Q1. IgE is present in low amounts and has a relatively short half-life (months) in the serum. However, IgE specific for an allergen can still cause dramatic symptoms of anaphylaxis many years after the sensitization period to an allergen. How would you explain this phenomenon. IgE binds to FcεRI on mast cells with high affinity which increases the half-life of IgE to many years. Binding of the allergen to the cell surface IgE triggers release of mast cell granules and causes anaphylaxis.

Q2. A delayed type of hypersensitivity (DTH) immune response can be both helpful and harmful during an immune response. A. What cells and cytokines are characteristic of a DTH response? Th1 cells, macrophages, IFN-γ, TNF-α. B. Describe an example of a DTH response that is immunopathogenic (harmful) to an organism. Type IV hypersensitivity with response to harmless foreign antigens (poison oak, metals, drugs) which cause inflammation and disease. Infections such as TB, schisto, can cause a DTH response that results in granuloma formation. C. Would you find Neutrophils at the site of a Delayed Type Hypersensitivity reaction? Why or why not? Not likely. Neutrophils are part of acute inflammation in contrast the chronic activation of antigen-specific Th1 cells is more likely to involve the release of chemokines that attract macrophages.

Q3. How does chronic inflammation differ from acute inflammation? Chronic inflammation requires adaptive an immune response to antigen. This is usually persistent antigen activating antigen specific Th1 cells and making cytokines that activate macrophages at the site of the antigen.

Q4. Why do high endothelial venules (HEV) express a different set of cell adhesion molecules (CAMs) than endothelial cells that are attracting cells to a site of inflammation? HEV express CAMs that will attract naive T and B cells to the lymph nodes or spleen (NOT neutrophils) whereas an inflammed endothelium will attract neutrophils/macs and ACTIVATED T cells.

Q5. IL-1, IL-6, and TNF-α play a crucial role in activating acute inflammation. On a systemic level they are capable of producing numerous effects on the host. How can IL-1, IL-6, and TNF-α interact with the liver to cause effects on the central nervous system? Acute phase response. Through the production of acute phase proteins that can activate hormones (such as ACTH) that will activate the "stress" response. Can also say will interact with adrenal, hypothalamus, pituitary axis

Q6. As a graduate researcher you have decided to study mechanisms of leukocyte homing. You make double knockout mice that have no E-selectin or P-selectin (E-P-selectin/-/−). You decide to test the immune responses of these mice for their ability to fight off extracellular bacterial infections. What changes might you expect to find in E-P selectin/-/− mice? The primary defect would be in the ability of neutrophils and activated effector T cells to attach (tether and roll) to activated or inflamed endothelium and extravasate at the site of infection. During an infection with extracellular bacteria the E-P selectin/-/− mice would have a reduced ability to initiate inflammation at the site of infection and a reduced immune response in general especially early phagocytic clearing of bacteria.
Q7. Neutrophils and macrophages are both very important in inflammatory immune responses. They have many similar functions and many different characteristics as inflammatory cells.

In the table below contrast the two different cell types.

<table>
<thead>
<tr>
<th>Example: Production of oxygen radicals</th>
<th>Neutrophils</th>
<th>Macrophages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Production of antibacterial enzymes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Longevity in tissues</td>
<td>Short-lived</td>
<td>Long-lived</td>
</tr>
<tr>
<td>Opsonization via Fc Receptors</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Respond to C3a, C5a</td>
<td>Yes</td>
<td>No. Responds to MIP-1α, MIP1-β</td>
</tr>
<tr>
<td>Secrete TNF-α</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Present antigen to T cells</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Respond to lipid mediators (PGE2, LTB4)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Q8. Transfusion reactions can occur if a person receives blood with the wrong ABO blood group. This is a Type II Hypersensitivity triggered by antibodies against the AB blood group antigens.

A. What are the ABO antigens and where are they located?
The A and B antigens are carbohydrate groups located on the surface of red blood cells.

B. What type of immune mechanisms can result from these antibodies binding to the surface of red blood cells? Where would you see the effects of this Type II response?
The immune mechanisms would be those directed through antibody binding. Primarily complement activation and ADCC (maybe opsonization) of targeted red blood cells. This would lead to a systemic inflammatory response and potentially immunopathology in liver and spleen.

Q9. A. In Type III Hypersensitivity why do you see an increase in Complement activation?
The immune complexes when not eliminated will activate complement via the many exposed Fc regions.

B. How does Complement activation potentially increase the symptoms seen in Type III Hypersensitivity?
C3a, C4a, and C5a are anaphylatoxins that increase the inflammatory response.

Q10. A. In what ways is a Type IV DTH response similar to a Type I Hypersensitivity?
They both require a sensitization period and both can activate inflammation.
Both are to innocuous small antigens.

B. In what ways is a Type IV DTH response different from a Type I Hypersensitivity?
Type IV is a T cell and macrophage mediated delayed immune response.
Type I is an IgE, Mast cells, Eosinophil mediated immediate immune response.
**Q10.** *Staphylococcus aureus* is a very common extracellular bacterial pathogen that causes a wide range of diseases ranging from strep throat to rheumatic fever and toxic shock.

**A.** What would be the primary **adaptive** immune response to these bacteria?

**Antibodies and Th2 cytokines.**

**B.** *S. aureus* infection can occasionally cause a systemic inflammatory response that can result in shock and organ failure. How could this bacteria cause this serious disease consequence?

The *S. aureus* has an exotoxin that can act as a superantigen and bind to TCR and MHC causing non-specific T cell activation. The release of cytokines by T cells can cause systemic macrophage activation/inflammation (probably through the acute phase response) leading to toxic shock.

**Q11.** Leishmania are protozoan parasites that cause skin diseases and potentially systemic infections that can be lethal. Leishmania primarily infect macrophages and live endosomally. It has been well-documented that certain strains of mice, such as BALB/c, are more susceptible to Leishmania infection whereas other strains of mice, such as C57Bl/6, are more resistant to infection.

**A.** Would you expect the resistant C57Bl/6 mice to mount a Th1 or Th2 response? Why would a targeted cytokine bias be beneficial in response to this parasite?

Th1 responses are very good at activating macrophages and stimulating a cellular immune response.

However, an **intracellular pathogen** spends the majority of its life within a cell where these mechanisms cannot penetrate. A Th1 response would mount a more robust CMI.

**B.** Propose an immune genetic difference that could help explain why BALB/c mice are more likely to mount an immune response that is less able to resolve Leishmania infection?

A difference in the promoter region of IL-4 that allows higher transcription. A stronger affinity IL-4R.

Many other possibilities including MHC, inflammation genes, IFN-γ, IL-12, GATA-3, T-bet, MyD88, TLR etc.

**C.** A new vaccine for humans has been developed using a recombinant fusion protein combining three antigens identified from the mouse model of disease. This vaccine is a single recombinant polyprotein comprising the sequences of all three open reading frames genetically linked in tandem. The resulting molecule comprises an open reading frame that codes for a 111kDa polypeptide. Would this vaccine require an adjuvant and what type of immune response would you expect this vaccine to elicit?

Yes. It would require an adjuvant because the untreated protein will not initiate inflammation on its own. (okay to say no PRR recognition/TLR activation, no inflammation from tissue injury etc.) This would primarily elicit ab and Th responses. Might be both Th1 and Th2. But not CTL.