_problem\\_set\\_2/problems2.htm](http://www.courses.ahc.umn.edu/pharmacy/6124/tutorials/glycoside_problem_set_2/problems2.htm)) at the beginning of the “Aminoglycoside Problem Set” lecture (to be given on January 29, 2009). Students handing in their problem set prior to class on January 29, 2009 will be awarded 20 points.

If a student is unable to pass the kinetics competency s/he will not receive a grade for the ID section of the class, making it impossible to pass PHAR 6124.

### TOXICOLOGY

This section of the class will be comprised of both lecture format and case study format presentations.

Case Studies: The students will be divided into 8 groups with each assigned a specific topic in toxicology. The groups will be informed of their topic on the first day of class. On a predetermined class period each group will be responsible for answering questions on a case involving that topic. These questions will come from the handout materials provided to the class in the syllabus. The group will be seated at the front of the class (the hot seat group) and asked a series of 8 questions pertaining to this topic by the instructor. Groups should get together to discuss potential questions and answers prior to their scheduled date to present. Use of notes during the actual case study session will not be allowed. A group leader will be assigned to each group and will be responsible for having individual group members answer questions during the case study. They will also be in charge of taking attendance for the group and turning this attendance sheet in at the end of class. For every correctly answered question by the group, each student of the group that is present will receive 4 points. The total number of points allotted will be 32 per topic and this will count as 20% of the total grade.

Class Attendance: Attendance will be taken each class period in which a case study is presented. Any points awarded during the case studies described above will only be awarded to the students that are in attendance that day.

Students will be given 1 hour to complete the final exam and midterm.

## QUIZZES

### INFECTIOUS DISEASES

There will be four quizzes throughout the infectious diseases section of the course. When announced, the quiz will be posted on WebCt/Vista. Students will have 24 hours to log in and take the quiz. Once you log in, you will have 30 minutes to complete the quiz. The quizzes may not be made up. There will be three opportunities to establish 100% competency in aminoglycoside pharmacokinetics. Each aminoglycoside pharmacokinetic exam will be posted on WebCT/Vista. Students will have 24 hours to log in and take the exam. You will have 60 minutes to complete the exam once logged in.

### TOXICOLOGY

Two exams will be given during the course, a midterm and a final. Exams will consist of both multiple choice and T/F questions. Each exam will be worth 64 points and 40% of your grade.

### HEMATOLOGY/ONCOLOGY

Quizzes in the hematology and oncology section are announced and will be given in the first ten minutes of class on scheduled days, or will be posted on WebCT. They will consist of true/false, multiple choice, and short answer questions, and may not be made up.

## EXAM POLICIES

- Use of programmable calculators is permitted so long as programmable features are not used providing an unfair advantage to other students. This would be an honor code violation.
- Your working area should be clear of all books, personal organizers, etc.. You need only your calculator, two #2 pencils, examination, and answer sheet. Graph paper will be provided if required.
- Once examinations begin, no one is allowed to leave the room (i.e. to go to the restroom, etc.) until they have completed the examination.
- Write your name and ID# on the test, answer sheet, and graph paper.
- Number your answer sheet with the number on your test and remember to fill in the dots corresponding to your name and ID#.
- If students have any questions that arise while taking the exam, then they should approach the test proctor alone.
- Hand in all three items: your exam, graph paper, and answer sheet at the end of the exam.
- No grade will be assigned until each exam item is returned.
- Exams and quizzes will not be graded on a curve

Letter grade assignments appearing on your transcripts are as follows: Common rounding rules will be applied to the final grade (as per Microsoft Excel® where 0.5 and higher values are rounded up).

A	≥ 93%
A-	90-92%
B+	87-89%
B	83-86%
B-	80-82%
C+	77-79%
C	73-76%
C-	70-72%
D	60-69%
F	< 60%

### Make-Up Policy

Please note: MAKE-UP EXAMINATIONS, QUIZZES AND OTHER ASSIGNMENTS WILL NOT BE OFFERED **EXCEPT** UNDER THE FOLLOWING CIRCUMSTANCES: illness, verified by a note from a licensed professional; a family emergency, verified by a note from the professional person in attendance; or a University-sponsored event, verified by a note from the leader of the sponsoring organization. Additional circumstances will be considered at the discretion of the course or section director, but are not likely to be granted. If a student is unable to attend the scheduled exam, the relevant section director must be notified (by email and phone) at least 24 hours in advance of the exam time (where possible). If you do not receive a reply to your request prior to the examination time, please do NOT assume that your request has been granted. Contact us again to confirm your request was received and processed. If an acceptable circumstance or adequate documentation is not provided within one week, a grade of zero on the exam, quiz, etc. will be assigned by the course or section director. Unless there are extenuating circumstances, students must contact the course or section director within 24 hours of the missed scheduled exam, quiz or other assignment in order to be considered for a make up assessment.

### Workload Expectations:

The University of Minnesota defines one credit as equivalent to an average of three hours of learning effort per week (over a full semester) necessary for an average student to achieve an average grade in the course. For example, a student taking a five credit course that meets for five hours a week should expect to spend an additional ten hours a week on coursework outside the classroom. You will get the most out of this course by actively participating in the assigned readings, pedagogical tools (quizzes, oral and written exams, review sessions, assignments, etc.).

### Disability Accommodations:

Any student with a documented disability (eg. physical, learning, psychiatric, vision, hearing, etc.) who needs to arrange reasonable accommodations must contact the course directors as well as each section director for the course. Documentation of the need for accommodations should be received within the first week of the course and at least 7 days before any exam or test. It is assumed that Disability Services (TC: <http://ds.umn.edu/>, 612-626-1333, Duluth: Access Center, <http://www.d.umn.edu/access/>, 218-726-8217) has been contacted to document the disability and quantify the necessary accommodations before the beginning of the Semester. All discussions concerning this issue will remain confidential.

### Class Etiquette:

The instructors expect all students to conduct themselves in a professional manner consistent with the University of Minnesota Pharmacy Student Code of Ethical Responsibility and Professional Behavior. Students will not engage in disruptive classroom conduct. This refers to behavior that substantially or repeatedly interrupts either the instructor's ability to teach or student learning. The classroom extends to any setting where a student is engaged in work toward academic credit or satisfaction of program-based requirements or related activities.

### Honor Code:

Each student is bound by the following specific provisions as part of the honor code: Academic misconduct is any unauthorized act which may give a student an unfair advantage over other students, including but not limited to: falsification, plagiarism, misuse of test materials, receiving unauthorized assistance and giving unauthorized assistance. Specifically, each student will be required to do their own work on all quizzes (on line or written), tests, oral and written exams.

### Exam Dates:

Exam dates will not be changed from those printed in the course schedule. Should the University be closed due to an unforeseen event the exam will be rescheduled.

### PROBLEMS/OFFICE HOURS

Any problems concerning the presentation of this curriculum or any problems related to this course should be directed to the section or course director. Teaching assistants are also available for feedback. All three section directors (Drs. Rotschafer, Kirstein, Sioris, Filandrinos, and Gualtieri) will have office hours by appointment. Please call any of them to make arrangements; they will be more than happy to get together with you.

### TEACHING ASSISTANTS

\*Office hours to be determined at a later date

Infectious Diseases: Mary Ullman, 612-626-6116 (ullma020@umn.edu)

Toxicology: Kelly Sioris, Pharm.D., 612-501-4961 (sior0003@umn.edu)

Oncology:: TBA

### COURSE WEB PAGE

The course webpage has been developed extensively and we will be relying on it as an integral tool in this class. <http://www.courses.ahc.umn.edu/pharmacy/6124/index.htm>

### EVALUATION OF INSTRUCTORS AND TEACHING ASSISTANTS

There is a great deal of time and effort devoted to the presentation of this curriculum. We are always looking for ways in which we might improve. We would greatly appreciate any comments you might have which might improve the way in which this course is presented to students. A formal evaluation will be held at the end of the course.

### BACKGROUND/EXPECTATIONS (Infectious Diseases)

A requirement for PHAR 6124 is a working knowledge of antibiotics listed below, which have been presented in previous courses (MedC 5164). Please review the following for both the midquarter and final exams. Further information on these antibiotics may not be given in class lectures.

You are responsible for:

- Mechanism of action
- Spectrum
- Mechanism of resistance (i.e., penicillin-resistant *Streptococcus pneumoniae*, vancomycin-resistant *Enterococcus*)
- Common side effects

### PENICILLINS:

Know the difference in spectrum and uses of penicillin, aminopenicillins (e.g. amoxicillin), penicillinase resistant penicillins, broad spectrum penicillins, and beta lactam/beta lactamase inhibitors combination products.

### CEPHALOSPORINS:

Know the difference in spectrum and uses of common first, second, third, and fourth generation cephalosporins. Pay particular attention to which agents have anti anaerobic activity, and which are active against *P. aeruginosa*.

### MISCELLANEOUS:

- Imipenem/cilastatin
- Aztreonam
- Daptomycin
- Tigecycline
- Rifampin
- Nitrofurantoin
- Clindamycin
- Doxycycline/Minocycline
- Trimethoprim/Sulfamethoxazole
- Metronidazole
- Vancomycin
- Chloramphenicol
- Erythromycin/ Azithromycin/ Clarithromycin
- Quinupristin/dalfopristin
- Linezolid
- Fluoroquinolones: older (e.g., ciprofloxacin), and newer (e.g., gatifloxacin, moxifloxacin)
- Polymyxins

### HEURISTICS (Infectious Diseases)

- Respiratory fluoroquinolones including levofloxacin, moxifloxacin, and gemifloxacin have increased activity against gram-positive bacteria (particularly *S. pneumoniae*) compared to older quinolones such as ciprofloxacin.
- Penicillin-resistant *S. pneumoniae* tend to show laboratory resistance to a number of other antibiotic classes.
- In the United States, 25%-30% of macrolide resistant *S. pneumoniae*.
- Methicillin resistant *S. aureus* (MRSA) also tend to be quinolone resistant.
- 10 to 40% of *Haemophilus influenzae* are ampicillin resistant.
- 80% of *Staphylococcus epidermidis* are methicillin resistant (MRSE).
- 50% of *Staphylococcus aureus* are methicillin resistant (MRSA).
- Almost all staphylococci are penicillinase producing.
- Enterococcus is preferably treated with a combination of penicillin or ampicillin or vancomycin plus either streptomycin or gentamicin when a systemic infection is suspected. Multiple antibiotic resistant enterococci are becoming much more common and traditional therapeutic approaches will usually not work for these organisms.
- Vancomycin is the drug-of-choice for methicillin-resistant *Staphylococcus epidermidis* (MRSE) and *Staphylococcus aureus* (MRSA) however, rising MIC values and alternative agents may change vancomycin's current status.
- No currently marketed cephalosporin should be used to treat methicillin resistant staphylococcal infections except ceftibiprole or ceftaroline.
- No currently marketed cephalosporin should be used to treat enterococcal infections.
- First and second generation cephalosporins do not provide adequate coverage for *Pseudomonas aeruginosa*.
- Of the cephalosporins only ceftazidime, cefepime, ceftibiprole and ceftaroline provide reasonable coverage for *Pseudomonas aeruginosa* infections. (Although these drugs may represent the cephalosporins of choice of *Pseudomonas* infections they may not be the drug of choice of *Pseudomonas* infections.
- Only some select third generation cephalosporins should be considered for treating meningeal infections (Selection of third generation cephalosporins should be based on the likely microorganism and penetration into cerebrospinal fluid and their CSF MIC.
- Of the currently marketed cephalosporins only ceftoxitin, cefotetan, and possibly ceftizoxime should be considered as adequate coverage for *Bacteroides fragilis* infections.

- No currently marketed cephalosporins should be considered as adequate therapy for *Listeria* infections especially central nervous system infections.
- The need for totally empiric or "blind" therapy is rare.
- The likely source of infection is a strong indicator of the likely cause of infection.
- The causes of community-acquired infection are different from the causes of hospital-acquired infection.
- The sources and causes of infection are more diverse in immunosuppressed patients than in normal hosts.
- Signs and symptoms of infection are more subtle and obscure in immunosuppressed patients.
- All empiric therapy regimens should be modified to a regimen appropriate for the susceptibility of the causative agent(s) once known.
- Antibiotic regimens should be the least toxic that is appropriate to the causative agent.
- The sicker the patient, the greater the need for immediate antimicrobial treatment.
- Neutropenic patients ( $100/\text{mm}^3$ ) require immediate institution of antimicrobial therapy if they appear to have infection.
- Infections of specialized body sites require special antimicrobial consideration (e.g. meningitis require high penicillin dosage to achieve adequate CSF levels endocarditis requires prolonged high dose therapy to prevent relapse).
- With a first order PK drug, an increase or decrease in dose will result in a proportional increase or decrease in serum concentrations.
- The time between the peak and the trough of an antibiotic given intravenously is  $T-t'$ .
- $K_0$  is an infusion rate and not a dose. Dose is equal to  $K_0 \times t'$ .
- With a first order drug, half-life and  $K_d$  are dose independent parameters. Any factor that prevents the patient from receiving the assumed dose of aminoglycoside will not change the determination of  $t_{1/2}$  or  $K_d$  providing post infusion data is used.
- Any factor that prevents the patient from receiving the assumed amount of aminoglycoside will result in an error in the calculation of distribution volume.
- Trough concentration drawn prior to the intravenous administration of an antibiotic must be extrapolated to the start of the antibiotic infusion.
- With aminoglycoside trough/peak checks, the trough concentration is used both in the calculation of  $K_d$  and in the calculation of volume of distribution at steady-state. Whereas with first- or second-dose kinetics the trough is used only in the calculation of volume of distribution.
- To accurately perform trough/peak pharmacokinetic studies, the patient must be at steady-state using the same dose, dosage interval, and infusion time while on the same schedule. The patient also must have received the drug for at least 5 half-lives and the clinical status (serum creatinine and fluid status etc.) are not undergoing dramatic change.
- An aminoglycoside dosage interval usually approximates two or three patient drug half-lives.
- The elimination rate constant, half-life, and distribution volume are similar between aminoglycosides (except for inactivation with beta-lactam antibiotics) i.e. pharmacokinetic data from one aminoglycoside can be used to develop a dosage and dosage interval for another aminoglycoside.

## ABBREVIATIONS

- AAPMC = Antibiotic associated pseudomembranous colitis
- ABW = Actual body weight
- AG = Aminoglycosides
- ARF = Acute renal failure
- AUC = Area under the antibiotic concentration curve
- BLIC = Beta lactam inhibitor combination
- caMRSA = Community acquired MRSA
- CLcr or CrCl = Creatinine clearance
- CNS = Central nervous system
- CRF = Chronic renal failure
- CSF = Cerebral spinal fluid
- DBW = Dosing body weight
- GISA = Glycopeptide intermediate S. aureus
- GNB = Gram negative bacilli
- HIV = Human Immunodeficiency Virus
- H-MRSA = MRSA hereroresistant MRSA
- LBW = Lean body weight
- LRTI = Lower respiratory tract infection
- MAC = Mycobacterium avium complex
- MBC = Minimum bactericidal concentration
- MIC = Minimum inhibitory concentration
- MOA = Mechanism of action
- MOR = Mechanism of resistance
- MRSA = Methicillin-resistant Staphylococcus aureus
- MRSE = Methicillin-resistant Staphylococcus epidermidis
- PAE = Post antibiotic effect
- PCN = Penicillin
- PD = Pharmacodynamics
- PK = Pharmacokinetics
- PMN = Polymononuclear cell
- SBE = Subacute bacterial endocarditis
- SBT = Serum bactericidal titer
- SDD = Single daily dosing
- SE = Side effects
- SIT = Serum inhibitory titers
- S/STI = Skin/soft tissue infection
- STD = Sexually transmitted diseases
- TB = Tuberculosis
- TMP/SMX = Trimethoprim/sulfamethoxazole (Bactrim/Septra)
- UA = Urinary analysis
- UO = Urinary output
- UTI = Urinary tract infections
- URTI = Upper respiratory tract infection
- VISA = Vancomycin intermediate S. aureus
- VRE = Vancomycin resistant Enterococcus
- VRSA = Vancomycin resistant S. aureus
- WBC = White blood cell(s)