Example-exam Basics of Infectious Diseases (NEM-20806) 2015/16:

Question 1: The 'disease triangle' is a conceptual model used to better understand the epidemiological dynamics of infectious diseases.

A. **What are the three factors that make the corners of the disease triangle?**

   [ANSWER (2 points): environment, infectious agent, and host]

B. **How can the disease triangle help to understand a sudden outbreak of an infectious disease?**

   [ANSWER (4 points): the epidemiological outcome of an infectious disease is determined by interactions between environment, pathogen, and host. Sudden outbreaks of infectious diseases always involve a change either in the environment, in the pathogen, or in the host. Changes in the environment may for instance enable the transmission of pathogen from a novel source (e.g. reservoir host in jungle). Specific genetic changes in pathogens may increase their virulence (e.g. mutations in virus surface proteins). Changes in host behaviour may enhance the transmission of the causal agent. For example, the current aggregation of thousands of people in refugee camps in drought stricken East Africa greatly enhances the likelihood of transmission of infectious diseases.]

C. **Apply the disease triangle to explain a recent pandemic of an infectious disease.**

   [ANSWER (2 points): the swine flu epidemic is thought to have occurred after a genetic recombination in the viral genome of an influenza virus (pathogen factor). People (host factor) lacked immunity to this new highly virulent virus, while international travelling (environmental factor) of carriers of the virus allowed for a rapid spread of the disease throughout the global community.]

Question 2:

Most people get microbial infections when their immune systems are weakened. Nevertheless, also people having a normal functioning immune system can get infected by pathogenic bacteria.

A. **Explain how bacteria can cause disease despite the presence of a functioning immune system (2 points)**
B. **Give examples of immune evasion mechanism (at least 3) (4 points)**
C. **Explain why the development of antibiotic resistance is a problem in healthcare (4 points)**

This question has been discussed in the lecture. See for answers lecture slides.

Question 3:

Despite the occurrence of many fungal species, fungi are not known as major human pathogens.

A. **Explain why fungi generally do not cause severe diseases on humans and animals. (4 points)**
B. **Once suffering from a systemic mycosis, mortality is generally very high. Explain why it is difficult to develop antifungal drugs. (3 points)**
C. **Systemic mycoses can be divided into true and opportunistic systemic mycoses. How many fungal species can cause true systemic mycoses and how many fungal species can cause opportunistic systemic mycoses? (3 points)**

This question has been discussed in the lecture. See for answers the lecture slides.

Question 4:

A. **What is the difference between a directly transmitted and an indirectly transmitted pathogen? (Use diagrams to illustrate your answer; 4 points)**

[ANSWERS: A directly transmitted protozoan passes from one host to another without the need for a vector. Direct transmission may be through a medium such as soil or water.

An indirectly transmitted protozoan parasite has a transmission cycle which involves a vector. The protozoan is transmitted from one host to another via a vector which may be an insect.]

B. **Give two examples of directly transmitted protozoan pathogens (2 points)**

[ANSWERS: Directly transmitted: Examples include, Giardiasis (*Giardia duodenalis and Giardia lamblia*), Toxoplasmosis (*Toxoplasma gondii*)]

C. **Give two examples of indirectly transmitted protozoan pathogens (2 points)**

[ANSWERS: Indirectly transmitted (vector borne): Examples include, Chagas disease (*Trypanosoma cruzi*), African trypanosomiasis (*Trypanosoma brucei spp*), Leishmaniasis (*Leishmania spp*), Malaria (*Plasmodium spp*).]

D. **What are some of the challenges involved in the control of protozoan pathogens? 2 points**

[ANSWERS: Antigenic variation, evasion of host immune system, natural reservoirs of infection, vectors become resistant to insecticides used to control them, parasites become resistant to the drugs used to treat infection.]

Question 5.

A. **List three ways in which arthropods may be of public health importance to humans and give one example for each. (6 points)**

[ANSWERS: Nuisance biting (e.g. head lice, mosquito bites, midges); Allergies to bite or sting (e.g. bee, wasp, ant, mosquito); Disease causing agent (e.g. Myiasis by the human botfly, Dermatobia hominis); Disease vector (e.g. mosquitoes transmitting malaria, ticks transmitting lyme disease).]

B. **What is the causative agent of Lyme disease and how is this disease transmitted? (2 points)**

[ANSWERS: Causative agent = *Borrelia* bacteria. Transmitted from one host to another through bites of infected ticks (the sheeptick *Ixodes ricinus).*]

C. **How can infection with Lyme disease be prevented? (2 points)**

[ANSWERS: Tick checks - remove tick within 24 hours of attachment; Use of DEET-containing repellents to prevent tick bites.]

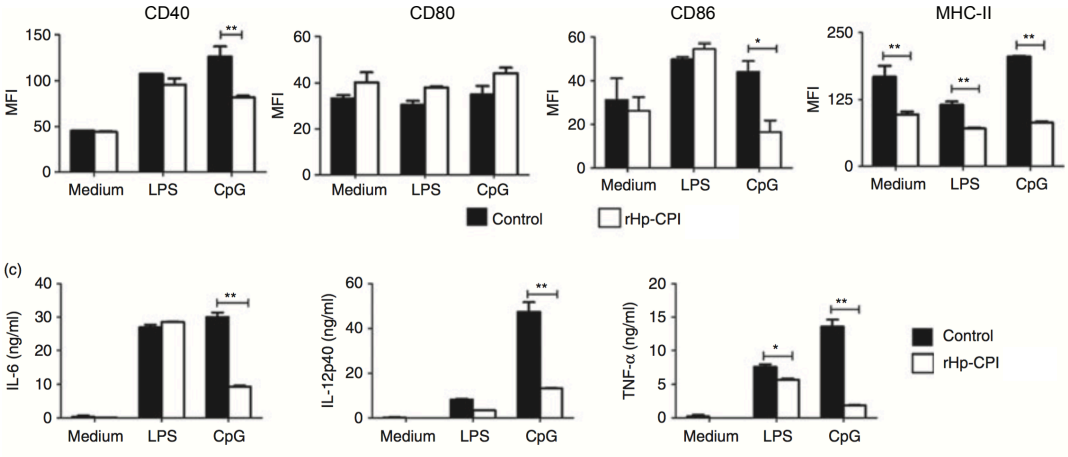
Question 6

A cysteine protease inhibitor from the murine parasitic helminth H*eligmosomoides polygyrus* (Hp-CPI) is able to modulate dendritic cell function and subsequent responses of the adaptive immune system.

A. **Describe step-by-step how foreign compounds (e.g. PAMP's or antigens) are being perceived by dendritic cells and ultimately lead to T helper cell activation? [2 points]**

[Answers: Perception by PRR's, endocytosis, fusion with lysosomes, loading onto MHC-II molecules, antigen presentation and T cell activation.]

In the figure below you can find the effect of recombinant (r)Hp-CPI on mouse bone marrow-derived dendritic cells, which are stimulated with ligands for TLR4 (LPS) and TLR9 (CpG).



MFI: mean fluorescent intensity (a measure for expression level)

B. Polarisation of T cells depends on three distinct signals given by antigen presenting cells. Which of these three signals are affected by Hp-CPI as stated in the figure? [2 points]

[Answers: Signal 1 – antigen presentation; Signal 2 – co-stimulation; Signal 3 – cytokines]

C. Knowing the effect that Hp-CPI has on dendritic cells, which type of T helper cell response will you expect? Furthermore, what do you expect to be the effect on the type of antibodies that will be produced by B-cells? [3 points]

[Answers: Reduction of IL-12 => suppression of Th1 responses; Reduction of IL-6 => suppression of Th17 responses, favoring Tregs; Th2 dominated immune responses are the result; Th2 type immunity will favor the production of IgE/IgG4 by B cells]

D. Besides the immunomodulatory properties illustrated above for Hp-CPI, helminths employ multiple other mechanisms to modulate host immune responses. Give at least 3 other examples. [3 points]

[Answers: Proteases, protease inhibitors, chemokine blockers and anti-oxidants to inhibit eosinophil recruitment and effector functions; antibody class switching from IgE to IgG4 to limit eosinophil degranulation; alternative activation of macrophages to block Th1 responses and induce wound healing; promoting regulatory T cell development; promoting lymphocyte hyporesponsiveness (anergy), cytokine mimics (e.g. TGF-b1), etc….]

Question 7:

Helminth parasites have a number of characteristic features that makes them different from other causal agents of infectious diseases.

A. **Helminth parasites cannot outpace the immune system of the host. Explain why.**

   [ANSWER (4 points): Helminths do not replicate inside a single host individual. The parasite load of an individual results from multiple infections with parasites/eggs. Unlike viruses and bacteria, replication of helminth parasites is not faster than normal response time of the immune system of the host.]

B. **Give two other characteristic features of helminth parasites.**

   [ANSWER (one point each):

   Persistence of individual parasites (several years), and the low mortality rates associated with parasitic diseases in the host]

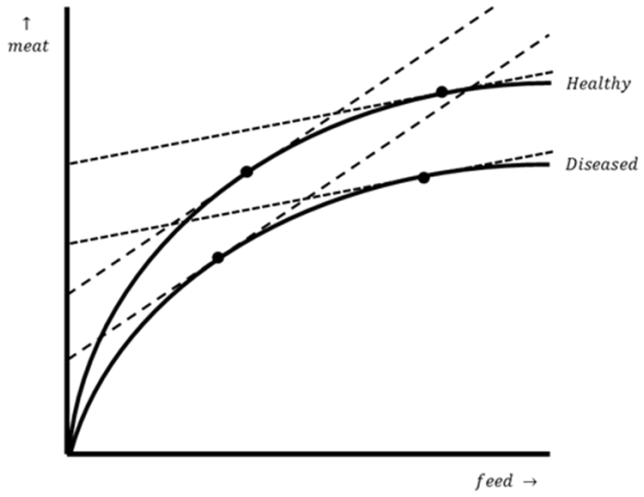
C. **Some helminth parasites can go into a developmental arrest. Give two reasons why a developmental arrest can be beneficial for a parasite.**

   [ANSWER (2 points for each good answer):

   Developmental arrest helps the parasites to survive adverse conditions in absence of a host (i.e. eggs of Ascaris survive >10 years), and developmental arrest is used as a means for demographic control to prevent that the build up of parasite infections in a host population become so high that it increases the mortality. Realize that helminth parasites are obligate parasites that want to persist for a long time in living host. Early death of a host is not a stable strategy for the parasite.]

Question 8:

A. **Draw the Production Function for livestock production and show the impact of disease on this Function (2 points).**



B. Mention at least 2 differences between production diseases and Highly Contagious Livestock Diseases (HCLD; 2 points).

[ANSWERS: Cause: disease agent <>loss of free status
Impacts: decreased production (efficiency)<>measures to control the disease
Aim: mitigation<>regain free status asap]

C. Mention the four categories of monetary costs that can be caused by an outbreak of a Highly Contagious Livestock Disease (HCLD; 2 points).

[ANSWERS: Direct Costs (DC); Direct Consequential Costs (DCC); Indirect Consequential Costs (ICC); Aftermath Costs (AC)]

D. Besides the monetary impacts discussed in Lecture 1, various other factors can affect the impact of a Highly Contagious Livestock Disease (HCLD); mention at least three of such factors (2 points).

[ANSWERS: Zoonotic nature of the disease; Hobby/Non-commercial farmers; Production structure; Region where the disease occurs; Control strategy applied]

E. If you compare Foot-and-Mouth Disease (FMD) and Highly Pathogenic Avian Influenza (HPAI), what is the most important difference with regard to impact on society? (1 point)

[ANSWER: Zoonotic nature of HPAI]

F. **Has the above answered difference the same importance in all countries all over the world? Provide together with your answer a short explanation or an illustration. (1 point)**

[ANSWER: No; see HPAI in SE-Asia: much more fear for human health, therefore use of vaccin; plus: infrastructure for control is quite different, therefore measures at village level.]

Question 9:

Kuru was a deadly prion disease in Papua New Guinea.

A. **How was Kuru disease transmitted between members of the Foray tribe? (1 point)**

[ANSWER: Via ritualistic cannibalism.]

B. **Why were more females infected with Kuru than men? (1 point)**

(ANSWER: More intensive role for women in the rituals.]

C. **Name 2 changes in tissues of the brain that characterize prion diseases. (2 points)**

[ANSWER: 1. vacuoles/spongiform tissues; 2. amyloid plaques/protein deposits/prion fibrils]

D. **Spell out the abbreviations PrPc, PrPsc, PrPsen, PrPres. (2 points)**

[ANSWER: **Pr**ion **p**rotein - **c**ellular, **sc**rapie, **sen**sitive, **res**istant]

E. **Dr. Charles Weismann performed crucial animal experiments to show specificity in the induction of prion disease (scrapie in mice). Which mouse develops severe disease when challenged ("infected") with hamster scrapie: transgenic mice expressing 5-10 times more prions or transgenic mice expressing hamster prions? Explain your answer. (4 points).**

[ANSWER: Transgenic mice expressing hamster prions, only these mice are susceptible to the disease. Mice expressing mouse prions do not develop disease upon challenge with hamster scrapie.]