

GMS6006 FINAL EXAMINATION

This is a closed book examination.
Answer ALL of the questions unless otherwise stated.
Please confine your answers to the space provided.
This examination will constitute 40% of your final grade.

	Score
Dr. Handfield's section (40 points = 40%): answer all question (#1-4)	_____
Dr. Condit's section (50 points = 50%): answer all questions (#5-9)	_____
Dr. Brady's section (10 points = 10%): answer all questions (#10)	_____
Total	_____

Student Name: _____

Code ID: _____

The use of code ID is to enhance a non-biased evaluation since individual lecturer will not know the identity of student during the grading process.

Dr. Handfield's section (40 points)

Lecture 10. Virulence Strategies of Bacterial Pathogens

1. (10 points) *Staphylococcus aureus*, a Gram positive human pathogen, makes a protein called "clumping factor" which converts fibrinogen into fibrin. This promotes the virulence of this pathogen by effectively coating the cell surface with a human protein recognized as "self" by the immune system. You've managed to clone the gene responsible for the fibrin binding protein in *E. coli*, a heterologous host commonly used in genetic engineering. How would you prove definitively that the clumping factor is an important gene in promoting the virulence of *S. aureus*? (5 points) Describe another approach that would allow you to demonstrate that this virulence factor is important during the entire infectious process as opposed to a specific step? (5 points)

2. (10 points)

Lecture 15. Opportunistic Paradigm: *Pseudomonas aeruginosa* (2.5 points per question)

i. Which of the following characteristics is NOT associated to *Pseudomonas aeruginosa*?

- a) It is ubiquitous in nature
- b) Has a flagellum
- c) Gram-positive
- d) It produces a pigment named pyocyanin
- e) None of the above. These are ALL *Pseudomonas* characteristics.

ii. *Pseudomonas aeruginosa* causes a number of different types of human infections in burned, immunocompromised, and cystic fibrosis patients. We explain why it causes so many types of infection with the following characteristics. **All of these are correct except one. Which one?**

- a) *Pseudomonas* has an outer-membrane
- b) Intrinsic antimicrobial resistance
- c) Nutritional versatility
- d) Numerous secreted enzymes
- e) None of the above. These are all relevant characteristics.

iii. Which of the following characteristics of alginate in *P. aeruginosa* pathogenesis is NOT relevant to cystic fibrosis?

- a) Contributes to airway obstruction
- b) Binds iron and other essential metals
- c) Neutralizes oxygen radicals.
- d) It's production correlates with reduced exoproducts
- e) None of the above. These are all relevant characteristics.

iv. Which statement is TRUE regarding biofilms?

- a) *Pseudomonas* biofilms only form *in vivo*, in infected human patients.
- b) Microbial biofilms are structures where microbes are attached to a surface and embedded in an exopolysaccharide (EPS) matrix.
- c) All *Pseudomonas* animal models perfectly mimic the biofilm formation stages including colonization, formation of microcolonies, evasion of the immune system and spread to underlying tissues.
- d) Bacteria growing as biofilms have the same minimal inhibitory concentration (MIC) to antimicrobial agents as compared to a planktonic matching strains.
- e) None of the above. ALL these statements are FALSE.

3. (10 points)

Lecture 16. Gram-negative paradigm: *Salmonella* spp.

Salmonella enterica serovar *typhi* and *Salmonella enterica* serovar *typhimurium* infections have a similar clinical manifestation in humans in the early phases of disease: nausea and vomiting, followed by abdominal pain, diarrhea and fever that may lead to septicemia and ultimately cause septic shock. Both bacteria are typically transmitted by contaminated foods. Although a *S. typhimurium* infection will typically show symptoms before a *S. typhi* infection, and persists much less in the host, *S. typhi* is more likely to cause a life-threatening systemic infection in humans as compared to its close cousin, and may persist in the host for up to 1 year. How do you explain such differences? Inspire yourself of the infectious process (8 points). Does that influence therapy? (2 points)

4. (10 point)

Lecture 17. Gram-positive paradigm (*B. anthracis*) (2.5 points per question)

i. Which fact is FALSE about *Bacillus anthracis*-associated infections.

- a) it produces a plasmid encoded antiphagocytic capsule
- b) it produces a heterogeneous toxin which is responsible for the clinical manifestations of anthrax
- c) it produces spores
- d) ALL of the above, these are all false.
- e) None of the above, these are all true.

ii. Which of the following characteristic of *B. anthracis* is TRUE?

- a) Forms long chains in clinical samples
- b) Sporulates after every round of cell division
- c) Large, Gram-positive bacillus
- d) ALL of the above
- e) NONE of the above

iii. Which statement is FALSE?

- a) The lethal factor (LF) affects mitogen-activated protein kinase-kinases (MAPKK) resulting in apoptosis
- b) LF and the EF are only active as a heterodimer
- c) The edema factor (EF) converts ATP to cAMP, resulting in edema
- d) These statements are all TRUE
- e) These statements are all FALSE

iv. Which route of infection is NOT associated with *B. anthracis* infections?

- a) Intra-muscular
- b) Intestinal
- c) Pulmonary
- d) ALL of the above are possible routes of infection
- e) NONE of the above are routes of infection

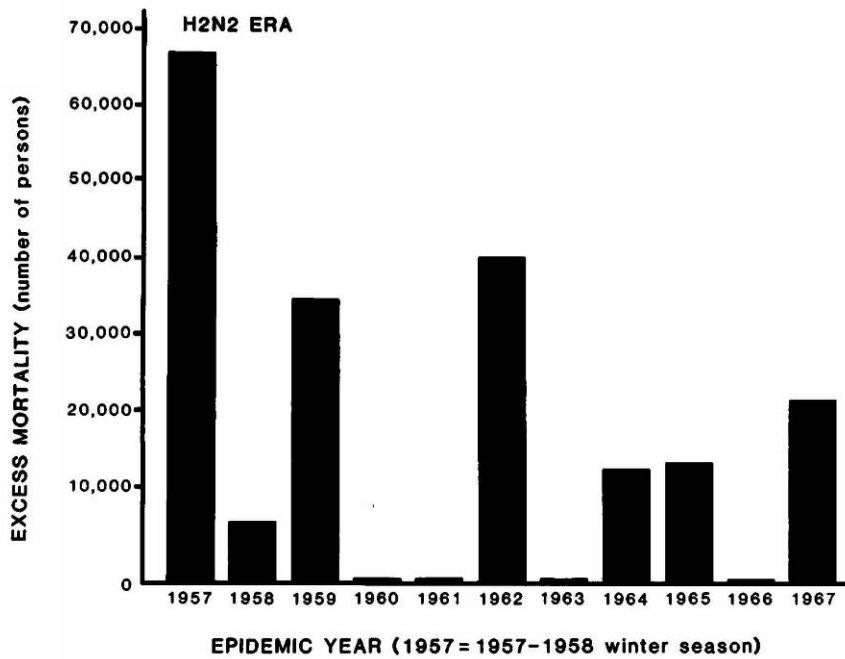
5. (10 points) Describe in detail how a hemagglutination inhibition test is used to quantify influenza antibody in patient serum. Be sure to state specifically what reagents are used in the test, how the test is set up, how it is read, and how the readings provide a measure of serum antiviral antibody titer. (Note: Read this question carefully. It is about the hemagglutination ***inhibition*** test, not the hemagglutination test.)

6. (10 points total)

Single stranded RNA viruses may package either the positive RNA strand, (+) ssRNA, or the negative RNA strand, (-) ssRNA, in virions, depending on virus family. Which of these two virus types, (+) ssRNA or (-) ssRNA, must also package an enzyme in the virion, and why? As you answer the question, please address not only why one virus group needs to package an enzyme, but also why the other virus group does NOT need to package an enzyme.

7. (10 points total)

The figure below shows excess mortality that occurred during the interval from 1957 to 1967 due to influenza virus. The viruses causing disease during this period were all of the H2N2 subtype. Please describe what changes are occurring in the virus during this period of time and how these changes give rise to the epidemiological pattern shown.

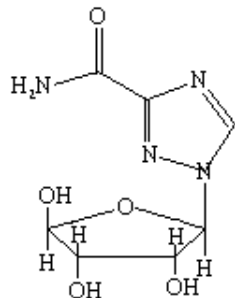


8. (10 points total)

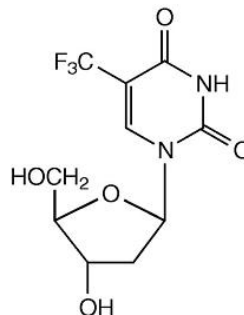
Acyclovir and other anti-herpesvirus medications reduce the duration and severity of an acute herpes virus infection, but they cannot cure a latent infection. Please explain why this is true.

9. (10 points)

Compound A inhibits replication of influenza virus but not herpesvirus. Compound B inhibits the replication of herpesvirus but not influenza virus. Both compounds inhibit replication of vaccinia virus. Please explain the specificity of these drugs for these viruses.



Compound A



Compound B

Dr. Brady's section (10 points)

10. As a researcher with grant funding from the Department of Defense you have been charged with the task of developing a vaccine against the SARS Coronavirus, a virulent pathogen with a potential for use as an agent of bioterror. Discuss the types of things you would want to consider during the development of an effective vaccine that could be safely administered to the general population and outline your rationale and an approach for achieving an optimal protective immune response.