1. (5 pts) Please do one of the following choices:
   **Choice A:** Briefly discuss how the high diversity of the B-cell receptor **or** the T-cell receptor genes is generated. Why is this diversity important for the normal functioning of the immune system?
   **Choice B:** Briefly discuss DNA rearrangements/changes that occur after B-cell activation. Why are these changes important in the immune response?

2. (5 pts) Briefly describe the molecular (e.g. protein-protein) interactions that would occur during the normal activation of a B-cell. Comment on the specificity of the key interactions and why the level of specificity is important.

3. (5 pts) Briefly discuss how the classical complement pathway is utilized in the defense against pathogens. You should discuss activation of the pathway by the innate and acquired system, the overall pathway, and how the products of the pathway lead to pathogen destruction. There is no need to discuss the detailed composition of protein assemblies, e.g. you don’t need to state that C3 convertase is made of C4bC2a.
4. (7 pts) Compare and contrast antigenic shift, antigenic drift, and multiple serotypes. Given one example of one pathogen that employs any of the three to evade the immune system.

5. (4 pts) Please do one of the following choices:
   - **Choice A:** Briefly describe one mechanism, besides those covered in the previous question, that bacteria utilize to evade the immune system.
   - **Choice B:** Briefly describe one mechanism, besides those covered in the previous question, that viruses utilize to evade the immune system.
   - **Choice C:** Briefly describe why the subsequent infection by a related serotype of the dengue virus can lead to a severe disease (dengue fever).
   - **Choice D:** An immune response to one serotype of the dengue virus prevents the efficient production of antibodies to a subsequent infection by a different serotype, why?

6. (8 pts) Describe the events that occur either during an antibody response to parasites or to allergens. Your answer should include information about the sensitization, activation, and response phases.
7. (1 pt) Please do one of the following choices:

**Choice A:** You are having dinner with some friends at a restaurant and during the meal one of your friends begins to have difficulty breathing. What has occurred, and how would you help your friend recover from this life-threatening situation?

**Choice B:** Describe one mechanism by which allergy shots reduce the immunological response to allergens.

8. (6 pts) A person was successfully treated for a bacterial infection with an antibiotic. They become infected with the same bacteria and are treated with the same antibiotic. Please answer one of the following choices [Each of the choices is related to one of the hypersensitivities; it is more important that you describe what is happening than state the number (e.g. 1-4) of hypersensitivity.]

**Choice A:** During the second antibiotic treatment they rapidly develop anemia and have traces of hemoglobin in their urine the day they start taking the antibiotic. Why is this happening?

**Choice B:** During the second antibiotic treatment they develop a severe rash over their entire body within an hour of taking the first dose. Why is this happening?

**Choice C:** During the second antibiotic treatment their small intestine becomes inflamed, but the inflammation only begins a few days after they started the second treatment. Why does this occur?
9. (16 pts) A person receives a liver transplant from a related donor and then is treated with immunosuppressant drugs after the surgery. (In liver transplants they don’t transplant the entire organ, just a lobe, and the missing lobe is regenerated in the donor). Please answer all of the following questions:
   i) Briefly describe one method by which the donor tissue would have been tested to see that it was compatible with the host (4 pts).
   ii) Several weeks after the transplant, the transplant surgeon notices from a biopsy the infiltration of macrophages into the surgical site – what has happened to cause this? What events have transpired to cause the host to recognize the donor tissue as foreign? (5 pts).
   iii) What could the surgeon have done to detect the infiltration besides a biopsy? (1 pt)
   iv) The surgeon increases the dose of FK506 and anti-IL2 receptor antibodies (e.g. basiliximab). What is the purpose of increasing these drugs? Select one and describe how it prevents rejection (2 pts).
   v) What could the surgeon have done that may have prevented the rejection, besides increasing the dose of FK506 or basiliximab? How would this have reduced rejection? (Hint: He could have learned this technique in Pittsburgh) (2 pts)
   vi) In spite of the surgeon’s best efforts, the liver is rejected after several weeks and the patient is in critical condition. In desperation, the surgeon uses the same donor tissue in a second transplant. The transplanted liver is rejected almost immediately, why did this occur? (2 pts)
10. (2 pts) Describe one event that occurs in central tolerance that reduces the possibility of autoimmune diseases?

11. (4 pts) Please do one of the following choices:

Choice A: The interaction of B- and T-cells occurs frequently in the lymph node. However, in the absence of an active infection, this interaction typically results in tolerance of the B and/or T-cell. What events (or rather the absence of events) lead to tolerance?

Choice B: How do T\textsubscript{REG} cells arise and what is their role in peripheral tolerance? How do they induce peripheral tolerance?

12. (5 pts) Please do one of the following choices related to autoimmune diseases:

Choice A: A female patient goes to her doctor complaining that she cannot hold her eyelids open. What is causing these symptoms?

Choice B: A patient goes to their doctor with vague systems related to metabolism. The patient is shown to have a high level of thyroid hormones. Why has this occurred?

Choice C: After a bacterial infection by a Strep species, a patient develops a heart murmur, due to scarring of the heart tissue. How did this occur?

Choice D: A patient comes to her doctor complaining of joint pain. The doctor also notices a rash on the face of the patient. What disease is she likely to have and why is it causing these symptoms?

Choice E: Your friend is in a car accident which causes severe damage to one eye. The surgeon states that although they could surgically repair the eye and restore limited sight they will remove the damaged eye – why?
13. (5 pts) Please do both parts of this question:
   i) One patient has SCID (severe combined immunodeficiency) and totally lacks B and T cells. What genetic deficiency might they have and why would it have caused this condition?
   ii) Another patient has B and T cells, but can only produce IgM antibodies and no B-memory cells. What genetic deficiency might they have and why would it have caused this condition?

14. (5 pts) A bone marrow transplant is performed to treat a patient with SCID. There are no technical problems with the transplant and the transplanted stem cells produce B, T, and APCs, yet the patient’s immune system remains non-functional - in that the T-cells produced from the transplanted stem cells cannot be activated. Why?

15. (2 pts) Please do one of the following choices:
   **Choice A:** How does a deletion in the CCR5 cytokine receptor lead to immunity from AIDS?
   **Choice B:** A patient was infected with HIV several years ago and begins to receive anti-viral drugs when they begin to notice they have trouble fighting common infections. Although the patients T-cell count rises, they die of AIDS a few years later. Why?
16. (4 pts) Pick any one of the drugs that is currently being used to treat HIV and briefly describe how it interrupts the lifecycle of the virus. There is no need to name the drug, just describe its general characteristics and how it interferes with the life cycle.

17. (2 pts) Please do one of the following choices:
   - **Choice A:** What is the most significant difference between passive and active immunization?
   - **Choice B:** What is an adjuvant and what is its role in immunization.
   - **Choice C:** Give two reasons why booster shots may be required for protective immunity?

18. (2 pts) A new political party is trying to get childhood immunizations banned because they claim that the vaccines are unsafe. In addition to putting their own children at risk, how are they putting other children at risk with this policy?
19. (6 pts) The following is a list of vaccination strategies. Pick any one from list A and any one from list B and briefly describe how they confer immunity. Give the relative advantages or disadvantages of the two that you selected.

**List A**
- Denatured Toxins
- Killed organisms
- Carbohydrate+protein
- Capsid Proteins
- ISCOMs
- Virus like particles

**List B**
- Attenuated virus
- Plasmid DNA
- Viral vector encoded (e.g. insertion of HepB genes into measles.)

20. (2 pts) Based on the typical immune response to HIV, why is a T-cell based vaccine likely to be more beneficial? Why have all vaccine trials failed at this point?
21. **Questions Based on Presentations** (4 pts). You can answer up to 4 questions, 2pts each. 2\textsuperscript{nd} two choices are bonus points. *Please indicate the four that you would like graded, otherwise the first four will be graded.*

a) How does Gardasil or Cervarix provide protection against cervical cancer?

b) Ibalizumab is an monoclonal antibody that is used to interfere with HIV growth. What protein does it bind to and how might this prevent HIV growth?

c) How is passive and active immunization combined to provide protection against the Procine Epidemic Diarrhea Virus (PEDV) in piglets?

d) How is the Newcastle disease virus, an avian virus, used to develop a vaccine for ebola virus?

e) What is one key limitation regarding the development of vaccines for birth control?

f) How can hookworms be used to treat autoimmune diseases that involve antibodies?

g) What are two key properties of the antigen that is selected for the development of anti-cancer therapeutic antibodies?

h) Why might the protective antigen from Anthrax be the most useful target for vaccine development?

i) What experiment was done to demonstrate the anti-cocaine catalytic antibodies are more effective in the treatment of cocaine than antibodies that simply bind cocaine?

j) Why are patients who are infected with HIV more susceptible to tuberculosis?

k) Why is suppression of apoptosis by N. Gonorrhoeae a useful advantage for the bacterium?

l) What experiment was done to show the linkage between Rag1/Rag2 expression and the severity of immunodeficienies?