FLORIDA ATLANTIC UNIVERSITY™

Graduate Programs—NEW COURSE PROPOSAL

UGPC APPROVAL _____
UFS APPROVAL _____
SCNS SUBMITTAL _____
CONFIRMED _____
BANNER POSTED _____
CATALOG _____

DEPARTMENT NAME: BIOMEDICAL SCIENCE

COLLEGE OF: Medicine

RECOMMENDED COURSE IDENTIFICATION:

PREFIX _____BMS_____ COURSE NUMBER ___ 6303_____ LAB CODE (L or C) _____

(TO OBTAIN A COURSE NUMBER, CONTACT MJENNING@FAU.EDU)

COMPLETE COURSE TITLE

CLINICAL MICROBIOLOGY

EFFECTIVE DATE
(first term course will be offered)

CREDITS: 3

TEXTBOOK INFORMATION:
***Medical Microbiology* 6th edition, Murray, Rosenthal, Pfaller 2009**

GRADING *(SELECT ONLY ONE GRADING OPTION)*: REGULAR ___X___ SATISFACTORY/UNSATISFACTORY _____

COURSE DESCRIPTION, NO MORE THAN 3 LINES: The overall objective is for the student to learn the relevant facts and principles underlying bacteria, parasites, pathogenicity, and host resistance. Armed with this fundamental information, the student will then capable of understanding and utilizing contemporary modes of treatment and prevention.

PREREQUISITES:	COREQUISITES:	OTHER REGISTRATION CONTROLS (MAJOR, COLLEGE, LEVEL):
MCB 3020		GRADUATE

PREREQUISITES, COREQUISITES & REGISTRATION CONTROLS SHOWN ABOVE WILL BE ENFORCED FOR ALL COURSE SECTIONS.

MINIMUM QUALIFICATIONS NEEDED TO TEACH THIS COURSE:
M.D OR PH.D.

Other departments, colleges that might be affected by the new course must be consulted. List entities that have been consulted and attach written comments from each. Department of Biology

Dr. Gary Rose, grose@fau.edu, 561-297-0675
Faculty Contact, Email, Complete Phone Number

SIGNATURES

Approved by:	*Date:*
Department Chair: _____	7-25-11
College Curriculum Chair: _____	7-14-11
College Dean: _____	7-19-11
UGPC Chair: _____	
Dean of the Graduate College: _____	

SUPPORTING MATERIALS

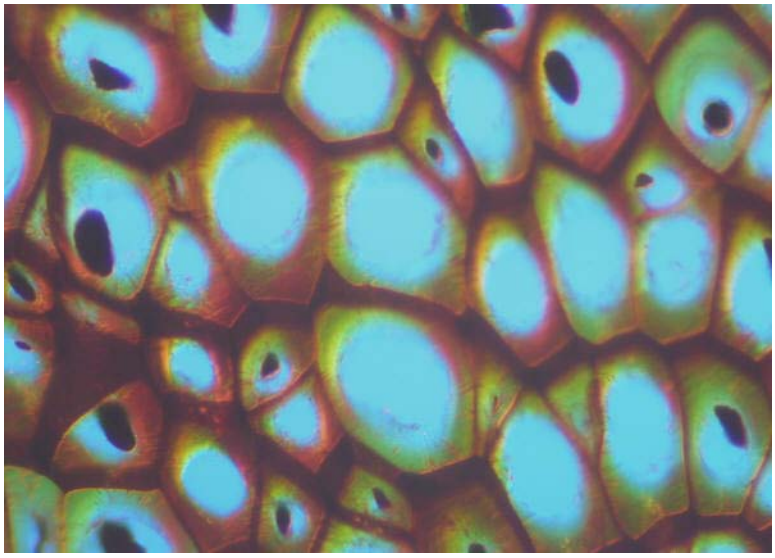
Syllabus—must include all details as shown in the UGPC Guidelines.

To access Guidelines and download this form, go to: *http://www.fau.edu/graduate/facultyandstaff/programscommittee/index.php*

Written Consent—required from all departments affected.

Email this form and syllabus to *diamond@fau.edu* one week ***before*** the University Graduate Programs Committee meeting so that materials may be viewed on the UGPC website by committee members prior to the meeting.

Clinical Microbiology



I. INTRODUCTION

Infectious diseases remain the single most important cause of human morbidity and mortality in the world. While significant inroads have been made by modern medicine into the treatment and prevention of many important infectious diseases, many more remain unconquered and cause untold misery and death. Yet the pathogens that cause these diseases represent only a very minor fraction of the enormous variety of microorganisms in the world. Many of these organisms are irrelevant to human beings, except insofar as they participate, both for good and ill, in the precariously balanced biosystem of earth. A significant number of organisms actually prove to be of crucial benefit to human beings - witness the commensal organisms that normally populate the gastrointestinal tract and thereby provide essential nutrients and vitamins. The idea that emerges from this consideration is that living organisms, both human beings and microbial agents, comprise integral participants in an interacting biological system in which competition for limited resources is intense. In this setting, genetically disparate species, even as vastly different as humans and bacteria, have come to discover that the survival of each may be enhanced by a symbiotic relationship in which each benefits from their interdependency. As in all such mutually dependent relationships, genetic or environmental factors can intervene to disrupt the balance, causing one or the other participant to gain temporary ascendancy. When the microorganism temporarily succeeds, human disease erupts.

However, not all relationships between microbes and humans are mutually beneficial. In order to establish a foothold in the biosphere, certain pathogenic microorganisms take unfair advantage of the human host. The more successful of these organisms exploit their human hosts for long periods of time, producing debilitation and morbidity, but usually not death. The less successful microbes exploit their human host with an imprudently aggressive attack that rapidly leads to death - both for the host and for the microbe. Since the strategies that microbial agents can use to take advantage of their hosts are exceedingly diverse, the study of Microbiology is broad in scope, deep in detail, and fascinating in its complexity.

Human beings are, of course, not devoid of protective mechanisms with which they can ward off successful microbial invasion. In fact, the strategies which human beings and other vertebrates, use to prevent and terminate infections with microbial agents are also exceedingly diverse and complex. It is convenient, if not always accurate to characterize microbe-human interactions as a contest in which the former achieves success in proportion to its "virulence" while the latter survives in health in relation to its "resistance". In general, the greater the imbalance of these opposing forces, the greater the likelihood that severe disease will result from an infection.

The ability of the physician to influence the outcome of this contest, in favor of the patient, depends upon the ability to (a) prevent the growth, multiplication and toxicity of the organism in the host and to (b) enhance the host's innate abilities to combat the pathogen by neutralizing its mechanisms of virulence.

In order to accomplish the first of these objectives, the physician must understand the structure and metabolism of the various agents that cause infectious diseases. From such understanding emerges pharmacologic approaches to interfering with growth/metabolism of the organism. For example, we can prepare a shrewdly designed semi-synthetic beta-lactam, ampicillin, being careful not to alter the acyl-D-analyl-D-alanine portion of the molecule which is a sensitive analog of the organism's peptidoglycan. When used in infected patients, this proves to be an exceedingly effective antibiotic. In addition, the physician must know the precise cellular and molecular strategy by which an organism exploits its host so that an effective plan for intervention can be designed.

II. COURSE DESCRIPTION

This Clinical Microbiology Course consists of Medical Bacteriology and Medical Parasitology.

III. OBJECTIVE OF THE COURSE

The overall objective is for the student to learn the relevant facts and principles underlying bacteria, parasites, pathogenicity, and host resistance. Armed with this fundamental information, the student will then capable of understanding and utilizing contemporary modes of treatment and prevention.

IV. TEXT BOOKS

The highly readable text**: Medical Microbiology 6th edition, Murray, Rosenthal, Pfaller 2009** is used as the reference text.

V. GRADING POLICY

Two examinations will be given in this 6 week course:
Exam 1: 50 points
Exam II: 50 points
The total points for Exams I and II = 100 points.

The Grading Scale is as follows:

90 – 100 = A
80 – 89 = B
70 – 79 = C
60 – 69 = D
< 65 = F

Please refer to the Florida Atlantic University Academic Calendar 2009 – 2010 for a complete listing of key dates for drop/add, withdrawal, etc.

Principles of Medical Microbiology

Bacterial Structure and Physiology

Lecture
Gary Rose, M.D.

Reading Assignment: Reference: Murray et al., *Medical Microbiology* 6th edition [9-23]

Role of Microbial Taxonomy

1- Association of specific organisms with disease
2- Accumulation of knowledge on disease management
3- Understanding mechanisms of pathogenicity and antimicrobial resistance
4- Recognizing new or emerging pathogens
5- Developing new anti-infective therapy

Identification Criteria and Characteristics for Microbial Classification

Morphology
-Macroscopic
-Microscopic
Staining characteristics
Environmental requirements
Nutritional requirements (vitamins, co-factors, CO2)
Antimicrobial resistance profiles
Bacteriophage susceptibility patterns
Analysis of structural components (proteins, fatty acids)
Antigenic properties (somatic and/or capsular)
DNA base composition (G+C ratio)
DNA base sequence analysis

Staining characteristics
-Gram's stain
-Acid –fast stain

Environmental requirements
-REDOX potential
aerobic……...high redox

-microaerophilic
facultative……high or low redox
anaerobic……low redox

-aerotolerant
-moderate obligate
strict obligate ……very low redox

capnophilic……C02 required/enhanced

pH requirement ……..<5 to >8 are selective for some organisms

NaCl requirement…….<0.5% to 10% (>1%= halophilic)

Temperature requirements

-psychrophilic…… 0-20o C
-mesophilic…….20-45o C
-thermophilic …… 45-80o C
Nutritional requirements

-carbon source
autotrophic =CO2 as sole source of carbon
photoautotrophic = photosynthetic bacteria
heterotrophic = derived from organic nutrients

-nitrogen source
-essential minerals e.g. Fe++

Energy Production and Metabolism [24-26]

1) Nutrient Uptake
a) active transport via carrier molecules on the cell membrane, energy dependent
b) substance translocation – energy dependent w/ substrate modification

2) Production of energy and precursor metabolites
a) Emden-Meyerhoff pathway (EMP);
b) Tricarboxylic acid pathway (TCA)
c) Pentose phosphate shunt (PMP)
d) Other alternative pathways

3) Energy production from carbohydrates
a) Substrate oxidized (glycolytic pathway; **EMP**) with
Production of high-energy intermediates (ATP) and metabolic intermediates (i.e. pyruvate)
b) oxidation of pyruvate to water and CO2 with the generation
of various intermediates and NADH and FADH (**TCA**) If the terminal electron acceptor is oxygen (**02**,) it is called aerobic respiration , if other inorganic compounds are used (NO3-, SO4-) it is called anaerobic respiration . Conversion of pyruvic acid into other end-products in the absence of O2 where the final electron acceptors are organic compounds is called fermentation (alcohols, acids. gas)

c) In aerobic respiration the NADH and FADH enter the electron transport system where cytochromes act as electron donor -acceptor compounds leading to the generation of ATP from ADP. Aerobic respiration yields more energy (38 ATP) than fermentation (2 ATP) per mole of glucose.

Energy Requirements of Obligate Intracellular Parasites

-Unable to generate full metabolic energy requirements and survive in a free- living state. Adapted to life internal to eukariotic cells.

Rickettsia, Ehrlichia = carrier –mediated transport system for key phosphorylated compounds

Chlamydia = unable to generate high-energy phosphate bonds. No Pentose shunt or TCA cycle. Heterotrophic for ATP

Structural Classification

Rigid Cell Wall

Cocci

Gram positive……Staphylococci, Streptococci

Gram negative……Neisseria

Bacilli

Gram positive

Spore producing……. Bacillus, Clostridium
Non-spore producing……..Listeria, Corynebacterium

Acid Fast…….Mycobacterium, Nocardia
Branching…… Actinomyces, Streptomyces, Nocardia

Gram negative……Enterobacteriaceae (many species)
Pseudomonas
Legionella
Haemophilus

Flexible , Spiral Cell Wall……Treponema, Borrelia, Leptospira

No Cell Wall…….Mycoplasma

Comprehensive Classification of Medically significant Bacteria—Examples of

Selected Genera

Gram Positive cocci in chains
Facultative anaerobe
Catalase not produced……Streptococcus
Group A carbohydrate present……Streptococcus pyogenes
M protein 2 present in cell wall……S. pyogenes M type 2

Gram Negative Bacillus, pleomorphic
Facultative anaerobe……..Haemophilus species
Require hemin and NAD……Haemophilus influenzae
Production of urease; no indole formation and no ornithine decarboxylase produced……..H. influenzae biotype III
Polyribose phosphate capsule present…… .H. influenzae serotype b, biotype III

Gram Positive Bacillus, pleomorphic, no spores
Acid Fast……Mycobacterium
Growth in < 7 days……..rapid grower
Production of Fe oxide from FeNH4Citrate……Mycobacterium fortuitum

<u>Molecular Basis of Taxonomy</u>

Genotypic classification

-Ratio of guanine-to-cytosine (G+C) ratio in DNA

examples: C. perfringens…….24-48
M. tuberculosis……..62-70
E. coli……..48-53

-Degree (%) of DNA relatedness among organisms define phylogenetic relationship as measured by DNA:DNA hybridization experiments. By convention, organisms within the same species have >70 % DNA:DNA relatedness.

-Nucleic sequence analysis
-amplification of a specific conserved target (i.e., 16S ribosomal RNA gene)
-nucleic acid base sequencing of amplification
-database search on known sequences for identification. Generally, <99% sequence homology between a minimum of 500 base pairs DNA sequenced suggests different species. Ideally, 1,500 bp segments should be examined. Other molecular targets such as normal house-keeping genes (e.g. rpoB) can be used.

Advantages of genotypic methods for classification:

-Independent of viability or growth in culture

-Independent of the expression of phenotypic characteristics

-Identification of previously unrecognized species

a) Mycobacterium genavense
b) Bartonella henselae
c) Tropherima whippellii

Microbial Structure

The Cell Envelope: [12]

Structural Components:

1. The capsule (selected strains)
2. The outer cell membrane (Gram negative organisms only)
3. The cell wall
4. The inner (cytoplasmic) membrane

The Capsule:[15]

-not essential for viability or growth
-produced by selected strains or species
-found in both Gram positive and Gram negative organisms
-confers mucoid appearance to colonial morphology
-production markedly affected by environmental and nutritional conditions
-composition variable –examples:

Streptococcus pneumoniae…… d-glucose, l-rhamnose d-glucuronicacid
Klebsiella pneumoniae…….glucose, fucose, glucuronic acid ,pyruvate
Haemophilus influenzae b…….polyribose-ribitol phosphate
Pseudomonas aeruginosa……..alginic acid
Yersinia pestis……protein
Staphylococcus aureus……..teichoic acid

Streptococcus pyogenes……..hyaluronic acid

Antigenicity:

-serologically distinguishable as “serotypes”
-some are poorly antigenic (e.g.,N. meningitidis type B)
-known as “**K**” antigens in the Enterobacteriaceae

Virulence potential:

-antiphagocitic
-inducer of host reaction
-antigen masking; avoidance of the effects of complement

<u>The Cytoplasmic Membrane:</u>

- composed of lipid bilayer and protein
- osmotic barrier for the cytoplasm
- mediates transport of solutes in and out of the cell
- location of enzymes responsible for outer membrane and cell wall synthesis
- location of enzymes involved in energy metabolism
- molecular sensor for changes in the environment

<u>The Gram Positive Cell Wall</u>

The Peptidoglycan Layer :[18]

1 - prominent murein (peptidoglycan) layer
2 - composed of alternating units of n-acetyl glucosamine (NAM) and n-acetyl muramic acid (MUR)
3 - NAM subunits are connected by a tetrapeptide with the third amino acid (i.e., lysine connected with the terminal alanine of another chain to from a peptidoglycan sheet
4- In organisms like S. aureus, peptidoglycan sheets are cross linked by an entending chain of five amino acids (polyglycine) from a diaminoepimelate or lysine component of one chain to the terminal d-alanine in the tetrapeptide of an adjacent sheet. This forms a petidoglycan lattice
5 -cross linking is mediated by membrane-bound enzymes which are susceptible to the action of penicillin and cephalosporin antimicrobial agents
6 -substitution of the terminal d-alanine with a lactate in some bacteria interferes with the action of glycopeptide (i.e. vancomycin) agents

Teichoic acids and lipoteichoic acid polymers: [17]

1- repeating units of glycerol or ribitol polymers combined with sugars & amino acids
2- teichoic acids are linked to NAM, lipoteichoic acids are linked to the outer cell membrane
3- serve as specific surface antigens
4- exert biological properties in part similar to endotoxin

The Gram Negative Cell Wall

1- murein layer is thin and separated from the cytoplasmic layer by a periplasmic space
2- some antibiotic-inactivating enzymes (β-lactamases) are found in the periplasmic space

The Outer Membrane:

1. is unique to Gram negative bacteria
2. composed of phospholipids and polysaccharides (40%) and proteins (60%)
3. protein components are often in the form of porins that control the passage of nutrients and other substances. Number and type vary with species, some are specific for certain substances. Porins are often antigenic.
4. contains the lipopolysaccharide (endotoxin) component of the cell envelope

The Outer Membrane Lipopolysaccharide (LPS) [18]

-hydrophilic and hydrophobic (amphiphylic) molecule
-consists of three regions:

a) lipid A (inner region) endotoxic component., a multiple effect biomodifier which is species-specific

1- fever induction
2- hematologic changes consistent with acute phase response to inflammation. Induction of IL-1, IL-6, TNF and other cytokine release. Rise in plasma cortisol levels. Disseminated intravascular coagulation, hypoferremia, leukopenia followed by leukocytosis
3- hypotension, decreased vascular perfusion

b) Core polysaccharide: (middle region)

1- composed of keto-deoxy octulosonic acid (KDO) bound to lipid A on one end and to chains of hexoses on the other. Necessary for organism viability and assembly of sugar side chains. The composition of KDO is moderately conserved among species

c) "O" polysaccharide chains: (outer region)

1- variable combination of polysaccharide chains
2- antigenic; species and strain-specific
3- known as "**O**" antigens in the family Enterobacteriaceae

The Cell Wall of Acid Fast Organisms

1- found in members of the Mycobacterium, Nocardia and related genera
2- cell wall resistant to decolorization of carbolfuchsin by acid-alcohol solutions
3- contain approximately equal amounts of peptidoglycan, arabinan and lipids
4- contain long-chain glycolipids known as mycolic acids that confer acid-fastness and protect the organisms against dehydration
5- may contain sulfolipids known as "cord factor" which is associated with virulence in *M. tuberculosis*
6- contain mycosides which are >34 specific surface peptidoglycolipid antigens

Other Microbial Structures

Flagella: protein fibrils arising from the cytoplasmic membrane that provide motility for the organisms. Can be found at the ends (polar) or throughout the cell surface (peritrichous). Known as "H" antigens in the Enterobacteriaceae

Pili (fimbria): perithrichous fine protein fibrils that mediate the attachment of many microorganisms to host structures. These are known as "adhesins" and are essential to pathogenicity. Specialized pili serve as conduits for DNA during bacterial conjugation (sex pili)

Spores: endosporulation is a form of cell differentiation, which is the property of some Gram positive bacilli (Bacillus, Clostridium). Endospores are dormant structures capable of long term survival and regeneration of the vegetative cell a given cell produces a single spore. Spores contain very low water content and no detectable metabolic activity. Spores contain large amounts of spore-specific dipicolinic acid (DIP) a chelating agent that accounts for about 10% of the weight of the spore. DIP intercalates into DNA/RNA displacing intra-molecular water. Regeneration of the replicative state occurs during favorable environmental conditions and is initiated by enzymes already present in the spore [21]

The Pathogenic Role of Microorganisms

The Natural Host-Parasite Relationship

- -The Normal Host
- -The Compromised Host
- -immunological: chemotherapy, immune modulators, cancer
- -physiological: ETOH, diabetes, cancer
- -physically: trauma, abrasions, foreign bodies, surgical wounds

-The Microbial Flora

- -transient colonizers
- -resident flora (commensals)

Microbial characteristics that contribute to colonization:

- -Survival vs. environmental conditions
- -localization in moist areas
- -protection within ingested or inhaled debris
- -Expression of specific metabolic faculties. e.g., high salt or low pH tolerance

-Attachment to host cell surfaces

Adhesins, pili or fimbriae, formation of biofilms

-Motility

-Competition factors

- -against other microorganisms = bacteriocins
- -against host = iron-binding proteins (siderophores)

-Ability to coexist with other organisms NOTE: ability to compete vs. other organisms as stated above also enhances potential for infection

Microbial characteristics leading to infection. (Virulence Factors)

- -Expression of specific attachment mediators
- -Invasion capabilities
- -inter and intracellular penetration (phagocytosis or pinocytosis)
- -tissue destruction

intracellular mutiplication
elaboration of exoenzymes (collagenases, nucleases, hyalorunidase)
elaboration of exotoxins

Microbial Exotoxins [182-184]

-Most commonly, but not exclusively associated with Gram Positive organisms
-Produced and actively released by living organisms
-Specific modes of action and host targets (eg., neurotoxins)
-May affect targets distant from the site of infection (eg., tetanus)
-Diverse mechanisms of action
-inhibition of protein synthesis
-interruption of cellular internal signals (e.g., cyclic AMP)
-interruption of neuromuscular interactions
-destruction of eukariotic cell membranes
-nonspecific antigenic stimulation (superantigens)

Survival Against the Effects of Inflammation

-Immunological anergy due to molecular mimicry
-antiphagocytic capsule and outer membrane proteins (OMP)
-facultative intracellular parasitism (macrophages)
-anticomplementary surface components (OMP'S)
-inactivation of humoral immune components e.g., IgA proteases

Modes of Transmission of Microbial Pathogens

-Passage from a natural reservoir to a susceptible host directly or via vectors,

Reservoirs include the environment (*Legionella pneumophila*), animals (*Mycobacterium bovis*) or humans (*HIV*, *Neisseria gonorrheae*). Vectors include water (*Shigella dysenteriae*) food (*entertoxigenic E. coli*) medical devices (*Mycobacterium chelonei*), Organ transplants *(Cytomegalovirus*) and insects (*West Nile Virus*, *Yersinia pestis*)

Structural and Physiological Basis of Microbial Identification [157-159,165-175]

In most laboratories detection and identification of microorganisms from clinical specimens is most commonly based on the study of specific structural and metabolic characteristics of microorganisms. This involves 1) culture of the organisms in artificial media and 2) identification by means of biochemical or occasionally immunological methods. Molecular techniques for detection and identification are coming into general use primarily in high-volume laboratories.

Detection:

Direct: - direct detection in tissues or other clinical specimens by histochemical, immunological or molecular techniques

Indirect: - Detection of microbial products i.e, capsular antigens by sensitized latex particle agglutination tests, or E. coli enterotoxins by enzyme immunoassay
- culture in laboratory media

Identification:

Determination of nutritional and atmospheric requirements
Susceptibility or resistance to key antibiotics

Determination of metabolic capabilities

-rapid single-enzyme tests i.e. catalase, cytochrome oxidase
-biochemical reactions: determination of nutritional uptake or acid production from carbohydrates by rapid or conventional methods .

conventional methods: dependent on growth of the organisms; may take > 18 hours
rapid methods: based on the presence of preformed enzymes

This takes approximately 4 to 6 hours. The results of biochemical reactions are subjected to analysis of metabolic profiles; comparison of biochemical tests results with database of known organsms' biochemical profiles

Identification: additional methods:

-chromatography (GLC or HPLC) of metabolic end products or cell wall fatty acid composition
-electrophoretic protein analysis of whole cell proteins or specific enzymatic proteins (multilocus enzyme electrophoresis; MLEE)
-molecular methods: nucleic acid probes with or without amplification (e.g , real-time PCR, probe microarrays etc.)

Microscopy

Medically Significant Gram Negative Bacteria

Lecture
Gary Rose, M.D.

Reading assignment: Murray et al. *Medical* Microbiology, 6th edition

Characteristics of gram negative bacteria that influence their medical significance
· epidemiological characteristics
· morbidity and mortality
· economic impact
· mechanisms to pathogenicity
· resistance to treatment
· diagnostic challenge

Mechanisms of virulence
· adherence (pili)
· invasion (outer membrane proteins)
· metabolic by-products (acids, gas)
· toxins (endotoxins, exotoxins)
· exoenzymes (proteases, siderophores)
· evasion of immune clearance (capsule, others)
· resistance to antimicrobials (β-lactamases, others)

Medically significant gram negative microorganisms:
· agents of respiratory tract infections
· agents of food and waterborne infections
· agents of urinary tract infections
· agents of chronic gastric infections
· agents of sexually transmitted infections
· agents of zoonoses

I. Agents of Respiratory Tract Infection
- *Legionella pneumophila* [365]
· causative agent of legionellosis and Pontiac fever
· common in environmental water
· multiple species/serotypes
· no person-person transmission
· no animal reservoir or vector
· acquisition by droplet inhalation
· severe (pneumonia) or mild, flu-like, presentation (Pontiac Fever)

II. Agents of Food and Waterborne Infections

Many gram negative bacterial agents can cause infections of the stomach or the intestinal tract . Included among these are the *Vibrios*, several species of *Helicobacters*, *Campylobacters*, *Aeromonas*, *Plesiomonas* and the family Enterobacteriaceae

<u>The Enterobacteriacea</u>

At least 30 genera with >120 species. Found in the soil, water and the intestinal tract of man and animals. Generally, they are motile by means of peritrichous flagella. Some species can be non-motile. They are Facultative aerobic/anaerobic. Antigenic classification based on **O** antigens. (cell envelope lipopolysaccharide), **H** antigens (flagella) and **K** antigens (capsule). Enteric pathogens in this group include some strains of *Escherichi coli*, the *Salmonellae*, the *Shigellae*, and some species of *Yersinia*

- *The Salmonellae* [307]

· causative agents of enteritis (*S. enteriditis*), bacteremia (*S. cholerasuis*) and enteric fever (*S. typhi*)
· source in foods of animal origin and a varied animal reservoir (*S. enteriditis*)
· some adapted to humans only (S. typhi)
· enteroinvasive infections
· no enterotoxin production
· occasional blood dissemination e.g. (S. typhi and S. cholerasuis; others rarely)

- *The Shigellae* [309]

· causative agent of bacillary dysentery
· human source only
· transmission by food, water, or direct contact
· enteroinvasive infections
· toxigenic (Shiga toxin)

- *Escherichia coli (EC)* [305]

· common inhabitant of intestinal tract
· human or animal source
· enterotoxigenic infections (ETEC, EHEC)
· enteroinvasive infections (EIEC)
· enteroadherent infections (EPEC, EaggEC)
· common agents of bacterial diarrheal disease including travelers' diarrhea
· virulence factors shared/derived from other bacterial enteropathogens

III. Agents of Sexually Transmitted Infections

- *Neisseria gonorrhoeae* [291]
  - · fastidious, environmentally labile organisms, obligate aerobic
  - · colonization of columnar epithelium of humans only
  - · no animal reservoir or vector
  - · agent of urethral, pharyngeal, and anal infections in men and women, cervicitis and PID in women, conjunctivitis in neonates
  - · no exotoxins produced
  - · no protective immunity to re-infection

IV. Agents of Opportunistic Infections [333]

- *Pseudomonas aeruginosa*

· causative agent of multiple types of infection in compromised, often hospitalized patients
· ubiquitous in the environment. Aerobic, oxidative metabolism
· occasionally a normal components of the human microflora
· multiple virulence factors
· many predisposing or risk factors for infection
· often resistant to various antibiotics

V.Agents of Zoonosis

- Zoonotic diseases:

Diseases normally of animals that can be transmitted to humans under natural conditions. These infections can be sporadic or epidemic. May be transmitted directly from animals or by food, water or insect vectors. There are specific populations at risk based on occupational, geographic or seasonal factors. Methods of control involve animal immunization, proper food processing, elimination of infected animals or insect control. Examples include Tularemia, Brucellosis, West Nile Virus encephalitis, bovine spongiform encephalitis (vCJD) and bubonic plague

- *Yersinia pestis* [312]

· agent of bubonic/pneumonic/septicemic plague
· Optimal growth at 28oC
· multiple animal (rodent) reservoirs
· insect vector (fleas)
· multiple virulence attributes; many expressed only at 37oC
· transmission by insect bite; occasionally human-human by droplet inhalation

GRAM POSITIVE BACILLI

Lecture
Gary Rose, M.D.

LEARNING OBJECTIVES

- To become familiar with gram-positive aerobic and facultative anaerobic bacteria that are associated with human disease
- To understand the role of bacterial exotoxins and other bacterial virulence factors in the pathogenesis of different bacterial infections
- To be able to recognize/diagnose the unique signs/symptoms orepidemiologic clues associated with select gram-positive bacterial infection

LECTURE OUTLINE

I. **DISEASE: DIPHTHERIA**

A. **Etiology Agent**: ***Corynebacterium diphtheriae***

1. Introduction
2. Epidemiology
3. Clinical Manifestations
4. Pathogenicity
5. Diphtheria exotoxin
6. Laboratory Diagnosis
7. Treatment and Prevention
8. OTHER CORYNEBACTERIA
    a. AKA: diphtheroids/coryneforms; contaminants; normal body flora
    b. Disease
    c. Etiologic Agents
        i. *Corynebacterium ulcerans:* pharyngitis, diphtheria
        ii. *C. pseudotuberculosis:* granulomatis lymphadenitis
        iii. *C. jeikeium*: septicemia, CSF, wound infections
        iv. *C. equi (Rhodococcus equi):* necrotizing pneumonia foals & AIDS
    d. Epidemiology
    e. Pathology
    f. Laboratory Diagnosis
    g. Treatment

II. **DISEASE: ANTHRAX (WOOLSORTER'S DISEASE, SIBERIAN FEVER)**

A. **Etiologic Agents**: ***Bacillus anthracis***

1. Introduction
2. Epidemiology
3. Clinical manifestations
    a. Cutaneous: 95% of cases; small macule develops in 2-3 days; changes from papule to vesicle; ruptures leaving a sharp walled, inflammatory ulcer (malignant pustule); bacilli multiply, migrate to lymph node; cause swelling/hemorrhage
    b. Pulmonary: inhalation of bacterial spores; progresses from a mild flu-like illness to severe manifestations of hypoxia and dyspnea; most patients die; a biological

warfare agent

c.Gastrointestinal: ingestion of contaminated meat; GI pain, bleeding; development of ascites; not reported from the U.S.

4. Pathogenicity
   a.capsule: antiphagocytic and an exotoxin (carried on plasmids)
   b.anthrax toxin = 3 proteins which synergize to be effective:
      i.PA protective antigen (active PA binds to cell suface)
      ii.EF edema factor (calmodulin-dependent adenylate cyclase)
      iii.LF lethal factor (metalloprotease; target MAPKK)
5. Laboratory diagnosis
6. Prognosis and Treatment

III. DISEASE: *BACILLUS CEREUS* FOOD POISONING

A. Etiologic Agent: *Bacillus cereus*

1.Introduction
2.Epidemiology
3.Clinical Manifestations
   a.diarrheal type: acute abdominal cramps & diarrhea in 4-16 hours
   b.emetic type: nausea and vomiting in 1 to 5 hours
4.Pathogenicity
   a.diarrheal type: heat-labile toxin (accumulation of cAMP)
   b.emetic type: heat-stable toxin that mimics staph. food poisoning
5.Prognosis and Therapy

IV. DISEASE: LISTERIOSIS

A.Etiologic Agent: *Listeria monocytogenes*

1.Introduction
2.Epidemiology
3.Clinical Manifestations
4.Pathogenicity
5.Virulence factors
   a.Internalin - invasion of epithelial/endothelial cells (entry)
   b.Listeriolysin O - thiol-activated cytolysin, hemolysin(escape from vacuole)
   c.Phospholipase C - aids in escape from vacuoles
   d.ActA - required for intracellular actin-based motility
6.Laboratory Diagnosis
   a.easily cultured
   b.gram-positive rod; nonspore former; beta-hemolytic, motile, catalase positive
   c.wide growth temperature range (2_C to 37_C)
   d.13 serotypes based on O and H antigens; 4b most prevalent
7.Treatment

V. DISEASE: NOCARDOSIS

A.Etiologic Agents *Nocardia asteroides, N.brasiliensis, N.otitidis-caviarum*

1.Introduction
2.Epidemiology
3.Clinical Manifestations

4.Histopathology
5.Laboratory diagnosis

a.Direct Examination
b.Isolation
6. Prognosis and Therapy

Ch. 24 p. 247-253; Ch. 25 p. 255-260; Ch. 26 p. 261-267; Ch. 27 p. 269-275

Gram-Positive Cocci

Lecture
Gary Rose, M.D.

LEARNING OBJECTIVES

•Become familiar with the gram-positive cocci that are associated with human disease and the diseases they cause.
•Understand the role of the different proteins, toxins and enzymes associated with virulence of the gram-positive cocci.

LECTURE OUTLINE:

I. *Staphylococcus aureus*

1) Clinical Syndromes

a) Localized infections.
Folliculitis, furuncle
Carbuncle (boil)
Impetigo
Wound infection
b) Localized infections with diffuse skin rash.
Scalded skin syndrome
Toxic shock syndrome
c) Endocarditis
d) Food poisoning
e) Osteomyelitis and Septic arthritis

2) Physiology and structure

3) Pathogenesis and Immunity

a) Toxins

Alpha toxin
Beta toxin
Delta toxin
Gamma toxin
Leukocidin
Exfoliative toxins
Toxic Shock Syndrome Toxin-1
Enterotoxins and Superantigens

b) Enzymes

Coagulase
Catalase
Hyaluronidase
Fibrinolysin (Staphylokinase)
Lipases
Nuclease - role in disease in unknown
Penicillinase

4) Epidemiology

II. Coagulase-Negative Staphylococci (*Staphyloccus epidermicus*)

1) Clinical syndromes

a) Endocarditis
b) Prosthetic Device Infections

III. Group A Streptococcus (*Streptococcus pyogenes*).

1) Clinical Syndromes

a) Suppurative Streptococcal Diseases

Pharyngitis
Scarlet fever
Streptococcal Toxic Shock Syndrome (STSS)
Pyoderma
Cellulitis
Necrotizing fasciitis

b) Nonsuppurative Streptococcal Disease

Rheumatic Fever
Acute Glomerulonephritis

2) Physiology and structure

3) Pathogenesis

a) Capsule
b) M Protein
c) Protein F
d) Pyrogenic exotoxins

e) Streptolysins S and O
f) Streptokinase
g) DNase
h) Hyaluronidase

4) Epidemiology

IV. Group B Streptococcus (*Streptococcus agalactiae*).

1) Clinical Syndromes

a) Early-onset neonatal disease
b) Late-onset neonatal disease

c) Postpartum sepsis

2) Physiology and structure

3) Pathogenesis and Immunity

4) Epidemiology

V. Viridans Streptococci.

VI. *Streptococcus pneumoniae*.

1) Clinical Syndromes

a) Pneumonia
b) Sinusitis and Otitis Media
c) Meningitis
d) Bacteremia

2) Physiology and structure

3) Pathogenesis and Immunity

a) Capsule
b) Pneumolysin
c) Neuraminidase
d) Purpura-Producing Principle
e) Autolysins

4) Epidemiology

VII. Enterococcus.

1) Clinical Syndromes

a) Endocarditis
b) Bacteremia

2) Antibiotic resistance

Ch. 21 p. 209-223; Ch. 22 p. 225-242; Ch. 23 p. 243-246

MYCOPLASMA

Lecture

Gary Rose, MD

Learning Objectives

1. To recognize the disease via symptoms and pathology.
2. To understand how mycoplasma causes disease.
3. To be familiar with the unique structure and morphology of mycoplama
4. To know the epidemiology of mycoplasma

Mycoplasma

- Classification and structure
- Physiology and pathogenesis
- Pathogenic mycoplasma
- Human disease
- Diagnosis and treatment

Mycoplasma pneumonia

- Overview
- Epidemiology
- Human disease
- Diagnosis and treatment

MYCOBACTERIUM

Lecture

Gary Rose, MD

Learning Objectives

1. To understand how mycobacteria cause disease.
2. To be familiar with the unique structure and morphology of mycobacteria
3. To know the epidemiology of mycobacteria
4. To recognize the disease via symptoms and pathology.
5. To be familiar with the diagnosis and treatment of mycobacteria

- **Runyon Classification**
  - **Group I - Photochromaogenic Slow Growers**
    - **Carotenoid pigments produced after exposure to light**
  - **Group II – Scotochromogenic Slow Growers**
    - **Pigments produced in light or dark**
  - **Group III – Non-chromogenic Slow Growers**
    - **Non-pigmented**
  - **Group IIII – The Rapid "Growers**
    - **Growth in culture in ≤ 7 days**

Mycobacterium tuberculosis

Transmission
Multiplication and spread. Hematogenous spread. Granuloma formation
Reactivation
Compromised host
Skin testing and delayed hypersensitivity
Diagnosis and Treatment

Mycobacterium avium-intracellure,
Mycobacterium kansasii
Mycobacterium fortuitum, chelonae
Mycobacterium leprae

SPIROCHETES
Lecture
Gary Rose, M.D.

LEARNING OBJECTIVES:

- To become familiar with the unique morphology and structure of the spirochetes
- To become familiar with members of the genera *Treponema, Borrelia* and *Leptospira* that are associated with human disease
- To understand the pathophysiology and recognize the clinical manifestations associated with the various stages of *T. pallidum* and *B. burgdorferi* infections
- To become familiar with the advantages and disadvantages of the various diagnostic tests used for syphilis and Lyme disease

LECTURE OUTLINE:

I. Classification of the Spirochetes
   A. Family Spirochaetaceae - Genus *Treponema*
   - Genus *Borrelia*
   B. Family Leptospiraceae - Genus *Leptospira*

II. Genus *Treponema*
human pathogenic treponemes:
Treponema pallidum subsp. pallidum - syphilis
Treponema pallidum subsp. endemicum - bejel (endemic syphilis)
Treponema pallidum subsp. pertenue - yaws
Treponema carateum - pinta

A. *Treponema pallidum*: Structure and Morphology
B. Pathogenesis
C. Growth requirements
D. Syphilis
1. Clinical manifestations of syphilis
2. Clinical stages of syphilis
   a. primary syphilis
   b. secondary syphilis
   c. latency
   d. tertiary (late) syphilis
   e. Congenital syphilis
3. Transmission of syphilis
4. diagnostic tests for syphilis
   a. Darkfield microscopy - spirochetes
   b. Serology _ "nontreponemal tests"
      1. VDRL _ Venereal Disease Research Laboratory test
      2. RPR _ rapid _plasma reagin test

c. "treponemal tests"

1. The fluorescent treponemal antibody absorption (FTA_ABS) test is the most widely
2. The microhemagglutination test for T. pallidum (MHA_TP) can also be used to detect antibodies specific for T. pallidum antigens

5. Treatment and prevention of syphilis

E. Genus *Treponema*
other human pathogenic treponemes

1. bejel (endemic syphilis)
   etiologic agent _ *T. pallidum subsp. endemicum*
2. Yaws

   etiologic agent _ Treponema pallidum subsp. pertenue
3. Pinta

   -etiologic agent _ *T. carateum*

III. Genus _ Borrelia

A. Introduction
B. Relapsing fever
   1. epidemic or louse_borne relapsing fever
   2. endemic relapsing fever
   3. Clinical manifestations of relapsing fevers
   4. Diagnosis, treatment and control of relapsing fevers

C. LYME DISEASE - *Borrelia burgdorferi*

1. Transmission: Tick bite (Ixodes species) - a small hard shelled tick
2. Disease Stages:
   a. Initial
   b. Second stage
   c. Third stage
3. Diagnosis
4. Treatment
5. Summary
6. Vaccine Development

IV. Genus Leptospira
A. Introduction
B. Leptospirosis
C. Clinical manifestations of Leptospirosis
D. Diagnosis, treatment and control of leptospirosis

Ch. 42 p. 405-419

Obligate Intracellular Pathogens

CHLAMYDIAE
Lecture
Gary Rose, M.D.

LEARNING OBJECTIVES:

•To understand the unique biphasic life cycle of *Chlamydia* spp.
•To understand how chlamydia exploit the intracellular environment of their host cells.
•To become familiar with pathophysiology and clinical manifestations associated with chlamydial infections

LECTURE OUTLINE

I. *Chlamydia*
- A. Introduction
- B. *Chlamydia* classification
  1. One family - *Chlamydiaceae*
  2. One genus - *Chlamydia*
  3. three major species: (human pathogens)
     - a. *C. trachomatis*
     - b. *C. psittaci*
     - c. *C. pneumoniae* (TWAR)
- C. Chlamydial developmental cycle
  1. Elementary body (EB)
  2. Reticulate body (RB)
- D. Chlamydial genomes
- E. Chlamydial diseases
  1. those transmitted by direct contact
     - a. *C. trachomatis* genital and ocular infections
     - b. STD - nongonococcal urethritis (serotypes D-K)
       -can lead to pelvic inflammatory disease (PID), salpingitis, ectopic pregnancy and sterility
     - c. Lymphogranuloma venereum - STD caused by *C. trachomatis* serotypes different from those associated with nongonococcal urethritis (serotypes L1,L2,L3)
  2. those transmitted by the respiratory route:
     - a. *C. psittaci* and *C. pneumoniae* respiratory infections - pneumonia
     - b. *C. pneumoniae* infection also associated with atherosclerosis and cardiovascular disease

F. Chlamydial pathogenesis
1. Chlamydial invasion
2. Chlamydial inclusion
3. Chlamydia nutrient acquisition
4. Effects of chlamydial growth on the host cell
5. Chlamydia mechanisms of disease
6. Chlamydial type III secretion system
7. Chlamydial cell envelope
8. Release of Ebs

G. Diagnosis, treatment and control of chlamydial infections

Rickettsia, Coxiella, and Ehrlichia

LEARNING OBJECTIVES:

•To understand the unique intracellular life cycle of the *Rickettsia*
•To understand how Rickettsia exploit the intracellular environment of their host cells.
•To become familiar with pathophysiology and clinical manifestations associated with rickettsial Infections

LECTURE OUTLINE

I. Rickettsia, Coxiella and *Ehrlichia*
II. *Rickettsia*
A. Introduction
B. *Rickettsia Spp*. associated with human disease
1. Rickettsia prowazekii
a. louse-borne or epidemic typhus.
b. vector: human body louse.
2. *Rickettsia rickettsii*
a. Rocky Mountain Spotted Fever
b. vector: tick
3. Other Rickettsial infections
a. endemic typhus - R. typhi; vector - flea
b . Rickettsial pox - R. akari; mites
c. Scrub typhus - R. tsutsugamushi; mites
C. Rickettsial pathogenesis
D. Rickettsial Invasion and Growth
E. Rickettsial Metabolism
F. Molecular Biology of *Rickettsia prowazekii*

III. *Ehrlichia*
A. Introduction
B. *Ehrlichia* - Host Cell Interactions
C. Ehrlichia epidemiology

D. Clinical Manifestations of Human Ehrlichiosis

IV. Coxiella
A. Introduction
B. Q fever (query fever)
1. *C. burnetii* - intracellular cycle
2. Q fever – epidemiology
3. Q fever - clinical manifestations and treatment

Readings/reference: Murray et al., Ch. 44 p. 427-433; Ch. 45 p. 435-440; Ch. 46 p. 441-449

Virus

PARASITOLOGY I.
Lecture
Gary Rose, M.D.

Learning Objectives for all of the parasites:

1. To recognize the disease via symptoms and pathology.
2. To understand how the parasite causes disease.
3. To understand the developmental cycle of the parasite in humans to correlate with the pathology.
4. To know how the parasite is transmitted.

PROTOZOA: Intestinal, Genital Murray: p. 821-824
Agent: ***Entamoeba histolytica***
DISEASE: Amebiasis

PROTOZOA: Blood and Tissue Murray: p. 835-840

Agents: *Plasmodium falciparum, P. vivax & P. malariae*
Disease: Malaria

PROTOZOA: Blood and Tissue Murray: p. 841-844

Agent: *Toxoplasma*
Disease: Toxoplasmosis

Protozoa: Blood and Tissue Murray: p. 845-848
Agent: *Leishmania*
Diseases: Cutaneous leishmaniasis & diffuse cutaneous leishmaniasis,
Mucocutaneous leishmaniasis,
Visceral leishmaniasis

PARASITOLOGY II
Lecture
Gary Rose, M.D.

HELMINTHS: Nematodes Murray: p. 855-856
Agent: *Ascaris*
Disease*:* Ascariasis

Helminths: Nematodes Murray: p.858-859
Agents: *Ancylostoma & Necator*
Disease: Hookworm

Helminths: Nematodes Murray: p. 853-855
Agent: *Enterobius*
Disease: Pinworm

HELMINTHS: Nematodes Murray: p. 856-857
Disease: Larva migrans
Cutaneous Larva Migrans - Dog and Cat Hookworms
Visceral types

Helminths: Trematodes (flukes) Murray: p.876-880
Agents : Schistosoma mansoni, S. japonicum & S. haematobium
Disease: Schistosomiasis
Blood Flukes

HELMINTHS: Tapeworms (Cestodes*)* Murray: p. 884
Agent: *Taenia saginata*
Disease: Taeniasis (Beef tapeworm)

HELMINTHS:Cestodes Murray: p. 886-888
Agent: *Echinococcus granulosus*
Disease: Hydatid cyst

Helminths: Tapeworm Murray: p. 881-882
Agent: *Taenia solium*
Disease: Taeniasis (Pork tapeworm)

Helminths: Tapeworms Murray: p. 882-883
Agent: *Taenia solium*
Disease: Cysticercosis

VIRUSES
Lectures
Gary Rose, M.D.

1. **Introduction to virlology**
2. **Viral replication**
3. **Respiratory viruses**
4. **DNA viruses**
5. **Hepatitis**
6. **Neurologic, gastro-enteric, and hemorrhagic fever viruses**
7. **HIV**

Mycology
Lectures
Gary Rose, M.D.

1. **Introduction to mycology**
2. **Pathogenesis of fungal disease**
3. **Superficial and cutaneous mycoses**
4. **Systemic mycoses**

Julie Sivigny

From: David Binninger [binninge@fau.edu]
Sent: Thursday, May 12, 2011 12:22 PM
To: Julie Sivigny
Subject: Re: Biomedical Science New Course Proposal - Clinical Microbiology

Good morning,

We offer an undergraduate course entitled *Medical Bacteriology* (MCB 4203) and there are numerous overlaps in the topics being presented. However, we do not have any graduate level medical microbiology courses so this new course will likely be of interest to some of our students.

I hope this is helpful and good luck with the course proposal.

Regards,
David

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On May 12, 2011, at 12:05 PM, Julie Sivigny wrote:

Dear Dr. Binninger,

Biomedical Science is submitting a new course proposal for our graduate-level Clinical Microbiology course. It has previously been offered under the special topics course number and we wish to make it part of our permanent course inventory.

The Department of Biology was identified as a department that might be affected by this new course. Could you please review the attached syllabus for any potential conflicts?

We appreciate your help with this matter. Please contact me if you need any additional information.

Thank you.

Julie A. Sivigny
Academic Program Specialist
Charles E. Schmidt College of Medicine
Florida Atlantic University
(561) 297-2216

<clinical microbiology syllabus NCP.docx>