Spring 2003 Immunology Exam #3 - Chapters 8 - 10

There is no time limit on this test, though I have tried to design one that you should be able to complete within 4 hours, except for typing. You are not allowed to use your notes, or any books, any electronic sources, nor are you allowed to discuss the test with anyone until all exams are turned in at class time on Wednesday April, 2. **EXAMS ARE DUE AT CLASS TIME ON WEDNESDAY APRIL 2**. The **answers to the questions must be typed on a separate sheet of paper** unless the question specifically says to write the answer in the space provided. If you do not write your answers on the appropriate pages, I may not find them unless you have indicated where the answers are.

When you are ready to take the exam, send me an email with the subject line of **Immunology Test**. This will generate an automated email telling you how to download the exam.

-3 pts if you do not follow this direction.
Please do not write or type your name on any page other than this cover page. Staple all your pages (INCLUDING THE TEST PAGES) together when finished with the exam.
Name (please print here):

Write out the full pledge and sign:

How long did this exam take you to complete (excluding typing)?

12 pts.

I. Define these terms: 1 pts each. Define the terms and demonstrate your knowledge. These terms can be define succinctly so using a lot of words is not the best way to demonstrate your fluency with these terms. You may combine words with pictures if this helps, but don't hand write the words unless you print VERY neatly. However, note that unlike the first test, I will not be grading these as harshly since they are worth fewer points.

primary focus – a collection of activated B and Th2 cells in the T cell zone and gathered around an APC displaying the peptide recognized by the Th2 cells. Some B cells will form plasma cells making IgM while other move on to form a germinal center.
recirculate – the movement of B and T cells from blood to lymph, over and over.
FasL – Fas ligand that binds to Fas. When FasL trimerizes three Fas receptors, the cells with Fas undergoes apoptosis. FasL is on NK cells and Tc cells, among others.
affinity maturation – after somatic hypermutation of B cells in germinal centers, those B cells with mutations that increase affinity for the antigen out compete those B cells with lower affinity for the same antigen. Without binding to antigen, B cells with lower affinity die due to lack of survival signal while those with increased affinity continue to live and produce antibodies wit the highest affinity.
TI antigen – an antigen that can activate a B cell in without a Th2 cells assisting. These antigens are multivalent, such as bacterial cell wall components.
colostrum – mammary secretion for the first ~ 3 days before milk begins flowing and contains IgAs, cytokines and even some leukocytes.
staple conformation – shape of IgMs when they bind to the surface of bacteria. This shape permits Iq1 to bind initiate the complement cascade.
FcRn – the protein that binds as a dimer to IgG and transports the IgG across the placenta.
ADCC – antibody-mediated DDD CC CCCC – when a NK cell kills target cells by binding to antibodies adhering to the surface of cells displaying antigens.
transcytosis – the movement of antigen (e.g. M cells) or IgA (via poly-IgA receptor) across cells through the cytoplasm and within vesicles.
M cells – microfold cells in the intestines that transcytose antigens from the lumen to the basolateral side and available to APC to activate the adaptive immune response.
T_H3 – stimulated by oral tolerance , these T cells suppress immune responses.

Part II

These questions are intended to be ones which require you to synthesize a lot of specific information. I decided to see how you can integrate this information rather than breaking it up into smaller unrelated questions.

10 pts.

1) Design a strategy to shift an allergic response to grass from an annoying one to a harmless response. As you outline your approach, connect your approach to theory or rules we have covered. An answer that lacks theoretical backing will be worth only half the number of points. Although I would be eternally grateful for a simple and readily available answer, I will evaluate your answer based on theoretical constraints rather than on

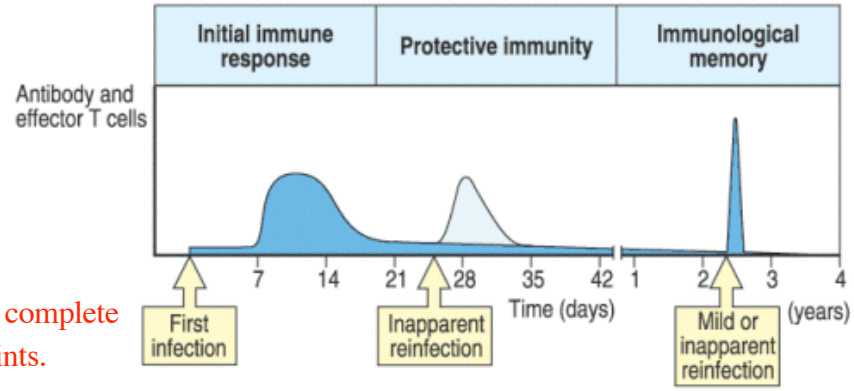
currently practiced immunotherapy.
You need to shift the immune response, not block it with antihistamines. There were several acceptable approaches. One answer was oral tolerance which meant you needed to induce Th3 and/or Tr1 cells. An alternative was to inject high does of antigen along with cytokines that shift CD4 differentiation towards Th1 and away from Th2.

10 pts.
2) Outline how you could immunize a person to elicit a cytotoxic T cell response instead of an antibody response. Use as your goal to eliminate a virus that infects muscle cells.
There were several options, but here is one:
a. vaccinate with DNA and adjuvant. DNA should enter APC and encode for viral protein.
b. APC makes protein and presents in MHCI which will activate CD8+ cells.
c. If muscle-virus infects muscles, there would be armed and/or memory CD8+ cells that would kill infected cells.

10 pts.
3) Outline how you could help someone infected with intestinal worms if the worms have been in the patient for over a year. These worms burry their sucker parts into your intestinal lining but the bulk of their body is within the lumen of your intestines. You cannot simply say give them drugs that kill worms. I want you to devise an immunology-based treatment. For this question, you have unlimited lab help and funding, so don't let something simple like purifying a protein or cloning a gene stop you.
Since intestinal worms can only be attacked by IgA which function primarily by neutralizing. Since the worm is already attached, the better target the mouth parts which have pierced the intestines. Purify mouth part proteins, and use these in a vaccine. Ideally, you would be able to shift the response towards an IgE response. This would arm mast cells and launch cytotoxic effects onto the worm. IgA and IgM are not effective responses since the worm is already attached.

35 pts.
4) OUTLINE a normal immune response to particular antigens listed below. To answer this multi-part question, use the following figure to guide your multi-part answers. One caveat, the timeline in this figure is in days and years, but your time line should be first exposure at day zero, second exposure 3 months later and final exposure 2 years after first exposure.

a. allergic response to a bee sting
b. anthrax infection in lungs
c. tuberculosis infection
d. Giardia in your intestines
e. bot fly larvae under your skin



The answers below are not intended to be complete answers but are meant to outline main points.

a. Allergic response tells you this is an abnormal response and probably IgE. The first exposure would activate B and Th2 cells. Perhaps IgE would be generated by the end of this exposure. This would lead to armed mast cells. Three months later, a more robust IgE-mediated response would be generated with normal release of histamine and other inflammatory molecules. The third exposure would re-activate memory cells and perhaps lead to systemic shock and perhaps death.

b. Anthrax spores land it lungs and generate an immune response that eventually produces an IgA response. In addition, bacterial toxins enter cells and would be presented in the context of MHC II. This would result in an IgG neutralizing effect and/or NK induced ADCC response. Subsequent infections would hopefully result in blocking of toxin and neutralizing of bacteria to prevent severe infection. Memory B cells would be ready to respond in later infections.

c. TB is also a lung infection but this bacterium lives inside macrophages. Ideally, you would produce a Th1 response to initiate killing of infected macrophage cells. Tc may help, but Th1 is the primary beneficial immune response. For subsequent infection, there may be some IgG-mediated blocking of bacteria prior to binding macrophages, but more than likely, memory Th1 cells would quickly respond and clear the infections.

d. Giardia is a unicellular, eukaryotic intestinal parasite that needs to be blocked by IgA. This would be too late for the first infection, but later infections should benefit from this response. Due to the diarrhea, we also know there is probably an IgE-mediated inflammation. Subsequent infections would hopefully block binding, but from personal experience, I know this is not always effective. Therefore, we would require additional means such as stress induced expression of MIC A and B proteins and □;□ T cells could bind and induced apoptosis. (In chapter 11, we learned that Giardia coats itself with host proteins which makes it especially hard to target and clear. This is why medication is required.)

e. Bot fly are multicellular parasites that are best cleared by IgE-armed mast cells. The process of producing these requires that APCs express parasite surface proteins that will activate Th2 cells and subsequently B cells. Memory B cells will be produced and mast cells will be armed and ready to attack the next infection.

6 pts.

5) Explain how your immune response to a virus can leave you vulnerable to serious infection under the following condition. This virus has 3 proteins on its outer coat and all 3 are needed to infect your cells. Each year one of these proteins mutates such that the protein still functions but your antibodies can no longer recognize the mutated protein. The first year you generate a strong humoral response but in year three, you get very sick.

The central component to this answer was original antigenic sin. You needed to state clearly that this only works on B cells producing Ig, probably IgG for neutralizing/blocking the virus from binding to host cells. Tc cells, which would kill virally infected cells, do not undergo suppression the way B cells do, however, if they used surface proteins presented in MHCI, we expect them to respond to each change as it occurred. These memory Tc should have lead to a fast clearance once the infection had taken hold unhindered by the loss of anti-virfus antibodies by the third year.

7 pts.

6) Outline how to vaccinate an infant against a new pathogen if the outer surface of the pathogen is composed of sugars only. Furthermore, explain the infant's immune system would respond after vaccination to successfully protect the infant from infection.

You needed to used linked recognition of sugar and protein, such as tetanus toxoid. The B cell would bind to the sugar and internalize the entire antigen. The toxoid portion would be displayed in MHC II and thus memory Th2 cells could quickly trap and activate the B cells in primary foci and later germinal centers. These memory B cells, with high affinity BCR should persist and protect the child from infection by neutralizing the viral pathogen.

6 pts.

7) Describe two components of the immune system where invariant TCRs appear to play a critical role in your immune system.

NK1.1 T cells bind CD1 and lipid antigen

□□ TCR bind MICA and B on stressed cells.

CD8+ □□ homodimer TCR bind to MHC class IB proteins.

Th3/Tr1 cells that lead to oral tolerance.

4 pts.

8) List as many examples as you can how a mothers boost the immunity of their children.

IgA through colostrum and milk

IgG across placenta and into fetal blood

symbiotic bacteria to line infant guts.

cytokines and leukocytes are also contained in the milk.

Bottom line – nurse your children!

+2 Bonus Points: With regards to our immune system, speculate what multicellular parasites must be able to do in order to survive in human hosts?

I was looking for a rapid change in surface proteins or surface decorated with human (self) proteins.