

NROSCI/BIOSC 1070 and MSNBIO 2070

Exam # 3

November 20, 2015

Total POINTS: 100	20% of grade in class
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- 1) Draw a schematic of a juxtamedullary nephron and label the major portions of the tubule. Then, assuming this is a normal, juxtamedullary nephron of a typically hydrated individual, note the osmolality of the fluid in each segment and the approximate volume of fluid passing through that segment each minute (*use volumes for the total of all juxtamedullary nephrons, not a single nephron*). **(10 points)**.

- 2) Loss of either ADH or aldosterone would cause an increase in urine volume. Other than measuring these two hormones, what could you measure in blood or urine that could inform you as to which hormone's function was lost? Explain your answer. **(10 points)**.

- 3) A patient is determined to have an inulin clearance of 100 ml/min and a PAH clearance of 400 ml/min. To the extent that these values are not normal, what do you think might be going on in this patient? **(10 points)**.

- 4) What are the two major stimuli for aldosterone secretion and how do these make sense in the context of the actions of aldosterone? In contrast, what are the two major stimuli for ADH secretion? **(9 points)**.

- 5) Mutations of proteins associated with Cl^- transport on the basolateral membrane of the ascending limb of the loop of Henle cause a syndrome of Na^+ loss and hypotension. Why should this happen as a result of changes in Cl^- transport at the basolateral membrane of this segment of the nephron? **(10 points)**.

- 6) A young child comes to the clinic suffering severe and widespread autoimmunity. When further testing is done it is determined that he suffers from IPEX syndrome, which is characterized by a loss of FOXP3. What suppressive immune cells would be detrimentally impacted by the loss of FOXP3? **(2 points)**.
- 7) Hematoxylin and Eosin (H&E) staining of a smear of peripheral blood or bone marrow is a common way to differentiate blood cell types and assess for changes indicative of infection and pathology. Name the innate cell indicated by the following physiological and histological descriptions. **(8 Points)**.
- a) Highly represented leukocytes that contain a multi-lobed nucleus and ample cytoplasm full of reddish-purple granules consisting of anti-microbial substances and enzymes.
 - b) Very rare white blood cells with dense blue granules and a bi-lobed nucleus.
 - c) These large white blood cells have significant cytoplasm, but lack pronounced granules and exhibit a bean or horseshoe shaped nucleus. A quick estimate suggests they represent about 10% of the leukocytes.
 - d) Relatively rare leukocytes (1-3% of white blood cells) with a bi-lobed nucleus and bright red granules containing major basic protein.

- 8) Immunoglobulin from one individual B cell comes with a single specificity due to their particular combination of Variable Light (V_L) and Variable Heavy (V_H) regions. Upon activation and appropriate interactions with other immune cells, however, that B cell can generate 5 distinct immunoglobulin isotypes. Each isotype has a distinct function that is shaped by the kinetics of its expression and structure. Identify each isotype described below. **(8 points)**.
- a) Which isotype is secreted as a pentamer and is important for agglutination?
 - b) Which isotype is often fixed to the surface of mast cells and supports degranulation of mast cells?
 - c) Which isotype is driven by B cell exposure to IL-5 and is found on the surface of mucosal surfaces
 - d) Which isotype is the first expressed by the B cell after its education in the bone marrow?

9) While much attention is given to the role of leukocytes in the immune system, protective physical barriers do the bulk of protecting the host from microbes. Describe how the following mechanisms help the barriers of the body prevent infections. **(8 points)**.

a) Lysozymes

b) Commensal microbes

c) Defensins

d) Mucus

- 10)** The loading of small peptides onto MHCI takes place in the endoplasmic reticulum (ER) of all nucleated cells of the body. The transporter associated with antigen presentation (TAP) pumps these peptides into the ER. TAP deficiencies limit MHCI loading. **(4 points)**.
- a) What subset of T cells would be detrimentally impacted by a TAP deficiency?
 - b) Decreased MHCI on the surface of all cells may open an individual open to a significant pathology mediated by which innate immune cell population?
- 11)** Individuals who lack recombination-activating genes (RAG) do not have functional T cells. Why? **(4 points)**.

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- 12) Why is the epitope specificity for an antibody produced by a B cell not altered by isotype switching? **(4 points)**.
- 13) Activated lymphocytes routinely use perforin and granzyme to precisely kill target cells. Explain the effector mechanisms of these two proteins. **(4 points)**.

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- 14) Describe the three types of potential transplant rejection responses that could occur after transplantation of a cadaveric heart, and briefly discuss the treatment (*if any*) that can be used to counteract each type of rejection. **(9 points)**.