Bio067 Study Question Key

Recommended use for optimal results:

- Only consult keys after you have a) studied and b) written out full answers to the questions.
- Do not memorize answers from keys; make sure you understand the concepts (i.e. that you can describe them to someone else in your own words). While similar ideas may appear on this year's midterm, the focus will be different. Quoting from previous keys will NOT be to your advantage.

1. A. What are the major differences between bacteria and viruses?

i) Bacteria are cells and their multiplication does not depend on host cell machinery. Viruses must infect host cells in order to multiply

ii) Bacteria are, on average, larger than viruses

iii) Bacteria use DNA for their genomes, viruses can use DNA or RNA

B. How do these differences affect how one identifies a microbe?

i) Since bacteria are cells, they can grow and multiply outside a host. Therefore, to identify a bacterium that causes a particular disease, you can transfer a sample from infected tissue to solid medium with appropriate nutrients and the bacterium should be able to multiply until it forms a colony (pile of bacterial cells). Viruses, however, require host cells for replication. Therefore you need to apply samples from infected tissue to host cells in a culture dish and allow the virus to enter the cells and replicate.

ii) Bacteria are usually large enough to be seen on a normal (light) microscope, whereas most viruses are so small that one needs a powerful electron microscope to see their structure.

iii) To identify and sequence bacterial genes, one can just use the polymerase chain reaction (PCR), whereas with an RNA virus, its genome must be reverse transcribed to get a DNA copy before PCR is used to make multiple copies of the microbial gene.

C. How do these differences affect how one fights a microbial disease?

i) Since viruses require host cell machinery to replicate themselves, many drugs to block viral processes will also block host cell processes and therefore be harmful to the host. Therefore, there are more drugs (antibiotics) that are effective against bacteria than against viruses.

ii) The smaller size (and host-dependence) of viruses can make them more difficult to identify and therefore more difficult to fight.

iii) RNA viruses and bacteria would use different machinery (proteins) to copy their genomes, therefore offering different targets for drug design.

2. There are a number of factors that can put one at risk for a certain disease. Choose one of the diseases we have discussed and give two examples for each of the following classes of risk factors. Make sure you explain *why* each factor increases one's risk of contracting the disease.

A. Agent (microbe)-based factors

Drug resistance. If the mycobacterium is resistant to the drugs usually used to fight the infection, the risk of the disease becomes higher since the bacterium can circulate unchecked in both individuals and the population.

Differences in genes that increase survival outside the host. Since mycobacterium can survive in water droplets when a patient sneezes, it can travel quite easily from host-to-host in enclosed spaces, being breathed in and getting deep into the lungs before people know they are at risk. Genetic differences that lead to increased survival outside the host (i.e. making a stronger or thicker cell well) could increase spread.

B. Host-related factors

Immune status. If a person is immunocompromised, their immune system cannot fight mycobacteria effectively at the beginning of infection and the bacterium will have a better chance of surviving to cause a full-fledged infection.

Diet. A well-balanced diet strengthens the immune system and increases overall health. Conversely poor diet can decrease one's body's ability to fight off infection.

C. Environmental risk factor

Work environment. Working in a TB clinic, prison, or other place with increased numbers of TB patients leads to increased exposure to mycobacterium and an increased likelihood of becoming infected.

Living conditions. Living in close quarters without much airflow increases the possibility that mycobacteria could be transferred from person to person.

3. Explain why exposing people to cowpox would put them at an advantage during a smallpox epidemic.

When a person is exposed to cowpox, B cells and T cells that recognize cowpox proteins will be activated to fight the disease. Memory B cells and T cells that are specific for cowpox proteins will also be produced. When a person is later exposed to smallpox, the similarity of smallpox proteins to cowpox proteins will allow the memory B cells and T cells to bind to smallpox proteins either on the surface of the virus itself (B cells) or from the inside of the virion (T cells). These memory cells will be activated much more quickly and will allow the body to fight off the smallpox infection. B cells will send antibodies around the body to bind to the invading virus and a) block the virus entering cells and b) act as a signal for phagocytes to eat and digest the invader, both of which can block smallpox infection. Cytotoxic T cells will recognize infected cells and send signals to kill them while helper T cells will send signals to help activate B cells, cytotoxic T cells and phagocytes.

4. As a new researcher at the Centers for Disease Control, you have been sent to the outskirts of Houma, Louisiana to investigate an outbreak of what appears to be a hemorrhagic fever. On your arrival:
First: You visit with numerous patients and inspect corpses of others who have already died.
Second: You are shown to a medical facility that is remarkably well equipped for research including microscopes, a wide range of experimental animals, and plenty of sterile growth media.

A. Outline the steps will you take to identify the microbe responsible for the outbreak

1. Take a sample of diseased tissue or blood and place it a) on solid growth medium (to look for bacterial growth) and b) on plates of cultured cells (to look for viral-induced cell death).
2. Purify the culture by transferring to fresh dishes for multiple rounds.
3. Look at the culture under the light or electron microscope to describe the possible agent.
4. Inject the pure culture into an animal and determine if the same disease symptoms (massive bleeding) occur in this model.
5. Reisolate agent from the animal and show that it is the same as the original (#3)
6. Try to find this agent (or antibodies that recognize it) in all people who have the disease.

B. When your collaborators arrive to look for the source of the microbe, they are given a tour of the environs, including the nearby Atchafalaya Swamp.

What should they look for on their tour?

They should look for animals that are present in areas close to human habitation and that are showing similar disease symptoms to humans (massive bleeding). Other animals in the area should also be considered, since the agent might not have the same effect on humans and animals.

What hypothesis might follow from their observations?

The working hypothesis would be that the animals showing disease symptoms are infected with the same infectious agent as the humans.

What follow-up experiments should they do to test their hypotheses?

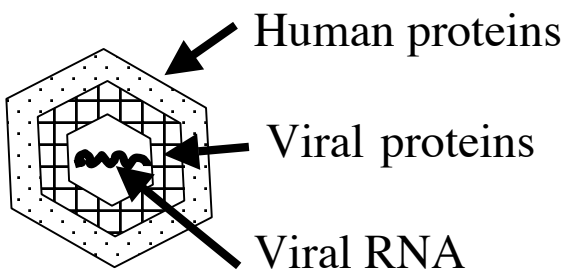
They can isolate possible agents from the animals and compare them to the agents isolated from the humans. Possible experiments include:

a) Visual comparison of microbes using light or electron microscope

b) Comparing genetic makeup (nucleotide sequence of genes) using molecular methods like RT-PCR.

c) Testing whether serum samples from humans have antibodies that recognize infected tissue from animals, or whether animal serum samples have antibodies that recognize the microbe from humans (see question 3)

5. You have discovered a new virus that looks like this:



Notice that all the viral proteins (boxes) and the viral RNA (squiggle) are surrounded by a coat of human proteins (dots).

How would the immune system react when this virus infected a human: which cells would be used to fight infection and why?

When this virus enters a human, there should be no B-cells or antibodies that can recognize it, since the outside of the virus is composed of human proteins (which the body should not see as foreign). However, once the virus enters a cell, pieces of the interior viral proteins should be able to be displayed on MHC class I molecules, which can then bind to killer T-cells that have T-cell receptors that are specific for those viral proteins. If the virus can be eaten by macrophages, display of viral proteins on MHC class II molecules will allow the activation of helper T-cells specific for the virus. These helper T-cells will then send chemical signals to the killer T-cells to help activate them. The killer T-cells will then kill cells infected with this virus. Therefore, the presence of human proteins on the outside of the virus causes the immune response to be a killer T-cell response, rather than a B-cell response.