

# GUIDELINES FOR THE MICROBIOLOGY/INFECTIOUS DISEASES COURSE

## ORGANIZATION OF THE COURSE

The overall goal of this course is to introduce you to the fields of microbiology and infectious diseases. It will cover a wide range of topics including bacteriology, virology, the pathophysiology and epidemiology of infectious diseases as well as the pharmacology of antimicrobial and antiviral agents (this latter part is a part of the pharmacology course). The intent is to provide an understanding of the medically relevant bacterial, fungal and viral pathogens and the diseases they produce. The emphasis will be on the pathophysiology of these diseases, the nature of host-parasite interactions and the different clinical syndromes caused by these pathogens. It is not the purpose of this course to teach the clinical management and therapy of infectious diseases.

### General Comments

A list of the entire faculty involved in this course is included at the front of the syllabus. If you have any questions, feel free to contact individual lecturers, case discussants or laboratory instructors. In addition, the course director (Frank Lowy) is available to discuss any questions or problems you have regarding the course. Drs. Christine Hogan, Michael Yin and Scott Hammer are co-directors of the course and are also available for assistance. Information for the class will be announced at lectures and sent out by email. One of the course directors or co-directors will be at all lectures. Dr. Lowy is available by email [fl189@columbia.edu](mailto:fl189@columbia.edu) or by phone (305-5787). Dr. Hogan is available by email [ch358@columbia.edu](mailto:ch358@columbia.edu) or by phone (305-6724).

For the **dental students** there are two advisors who will assist with the course - Dr. Hamish Young [csy1@columbia.edu](mailto:csy1@columbia.edu) and Dr. Steven Lee [s12385@columbia.edu](mailto:s12385@columbia.edu). They will be available to answer questions during the course. In addition Dr. Lee will arrange to have several lectures/discussions that are more directly relevant to oral microbiology.

The **case discussions** have been designed to give you an opportunity to apply the information you have learned in the lectures to clinical cases. The cases have been selected to illustrate many of the classic manifestations of relatively common infectious diseases. As such, it will be necessary for you to integrate your knowledge of specific pathogens and their particular mechanisms of virulence with the different clinical presentations caused by these microorganisms. In addition, one of the discussions deals with the use of antimicrobial agents in the clinical setting. Most (but not all) of the material discussed in these sessions will be covered in the lectures prior to the case discussions. Slides accompanying the cases are posted on the course website.

To assist with the discussion of these cases, different groups of students are assigned to lead each of the case discussion sessions. The assignments can be found at the end of the case discussion section of the syllabus. **Assigned students are expected to lead these discussions. This is a course requirement.** Failure to participate in the assignment will result in an incomplete for the course. Assigned students should supervise the session. They should be familiar with the material and be prepared to guide the discussion. They are not responsible for providing all the answers but should instead encourage participation of the entire group. The faculty will be there to assist with the discussions but they will not be responsible for leading the sessions. If you have questions or would like further assistance prior to a particular small group session, you may call the faculty advisor for your group.

The **laboratories** are designed to familiarize you with the basic techniques used to isolate and identify organisms from clinical specimens. Please remember all clinical specimens should be handled with care (*i.e.* wear gloves, no food *etc.*). These exercises will include the recognition of different microorganisms,

plating of potentially infectious secretions, learning how microorganisms are identified and how their antimicrobial susceptibility is determined. In order to provide you with more "hands on" time, much of the information you will need has been included in the manual. **Please review the material for each session in your laboratory manual prior to the laboratory sessions.** These sessions have been designed to provide you with exposure to typical infectious diseases problems. You will be given demonstration material to examine followed by brief case histories and clinical specimens. Your mission (which you will accept) is to identify the different unknown pathogens. A clinical microbiologist and infectious diseases specialist will be present in each laboratory to assist you.

One program entitled Gram Stain-Tutor is available on the school network. All students should review it at some point during the course (it would be a very good idea to do this before the final exam). There are a number of other useful programs included in this package that you may want to explore. The URL address for the site is:

<http://library.cpmc.columbia.edu/medtraining/start.html>

The user name (email address) is: **library** The password is: **cumed**  
Ignore the domain request.

#### **N.B. System Requirements:**

Microsoft Windows running Internet Explorer 5 or higher  
Microsoft Windows Media Player 6.4 or higher  
The program does not work with Macs (go figure).

This program, developed by the University of Washington provides instruction in the performance and interpretation of Gram stains.

Several study aids kindly donated by students from the Class of 2006 are posted on the course website. This material has not been vetted by the MID course faculty.

**Reading Assignments:** The recommended (but not required) text is: **Medical Microbiology 4<sup>th</sup> edition edited by Murray, Rosenthal, Kobayashi and Pfaller.** It should be used as a study guide. The reading assignments are optional. You are responsible for the material in the lectures, syllabus, small groups and the laboratories. Several copies of the text have been placed on reserve in the library. PowerPoint slides for the lectures will be made available on the course web site. Several additional texts that may prove useful as references or for issues you may want to pursue further are listed below.

1. Mandell, Douglas, Bennett. **Principles and Practice of Infectious Diseases**, 5th edition, Churchill Livingstone, 2000.

An encyclopedic text of infectious diseases. This will be useful for the case discussions. The sections on antimicrobial agents are also excellent.

2. Mims *et al.* **Pathogenesis of Infectious Diseases**. Academic Press, 2000, 5<sup>th</sup> ed'n.  
A well-written discussion of host-parasite interactions.

3. Bernard Roizman Peter M. Howley Stephen E. Straus, *et al.* **Fields Virology**, Raven Press, 4<sup>th</sup> edition, 2001.  
The definitive text on virology.

4. **UptoDate Clinical Reference Library** CD rom and Web site.

Nice reviews of selected medical topics including the pathogenesis and clinical presentation of infectious diseases. Available through Columbia Web site

5. Dale and Federman, **Scientific American Medicine**

Concise summaries of infectious diseases and antimicrobial agents.

**Examinations and Determination of the Final Grade**

There will be two examinations for the course. The first examination will include material from lectures 1–28 (up to and including Anti-TB and fungal agents), Case discussions 1-5 (including antimicrobial session) and laboratories 1-2 (including Gram negative bacteria). The second examination will cover the remainder of the course material. The examination will be in the format of the National Board Exams (to help prepare you for the NBME). Questions will be single best choice (1 of 5-15 possible answers). All examinations will be sequestered (*i.e.*, returned at the end of the exam). Sample exam questions are provided at the end of this introduction. There will generally be 3-4 questions/lecture, laboratory or case discussion.

There will be two practice sample exams given during the course. These will be conducted using the audience response system. This will provide an opportunity for you to see how the questions are structured and to see how you and your buddies are doing.

The passing grade for the course will be based on a determination of the performance of the class on the exam. It will roughly be 1 1/2 – 2 standard deviations from the mean. There is no separate honors grade for this portion of the pathophysiology course but your performance in MID will contribute to your overall course evaluation.

**What you need to know!**

There is a guide provided at the end of this section summarizing what you should study for the different topics covered in the course (*i.e.* objectives). Several tables summarizing the bacterial, viral and fungal pathogens as well as antimicrobial and antivirals are also provided as study guides. **As a general rule you should focus on the material emphasized in the lectures, cases and laboratories as a basis for what is considered important.** Since the examination questions are very much in the format of the cases in the small groups it is in your interest to attend these sessions.

**Re-examinations and Make-up Examinations**

The 2nd year faculty committee will make a decision regarding make-up exams for students who fail or miss the final exam. The course directors do not make this decision.

**Exam Reviews**

If there is sufficient interest, there will be a closed book (*i.e.*, no notes taken) review of the exam questions shortly after the exam. The purpose of this review is educational. The questions that caused the greatest difficulty or interest will be discussed.

**Course evaluations**

Forms for evaluation of the individual lectures are included in the syllabus. Lectures can therefore be evaluated on the day of the lecture. **All input is welcome.** Feel free to discuss any concerns, criticisms or the rare positive comment with Drs. Lowy, Hogan, Yin and Hammer at anytime during the course.

## SAMPLE EXAMINATION QUESTIONS

The questions below are illustrations of both the form and content of questions. Examples are provided from different sections of the course. The questions are prepared in the same format as are used in the National Boards.

Question type:            Single best answer. Select one answer.

1.        Which type of mutation results in the failure to synthesize an amino acid?
  - a.        nonsense
  - b.        deletion
  - c.        missense
  - d.        regulatory
  - e.        antisense
  
2.        Which type of mutation can be suppressed by a mutated tRNA gene?
  - a.        nonsense
  - b.        deletion
  - c.        missense
  - d.        regulatory
  - e.        antisense
  
3.        Which bacterial component is unique to Gram-positive rods?
  - a.        Penicillin-binding proteins
  - b.        Porins (outer membrane proteins)
  - c.        Spores
  - d.        Flagella
  - e.        Mesosomes
  
4.        Which bacterial component is involved in cell wall assembly?
  - a.        Penicillin-binding proteins
  - b.        Porins (outer membrane proteins)
  - c.        Spores
  - d.        Flagella
  - e.        Mesosomes
  
5.        Which bacterial component is necessary for transport of solutes across the outer membrane?
  - a.        Penicillin-binding proteins
  - b.        Porins (outer membrane proteins)
  - c.        Spores
  - d.        Flagella
  - e.        Mesosomes

6. Which toxin acts on the neuromuscular junction by inhibiting the release of acetylcholine?
- Cholera
  - Tetanus
  - Botulism
  - Diphtheria
  - Enterotoxin
7. Which toxin interferes with protein synthesis by preventing peptide elongation?
- Cholera
  - Tetanus
  - Botulism
  - Diphtheria
  - Enterotoxin
8. A 48 year old male who had an aortic valve replaced 2 months ago presents with symptoms of endocarditis. Which of the pathogens below would be the most likely pathogen?
- |                           |                             |                          |
|---------------------------|-----------------------------|--------------------------|
| a. <i>S. aureus</i>       | f. <i>L. rnonocytogenes</i> | k. <i>S. sonnei</i>      |
| b. <i>S. epidermidis</i>  | g. <i>E. coli</i>           | l. <i>C difficile</i>    |
| c. Gp. A streptococcus    | h. <i>K. pneumonia</i>      | m. <i>B. fragilis</i>    |
| d. <i>H. influenzae</i>   | i. <i>P. aeruginosa</i>     | n. Viridans streptococci |
| e. <i>N. meningitidis</i> | j. <i>E. faecalis</i>       | o. <i>C tetani</i>       |
9. A 78 year old male on antibiotic (a cephalosporin) therapy for pneumonia develops profuse diarrhea in the hospital. Which of the pathogens below would be the most likely pathogen?
- |                           |                             |                          |
|---------------------------|-----------------------------|--------------------------|
| a. <i>S. aureus</i>       | f. <i>L. rnonocytogenes</i> | k. <i>S. sonnei</i>      |
| b. <i>S. epidermidis</i>  | g. <i>E. coli</i>           | l. <i>C difficile</i>    |
| c. Gp. A streptococcus    | h. <i>K. pneumonia</i>      | m. <i>B. fragilis</i>    |
| d. <i>H. influenzae</i>   | i. <i>P. aeruginosa</i>     | n. Viridans streptococci |
| e. <i>N. meningitidis</i> | j. <i>E. faecalis</i>       | o. <i>C tetani</i>       |
10. Match the fungus *Histoplasma capsulatum* with the most consistent clinical setting:
- A 35 year old AIDS patient develops fever, headache and a positive India ink preparation of his cerebrospinal fluid.
  - A 44 year old stockbroker who is an avid weekend gardener develops a hard nodule on his forearm with red streaks radiating upward.
  - A 50 year old Filipino man living in San Diego, California, develops severe left arm and elbow pain, with x-ray showing destruction of the proximal humerus and joint space.
  - A 24 year old pregnant woman develops a white vaginal discharge and severe perineal pruritus.
  - A 75 year old subsistence farmer in Indiana develops fever

11. Match the fungus *Sporothrix schenckii* with the most consistent clinical, insidious weight loss and a pattern on chest x-ray that resembles miliary tuberculosis. setting:
- A 35 year old AIDS patient develops fever, headache and a positive India ink preparation of his cerebrospinal fluid.
  - A 44 year old stockbroker who is an avid weekend gardener develops a hard nodule on his forearm with red streaks radiating upward.
  - A 50 year old Filipino man living in San Diego, California, develops severe left arm and elbow pain, with x-ray showing destruction of the proximal humerus and joint space.
  - A 24 year old pregnant woman develops a white vaginal discharge and severe perineal pruritus.
  - A 75 year old subsistence farmer in Indiana develops fever, insidious weight loss and a pattern on chest x-ray that resembles miliary tuberculosis.
12. Which of the following is the most effective type of vaccine presently available to prevent measles?
- Live attenuated vaccine
  - Formalin killed vaccine
  - Recombinant antigen vaccine
  - Polysaccharide vaccine
  - Polysaccharide-protein conjugate vaccine
13. Which of the following is the most effective type of vaccine presently available to prevent *Hemophilus influenzae*?
- Live attenuated vaccine
  - Formalin killed vaccine
  - Recombinant antigen vaccine
  - Polysaccharide vaccine
  - Polysaccharide-protein conjugate vaccine
14. In clinical settings, the acquisition of multiple antibiotic resistance by enteric gram-negative bacteria most often Involves
- conjugative plasmids.
  - generalized transducing phage.
  - nonconjugative plasmids.
  - spontaneous mutation.
  - transformation by R-factor DNA.
15. A 1 year old boy is admitted on January 25th to Columbia Presbyterian Medical Center with 7% dehydration. The mother states that he has had a low grade temperature, one day of vomiting and 2 days of diarrhea. He is having approximately 10 watery stools/day. There is no blood or mucous in the stool. His playmate is also ill, but all the parents are well. The most likely agent is:
- An Enterovirus
  - Norwalk virus
  - Campylobacter spp.*
  - Shigella
  - Rotavirus

16. A 30 year old woman has a urinary tract infection caused by *Escherichia coli*. She has a history of allergy to penicillin and sulfa drugs. The physician elects to treat the patient with oral tetracycline, 250 mg, four times daily for 10 days. It is appropriate to advise the patient
- to avoid the use of antacids.
  - to avoid alcoholic beverages.
  - to take the drug with milk.
  - that the urine may take on an orange hue.
  - that a rash due to cross-reactivity to sulfonamides may occur.
17. Which one of the following statements about occupational exposures to HIV is true?
- AZT is uniformly effective in preventing HIV infection following a needle stick.
  - Recapping of needles is essential because it reduces the incidence of needle sticks among housekeeping staff emptying receptacles.
  - A needle stick carries approximately a 1/50 chance of transmitting HIV.
  - No documented cases of occupational acquisition of HIV have yet occurred.
  - The risk of acquiring HIV from a needle stick is significantly less than that of acquiring hepatitis B.
18. You are beginning to educate a new patient with HIV about the risk of opportunistic infections. You explain that because his CD4 count has dropped to 185 you will need to institute antimicrobial prophylaxis against which of the following pathogens (in addition to initiating his antiretroviral therapy)?
- Pneumocystis jiroveci* (formerly *carinii*)
  - Cryptococcus neoformans*
  - Toxoplasma gondii*
  - Mycobacterium tuberculosis*
  - Mycobacterium avium* complex (MAC)
19. The adenovirus E1A and E1B genes are thought to participate in oncogenesis by which of the following mechanisms.
- Insert in the host DNA and upregulate cellular oncogenes.
  - Contribute to recombination between various gamma globulin promoters and cellular oncogenes.
  - Inactivate antioncogenes such as the retinoblastoma and p53 genes by binding to the protein products of each of these genes.
  - Increase growth factor receptor genes on the cell surface.
  - Activate a cascade of transforming events by increasing the level of tyrosine kinases.
20. The mode of transmission of *Chlamydia trachomatis* is:
- inhaled droplet
  - waterborne
  - person to person contact
  - fomite
  - foodborne

**ANSWERS TO SAMPLE EXAMINATION QUESTIONS**

- |     |   |     |   |
|-----|---|-----|---|
| 1.  | A | 11. | B |
| 2.  | C | 12. | A |
| 3.  | C | 13. | E |
| 4.  | A | 14. | A |
| 5.  | B | 15. | E |
| 6.  | C | 16. | A |
| 7.  | D | 17. | E |
| 8.  | B | 18. | A |
| 9.  | L | 19. | C |
| 10. | E | 20. | C |

## **WHAT YOU NEED TO KNOW!**

### *Bacterial, Fungal and Viral Pathogens*

You should be familiar with the following information for each of the pathogens covered in the course.

1. General microbiology/virology of the organism. This includes its classification, morphology (*e.g.* on Gram stain), how it is identified (major biochemical tests, *e.g.* beta hemolysis for Group A streptococci).
2. Epidemiology. Habitat, Types of exposure necessary for disease acquisition. Means of transmission of the disease.
3. Host-parasite interactions. Mechanisms of bacterial or viral virulence and their interaction with the host. What are the unique virulence factors associated with the pathogen? What is the host response to infection?
4. What are the most common clinical settings in which the pathogen is encountered?

### *Antimicrobials. Antifungals and Antimycobacterial Agents*

The information as outlined below in general refers to "families" of compounds. This means that you will not be expected to know differences between specific drugs (*e.g.* gentamicin and tobramycin) which basically have the same pharmacology and mechanism of action. For the penicillins and cephalosporins you will be expected to know the differences between the "generations" of these antibiotics. For example, the third generation cephalosporins are more active against a wider variety of pathogens than the first generation cephalosporins.

1. What are the mechanisms of action for these drugs?
2. What are the mechanisms of resistance to these antibiotics?
3. Against which pathogens does the antimicrobial have activity?
4. What is the pharmacology of the compound? This includes: primary method of administration, distribution into different tissues and mode of excretion.
5. What are the major toxicities of the drug?
6. What are the general indications for its use?

### *Infectious Diseases Syndromes*

The following information should be known for the different infectious diseases syndromes.

1. What are the pathogens most commonly associated with the disease?
2. What is the pathogenesis of the disease? This includes both bacterial/viral pathogenetic mechanisms as well as the host response to these pathogens.
3. What is the epidemiology of the disease? What are the predisposing factors that contribute to development of the disease? Are there seasonal or age-related issues associated with the disease?