

## Master Answers for Clinical Immunologic Assays-I

### I. Basic Concepts of primary and secondary immune responses.

1. *Active military personnel are always current with regard to vaccinations. So the 20 year old on active duty will have **vaccine immunity**. This dog bite is superficial and was cleaned easily. Since the wound is not penetrating, there is no suitable environment for the tetanus organism to grow and produce the toxin. Ergo, no vaccine booster is needed.*
2. *On the other hand, the mountain man has a problem. His wound is deep and “dirty”. This type of wound is highly conducive to tetanus growth and toxin production and he is at extremely high risk because he has no existing immunity because he has never been vaccinated. He needs “instant” immunity and this can only be provided by **infusing human antitetanus antibodies** into him. This provides **passive immunity** and for the long term he can then be immunized for long lasting **active immunity** in case the bear returns.*
3. *There could be several answers to this one but the concept to remember is that basic research has shown that anthrax pathogenicity is markedly reduced if the shuttle vehicle is not present to transport the toxins into macrophages. Exploiting that fact, **a vaccine made to the shuttle protein** should prevent anthrax-mediated disease by **inducing active immunity**. The vaccine would have to be immunogenic and **given prior** to exposure to anthrax.*
4. *To be a successful clinician, you have to be creative and use what the situation gives you. In this case, we know that a group of patients survived a highly lethal infection with Ebola Virus. Although you may not know the exact immunologic mechanism(s) that provided them protection, it would be logical to assume they generated protective antibodies during their infection. Once the virus spread to susceptible lab personnel, infusing the plasma you had in the freezer (or draw more plasma from survivors) that had been drawn from the Ebola survivors could be life-saving because it might **provide passive immunity**.*
5. *The letter to the editor posted on the HD website is a real-life application of a clinician providing **passive immunity** to a lethal influenza virus that allowed the patient to survive the acute phase of the illness. The passive immunity provided a window of time that allowed the patient to then develop **active immunity** to the actual, but attenuated (by the infused survivor antibodies) viral infection. Since infused antibodies from a*

*survivor will last ~20 days, you can infer that the patient developed active immunity to the virus because antibody was present at 6 months.*

## **II. Seroimmunology**

1. *Antibody titers simply reflect the quantity of specific antibody present in the serum of the tested individual. The classical expression however is confusing because a fraction, example-“ a patient has a titer of 1/2000 to influenza A virus”, is used. The easiest way to remember what it means is **that the larger the denominator the more the antibody present**. For example, if one part serum has been added to 1999 parts of (non-antibody containing) diluent and reacts with the antigen in question, that tells you there is still enough antigen specific antibody present to be detectable by the assay and the titer is 1/2000. You can do serial assays over time to tell you whether the patient is making IgM or IgG antibody to the antigen. This tells you whether the infection has occurred in the past or is a primary response (new infection). This archaic “titer” terminology is rapidly being replaced with units so this will not be as large a problem when you are housestaff but the principle remains the same.*

## **III. HIV TESTING**

1. *At this point in your medical school life all you need to remember is that many initial testing methods employ high sensitivity to detect all possible reactors at reasonable cost and speed. ELISA is a very common screening assay used in patients with suspected infectious diseases. If an ELISA is negative, there is a very high probability (assuming the patient can make antibodies) that the patient does not have the infection in question. On the other hand, a positive test in this type of assay alerts the physician to the fact **that subsequent highly specific testing must then be done to make a precise diagnosis**. HIV is used here as a stark example. Telling a patient that he or she has HIV based on a test with low specificity like an ELISA creates multiple serious problems for the patient, the physician and society.*