# Answer Key

**NROSCI/BIOSC 1070 and MSNBIO 2070**
**Exam # 3**
**November 14, 2014**

**Total POINTS: 100 20% of grade in class**

**1)** The following table reports arterial blood gas levels measured in patients. For each set of readings indicate whether the:
   a. Patient suffers from acidosis or alkalosis.
   b. Whether the change in pH is respiratory or metabolic in origin.
   c. Whether compensation has occurred for the condition.

| Blood Chemistry | | | Acidosis or Alkalosis | Metabolic or Respiratory | Compensated or Uncompensated |
|---|---|---|---|---|---|
| pH | $pCO_2$ | $HCO_3^-$ | | | |
| 7.51 | 40 | 31 | Alkalosis | Metabolic | Uncompensated |
| 7.33 | 29 | 16 | Acidosis | Metabolic | Compensated |
| 7.48 | 30 | 23 | Alkalosis | Respiratory | Uncompensated |
| 7.30 | 59 | 28 | Acidosis | Respiratory | Compensated |

***(1 point each; 12 points total).***

# Answer Key

**2)** A patient is admitted to the hospital with an arterial $PaO_2$ of 55 mmHg. While talking to the patient's relatives, the physician learns that the patient has smoked for over 30 years, and has suffered from considerable shortness of breath for several years.

**a)** The patient's arterial oxygen saturation would likely be *(circle the best answer, **2 points**)*:

**i)** Approximately 55%

ii) Approximately 65%

ii) Approximately 75%

ii) Approximately 85%

ii) Approximately 95%

**b)** Would you expect for the patient's blood oxygen content to differ appreciably from normal levels? Provide a brief explanation for your answer. ***(3 points)***.

Blood oxygen content should be near normal, since there would likely be an increase in hematocrit associated with the patient's hypoxia. Although each hemoglobin molecule has lower $O_2$ saturation, there will be more hemoglobin in the circulation, such that the total circulating $O_2$ will remain fairly consistent.

**c)** It is estimated that the patient's pulmonary artery pressure is 35/20 mmHg, but the physician is not surprised. Why is the patient's pulmonary artery pressure at this level? ***(5 points)***.

Pulmonary artery pressure is extremely high, which is due to very high resistance in the pulmonary circulation resulting from hypoxia (hypoxia causes vasoconstriction of pulmonary vessels).

***Question Continues on the Next Page***

**d)** The physician prescribes a treatment for the patient that includes oxygen therapy and the administration of Warfarin *(Coumadin)*, Iloprost *(Ventavis, a analog of prostaglandin $PGI_2$)*, and Furosemide *(Lasix, a "loop diuretic")*. Briefly describe how each of these treatments is of benefit to the patient. ***(2 points each; 8 points total)***.

| Treatment | Benefit to Patient |
|---|---|
| **$O_2$ Therapy** | Vasoconstriction in pulmonary arterioles is dependent on alveolar $PO_2$. Oxygen therapy will increase alveolar $PO_2$, resulting in vasodilation and decreased pulmonary artery pressure. This will reduce the potential of congestive heart failure. |
| **Warfarin** | This patient is at risk of right-sided congestive heart failure and buildup of blood in the venous system. Whenever blood stagnates in the vasculature, there is a danger of blood clots forming. In this case, blood clots could form in the systemic veins, resulting in pulmonary embolism. It is thus prudent to reduce this risk with an anticoagulant such as Warfarin. |
| **Iloprost** | Prostaglandins, particulary prostaglandin $PGI_2$, are paracrines in the pulmonary vasculature that promote vasodilation. Lung damage caused by cigarette smoking results in reduced release of $PGI_2$. Providing inhaled Iloprost replaces the lost prostaglandins, and causes pulmonary vasodilation. |
| **Furosemide** | Furosemide is a classic diuretic. The pumping mismatch between the two sides of the heart in congestive heart failure is diminished when blood volume is lowered. Thus, giving a diuretic is helpful to the patient in reducing the risk of heart failure. |

# Answer Key

**3)** Breathing is altered by changes in arterial $pO_2$, $pCO_2$, and pH. Which of these factors are most effective in altering alveolar ventilation. Provide a brief explanation for your answer. ***(5 points).***

$pCO_2$. Both peripheral and central chemoreceptors are sensitive to changes in arterial $pCO_2$, whereas oxygen levels and pH are only sensed by the peripheral chemoreceptors. Furthermore, changes in $pCO_2$ cause an automatic change in pH, generating another stimulus that induces a change in breathing.

**4)** How does activity of neurons in the Pre-Botzinger complex (rostral portion of the ventral respiratory group) change during vomiting? Provide a brief explanation for your answer. ***(5 points).***

The breathing pattern generator is suppressed during vomiting, to allow a different pattern generator to control the contractions of respiratory muscles. Since the pre-Botzinger complex contains the core of the breathing pattern generator, many neurons in this region are inhibited during vomiting.

# Answer Key

**5)** Briefly describe how transection of the spinal cord at L1 alters the following ventilatory parameters, or if there is no change in the parameters. Provide a brief explanation for your answers. ***(2 points each; 6 points total)***.

| | |
|---|---|
| **Vital Capacity** | Transection of the cord at L1 causes a loss of control of the abdominal muscles, but not the other respiratory muscles. As a result, inspiratory volumes will remain fairly constant, but expiratory reserve volume is smaller. Thus, vital capacity decreases. |
| **Tidal Volume** | Tidal volume is not influenced by abdominal muscle contractions, and will remain constant. |
| **Transpulmonary Pressure** | The elasticity of the lungs is unaffected, and thus transpulmonary pressure remains constant. |

**6)** Patent ductus arteriosus can be treated medically by the administration of Indomethacin, a potent nonsteroidal anti-inflammatory drug (NSAID). Based on your knowledge of the physiology of ductus arteriosus, describe the mechanism of action of Indomethacin. ***(4 points).***

The patency of ductus arteriosus is dependent on the release of prostaglandins from the placenta (the prostaglandins cause relaxation of smooth muscle in ductus arteriosus). Loss of these prostaglandins is usually sufficient to cause ductus arteriosus to collapse, but sometimes endogenous prostaglandins in the newborn maintain the patency of the vessel. NSAIDs are prostaglandin synthesis inhibitors, and suppress the formation of endogenous prostaglandins.

# Answer Key

**7)** There are numerous critical differences between the innate and adaptive immune systems. Please provide a short statement (1-2 sentences) explaining the key differences between the innate and adaptive immune system for the 5 categories listed below. ***(10 points).***

**a)** The receptors used to differentiate self from non-self

Innate cells use pattern recognition receptors (PRR) that are fixed in genome at birth. These include cell surface receptors particularly the toll-like receptors (TLRs) and the mannose receptor. These also include soluble PRR such as C-reactive protein (CRP), or mannan-binding lectin (MBL). Innate cells also express other conserved receptors (killer activation receptors (KAR), killer inhibition receptors (KIR), complement receptors, Fc receptors, cytokine receptors).

Adaptive immune receptors include, the T cell receptor (TCR) and B cell receptor (BCR, or antibody), are highly diverse and generated via somatic gene rearrangement through life. The BCR can be secreted by plasma cells.

**b)** What the receptors recognize (i.e. to distinguish what is self and non-self)

PRRs detect conserved molecular pattern that are not found on host cells and shared by microbes – Pathogen-Associated Molecular Patterns (PAMPS). "Self" is very broad (human vs. non-human). Things such as the KAR and KIR which allow the innate immune system to respond to altered or "not normal" self (damaged tissues, cancer, inflammation, stress).

Adaptive cells see epitopes of specific antigens. In the case of T cells these are peptides presented on MHC. In the case of B cells these could be any free Ag, but particularly proteins and carbohydrates. "Self" equals you to the adaptive immune system.

**c)** The diversity of receptors on adaptive and innate immune cells at birth and over time

Innate receptors are non-clonal meaning all cells of a class are identical. Innate cells are the same across individuals and unchanged over life.

Adaptive immune cells are clonal, meaning each cell expresses a unique receptor. Where as adaptive immune system is unique to each individual and altered over time.

**d)** 1st response to non-self

Innate cells respond with immediate activation of effectors and responses happen in minutes to hours. Activation only requires a single signals and the response is mediated by the actual activated cell.

Adaptive responses take a long time to develop (Days-weeks). Multiple permissive signals are required to Stimulated cell can undergo clonal proliferation to amplified immune responses and generate a population of cells that can respond to the antigen.

**e)** Repeated responses to the same non-self

Upon secondary exposure to the same non-self material the same class of innate cells will respond with a response identical to primary response.

Adaptive cells will respond to the same non-self material the second time with a much more rapid and robust response. This is the principal behind immunological memory and vaccination.

# Answer Key

**8)** Briefly describe the difference between an antigen and an epitope. ***(5 points).***

An antigen (Ag) is the material that is recognized by the immune system (i.e. organisms or molecule). It is a collection of ligands recognized by cells of both the innate and adaptive immune systems. An epitope is smallest individually identifiable part of an antigen that is bound by a receptor (i.e. amino acids recognized by TCR, or carbohydrate sequence recognized by BCR).

**9)** An antigen-presenting cell (APC) engulfs a dead bacteria and breaks it down in lysosomes. How would it present the resultant peptides to the immune system?

On MHC class II

A second APC is infected with the Epstein–Barr virus (EBV), an intracellular pathogen. How would viral peptides arising inside this APC be presented to the immune system? ***(5 points).***

On MHC class I

# Answer Key

**10)** Given the profound epitope diversity generated during the process of lymphocyte antigen receptor generation, it is certain that self-reactive receptors will arise. Thus, an "education" process is needed to make sure T cells detect MHC appropriately, but have little potential for self reactivity. Describe the steps of central tolerance, including the location and cells of the body involved in this process that results in mature, functional $\alpha/\beta$ T cell. ***(10 points).***

1. Arising from hematopoietic stem cells in the bone marrow, T cell precursors, known as prothymocytes, migrate from the bone marrow to the thymus. These cells are double negative (DN) and do not express CD4, CD8, CD3, or T cell receptor (TCR).

2. In the thymus a large number of DN lymphocytes proliferate and begin to differentiate and generate and express TCRs and CD3 molecules. At this time, they begin to simultaneously express both CD4 and CD8 molecules and are known as "double positive" (DP) T cells.

3. The DP $\alpha\beta$ thymocytes undergo a set of selective processes referred to collectively as thymic education as they travel through the thymus and interact with cells expresses MHCI or II. Most DP T cells die within 3-4 days unless they recognize MHCI with help of CD8 or MHCII with help of CD4. This is referred to as "positive selection".

4. $CD3^+$ $CD4^+$ or $CD3^+$ $CD8^+$ cells whose T cells then interact too strongly with MHC have the potential to be autoreactive. These are induced to undergo apoptosis and removed. This process is called "negative selection"

5. Mature double positive (DP; $CD3^+$ $CD4^+$ or $CD3^+$ $CD8^+$) T cells exit the thymus and inter the circulation as fully functional T cells. Only about 5% of DN cells will progress to functional DP T cells.

# Answer Key

**11)** Immunoglobulin from one individual B cell comes with a single specificity due to its particular combination of Variable Light ($V_L$) and Variable Heavy ($V_H$) regions. ***(8 points).***

**a)** Upon activation and appropriate interactions with other immune cells, however, that B cell can generate 5 distinct immunoglobulin isotypes by doing what?

Immunoglobulin isotypes generated by DNA rearrangements where distinct heavy chain constant genes are combined during DNA rearrangements with the VDJ genes making up the $V_{H.}$

**b)** Each isotype has a distinct function that is shaped by the kinetics of its expression and structure. Which isotype can cross the placenta and mediates maternal passive immunity of infants?

IgG

**c)** Which isotype is both expressed on the surface of B cells and later secreted as a pentamer?

IgM

**d)** What isotype is often fixed to the surface of mast cells and supports degranulation of mast cells?

IgE

# Answer Key

**12)** The adaptive immune response relies on two major histocompatibility complex molecules (MHC). Where do you find MHC class I and class II expressed? ***(2 points).***

MHC class I is found on all nucleated cells. MHC class II is expressed only on antigen presenting cells (APC), including dendritic cells, macrophages, and B cells.

**13)** Which lymphocytes can undergo somatic hypermutation during reactivation and proliferation? ***(2 points).***

B cells

**14)** A common immune evasion strategy by tumor cells is to down regulate MHC class I molecules on their surface. This would make them invisible to which adaptive immune cells, but subject to removal by what innate immune cell? ***(4 points).***

Invisible to CD8 T cells (or CTLs) and subject to NK cell removal

# Answer Key

**15)** Two subsets of T cells are defined by cluster of differentiation molecules (CD) and their MHC specificity. Besides being phenotypic markers, CD can also be functional molecules. ***(4 points).***

**a)** List a CD molecule that is found on both MHC class I and class II restricted T cells and helps support antigen receptor signaling.

CD3 or CD247

**b)** Name the distinguishing CD markers for MHC class I and MHC class II restricted T cells. What is the function of these molecules?

MHC class I restricted T cells are distinguished by CD8, while MHC class II restricted T cells are distinguished by the CD4 molecule. Both are co-receptors that interact with the MHC molecule and stabilize the interaction of the TCR with MHC