May 11, 2001

Medical Microbiology Exam—Bacteriology Block

Instructions:
1. Fill in name and count pages—there should be 10 pages (45 questions).
2. Read questions carefully—format varies.
3. For multiple matching format, read through all the choices in order to pick the one that best, i.e., most specifically, fits each statement.

Short answer section. (Total of 33 points)

1. (9 pts.) *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*, type B, are three organisms that cause meningitis.

   A. Identify the very first site of infection by these pathogens in humans.
      Epithelia of nasal/oral/pharynx (upper airway)  

   B. Identify one virulence factor, encoded by each of the three pathogens that promotes infection at this (initial) site.
      pil for attachment
      Answer: IgA protease, adhesin, adhesive protein

   C. What site/body compartment must then be colonized prior to invasion of the CNS?
      Blood

   D. Identify one virulence factor, encoded by each of the three pathogens that promotes infection of this site/body compartment.
      Capsule

   E. How does this virulence factor promote infection of this site/body compartment work, i.e., what host defense does it inhibit? (complement)
      Prevents complement binding decreases opsonization, so have less phagocytosis

   F. Is humoral immunity, cellular immunity, or both, important for clearance and prevention of invasive disease?
      Both
      Humoral immunity needed to prevent disease as explained below, but cellular immunity is probably needed to clear infection and help boost humoral response.

   G. Name the protective antigen (don't need chemical structure).
      TI Antigens (carbohydrates in capsule)

   H. Why is it that young children (e.g., 6 m to 2-4 y) are particularly susceptible to invasive disease by some of these pathogens? What protects them prior to 6 months? After 2-4 years?
      Young children (6 m-2-4 y) cannot make Ab against TI Ag (carbs) 1 so are susceptible to invasive disease. Prior to 6m are protected by maternal Ab that crossed placenta and after 2-4 y start making Ab against TI Ag so can fight off bacteria with capsules.
I. Invasive infection by *Haemophilus influenzae*, type B decreased 90% in the last 15 years due to the development of a vaccine effective in young children. What does the vaccine consist of?

The vaccine is the carbohydrate from the capsule conjugated to a protein (to elicit a response in young kids).

2. (2 pts.) Although *Shigella* and *Listeria monocytogenes* use very similar mechanisms to exploit the intracellular environment of host cells and transmit themselves from cell to cell, *L. monocytogenes* is far more likely to produce systemic infection.

A. Why is that?

*Shigella* causes the macrophages it infects to die by apoptosis, so it doesn't spread, but *Listeria* invades macrophages and does not kill them and spreads throughout the body (via macrophages).

B. What group of individuals is most commonly affected in outbreaks of listeriosis? pregnant, fetus, neonates, immunity compromised (AIDS patient).

3. (3 pts.) The Enterics.

A. The EHEC (enterohemorrhagic *E. coli*) and the salmonellae manipulate host cells with which they make contact. What common mechanism do they use? Type III secretion (direct into host cell) of a protein/receptor for themselves, which allows for their attachment.

B. EHEC and *Shigella* share a property that dramatically enhances transmissibility. What is this property? Cause diarrhea that contains infectious bacteria so the actual bacteria are not killed by stomach acid.

C. EHEC and one species of *Shigella* can produce hemolytic uremic syndrome, or HUS, the triad of hemolytic anemia, thrombocytopenia, and kidney failure. How do they cause this?

Both make shiga toxin which can cause HUS.

4. (4 pts.) Compare gram positive and gram negative bacteria in terms of:

A. Thickness of cell wall.

Gram+ have thick wall. Gram−: thin wall.

B. Number of membranes.

Gram+ have 1

Gram− have 2

C. Presence of lipopolysaccharide.

**Only** Gram− have LPS. Gram+ NO LPS

D. Presence of endotoxin.

Gram+ have endotoxin, Gram− NO endotoxin.

5. (5 pts.) Although tetanus toxin (tetanospasmin) and botulin toxin are highly homologous toxins that block neuroexcitocytosis (release of neurotransmitters).

A. In general terms, how do they work? (2 pts)

Both are AB toxins that release the A part into the neurons. The A subunit is a protease that damages the proteins involved in synaptic vesicle release (ex.: Synaptobrevin)
B. Which one produces flaccid paralysis and which spastic paralysis? (1 pt)
- Tetanus → Spastic paralysis
- Botulin → Flaccid paralysis

C. Why do they have such different physiologic effects? (2 pts)
They have different effects because of different B subunits, which target different receptors on neurons. Tetanus toxin is taken up at the NMJ and transported up into CNS, blocks release of GABA vesicles, therefore get spastic paralysis. Botulin toxin is targeted to Ach containing neurons in the periphery, so therefore get flaccid paralysis.

6. (3 pts.) Cholera.
A. What is the enzymatic activity of cholera toxin?
Cholera is an AB toxin that targets the intestinal epithelium. The A subunit ADP ribosylates (steals ADP from NAD) ES, keeping it inactive state by blocking its ability to hydrolyze GTP.
B. What is the physiologic effect of this activity?
The increased activity of ES ends up increasing cAMP levels, which in turn increase fluid intake and fluid secretion, so end up losing water and electrolytes.
C. What is the most important treatment modality for victims of cholera?
Oral rehydration therapy + Na+ + glucose

7. (4 pts.) Group A streptococcus infection can be associated with toxic shock syndrome.
A. What is the class of toxin causes this syndrome?
Spe A (exotoxin)
B. What is the mechanism of action of this class of toxin?
It acts on the surface of cells not inside cells like AF toxin
Spe A specifically activates B cells so get a big, non-specific immune response.
Answer: SuperAntigens promote interaction of MHC II + TCR + induce cytokine release.
8. (3 pts.) Define $LD_{50}$, i.e., lethal dose 50?
LD$_{50}$ is the dose of bacteria inoculum needed for 1/2 of the animals to die.
It measures lethality.
Pathogen A has an $LD_{50}$ of 10, Pathogen B has an $LD_{50}$ of 1000. Which is more virulent?
The one w/ $LD_{50}$ of 10 is more virulent.
(The smaller the $LD_{50}$ the more deadly.)
Multiple choice section. (Total of 37 points.)

Read questions carefully-- format varies.
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Questions 9 - 12. Pick from the list of choices given below the one that best fits each statement. Each answer may be used once, more than once, or not at all.

A. Enteropathogenic *E. coli* (EPEC)
B. Enterotoxogenic *E. coli* (ETEC)
C. Enterohemorrhagic *E. coli* (EHEC), serotype O157:H7
D. Enteroinvasive *E. coli* (EIEC)
E. *Treponema pallidum*
F. *Shigella sonnei*
G. *Salmonella typhi*
H. *Clostridium difficile*
I. *Clostridium tetani*
J. *Legionella pneumophila*

9. Common cause of traveler’s diarrhea in Central and South America.  
   - [B]  

10. Colonization of the intestinal epithelium cells by this organism results in cytoskeletal rearrangements including disappearance of microvilli (attachment and effacing lesion), but not in hemolytic uremic syndrome (HUS).  
   - [A]  

11. Colonization of the gall bladder by this organism can result in a persistent carrier state.  
   - [G]  

12. Produces a toxin closely related to *cholera* toxin.  
   - [B]
Questions 13 - 16. Pick from the list of choices given below the one that best fits each statement. Each answer may be used once, more than once, or not at all.

A. Listeria monocytogenes
B. Streptococcus pneumoniae
C. Group A streptococcus (GAS)
D. Vibrio cholerae
E. Clostridium tetani
F. Clostridium difficile
G. Clostridium botulinum
H. Escherichia coli
I. Salmonella typhi
J. Neisseria gonorrhea (gonococcus)

13. Injects proteins directly into the cytoplasm of intestinal epithelial cells, causing the cells to engulf the bacteria. The bacteria later emerge from the basal surface of the cells and grow outside of cells in the lamina propria. **I**

14. Enter into host cells and escapes from the phagosome, then replicates in the cytoplasm and spreads from cell to cell via polymerization of host cell actin. **A**

15. Antiphagocytic capsule is essential for this organism's tendency to cause high level bacteremia and meningitis. **B**

16. Famous for its association with nonsuppurative sequelae, i.e., clinical manifestations that are not directly due to the presence of live bacteria at the site of damage. **C**
Questions 17 - 21. Pick from the list of choices given below the one that best fits each statement. Each answer may be used once, more than once, or not at all.

A. Opa protein
B. Superantigen
C. M protein
D. Listeriolysin O
E. Streptokinase
F. IgA protease
G. Flagella

17. Activates plasminogen, a host protease that degrades fibrin clots. E ✓

18. Bacterial surface protein that mediates bacterial entry into host cells. A ✓

19. Promotes resistance to complement. C ✓

20. Mediates escape of the bacterium from phagosome into the cytoplasm. D ✓

21. A secreted protein that is thought to promote colonization specifically at mucosal surfaces. F ✓
Questions 22 - 29. Pick from the list of choices given below the one that best fits each statement. Each answer may be used once, more than once, or not at all.

A. *Neisseria meningitidis* (meningococcus).
B. *Borrelia burgdorferi*
C. *Bacteroides fragilis* (an anaerobe)
D. *Vibrio cholerae*.
E. *Treponema pallidum*.
F. *Legionella pneumophila*.

22. Aerosolization from a water source is an important factor in outbreaks of this infection.  
23. Transmitted by human secretions, and a crowded living environment is an important risk factor for infection.  
24. Congenital infection can lead to prematurity, characteristic bony deformities.  
25. Transmission is fecal-oral.  
26. Bite of an arthropod vector is essential for transmission.  
27. Significant rate of asymptomatic carriage in pharynx.  
28. Vaccine is based on a protein that is not expressed when the bacterium is in the human.  
29. Associated with the presence of a foul odor in a wound.
Questions 30 - 36. Pick from the list of choices given below the one that best fits each statement. Each answer may be used once, more than once, or not at all.

A. Enterohemorrhagic E. coli O157:H7
B. Legionella pneumophila
C. Salmonella enteritidis
D. Shigella dysenteriae
E. Mycoplasma pneumoniae
F. Bacteroides fragilis
G. Treponema pallidum
H. Borrelia burgdorferi
I. Clostridium tetani
J. Clostridium botulinum

30. The capsular polysaccharide of this organism promotes the development of abscess formation.  **B**

31. The disease caused by this bacterium is most often a toxemia, i.e., no live bacteria are present in those affected.  **J**

32. This bacterium inhibits phagosome-lysosome fusion within the macrophages.  **B**

33. Attaches to respiratory epithelium of healthy hosts without invading.  **E**

34. Major cause of kidney failure in children under 10.  **A**

35. Infection is acquired by contact with infected secretions of host with self-limited illness.  **E**

36. This bacterium has no cell wall.  **E**
Questions 37 - 41. Pick from the list of choices given below the one that best fits each statement. Each answer may be used once, more than once, or not at all.

A. *Group A streptococci*
B. *Hemophilus influenzae*
C. *Neisseria meningitidis*
D. *Mycoplasma pneumoniae*
E. *Mycobacterium tuberculosis*
F. *Streptococcus pneumoniae*
G. *Legionella pneumophila*

37. Grows within macrophages and can spread to diverse sites, resulting in many different manifestations of infection. **E**

38. This organism diminishes complement deposition by adding a sialic acid (N-acetyl neuraminic acid; NANA) moiety to its LPS and by producing a polysaccharide capsule. **C**

39. Infected people may remain asymptomatic indefinitely with the only marker of infection demonstrated by a test of skin reactivity involving cell-mediated immunity. **E**

40. Horizontal genetic exchange has resulted in substantial diversity among strains of this pathogen, and probably has contributed to this pathogen's ability to be isolated from patients with diverse infectious syndromes. **A**

41. Often infects young adults. Important cause of “atypical” pneumonia, which usually is not severe or life threatening. **D**

**SEXUALLY TRANSMITTED DISEASES. Questions 42 - 45. Note different format: Modified True-False.**

A. *Neisseria gonorrhoeae.*
B. *Treponema pallidum. syphilis, spirochete*
C. Both of the above.
D. Neither of the above.

42. Human is only host. **C**

43. Obligate intracellular pathogen. **D**

44. Antigenic variation is a major contributor to its ability to cause chronic disease. **A**

45. Scarcity of exposed antigenic targets is a major contributor to its ability to cause chronic disease. **B**