February 3, 2020

BCH 4123 Pathological Assignment #1

*Answer **all** questions fully. Your answers may be in paragraph form, point form or if applicable a table or diagram. Remember if you use a table or diagram it must be appropriately labelled and clearly answer the question.*

Pages must be **numbered** and each page should include your **NAME** and/or **STUDENT NUMBER.** Acceptable formats are Word or PDF **only**.

*The completed exam is due **Monday February 10** by 5:00pm. **Please upload to Blackboard.** If unable to upload to Blackboard email your exam to me (rbooth@uottawa.ca), it **MUST** be **received** by 5:00pm February 10. **Please retain the sent email as proof of submission in case there is an issue.***

Question 1 [15 marks]
A 42 year old male with a oligoastrocytoma is on chemotherapy treatment with temozolomide (TMZ). Two months after initiation of TMZ the patient presents with polydipsia, polyuria and nocturia. Laboratory testing revealed hypernatremia and hyperosmolarity. An overnight water deprivation tests was attempted, but was not completed. Anterior pituitary function was assessed and shown to be normal. The patient was empirically placed on 1-desamino-8-D-arginine vasopressin acetate (DDAVP) which resolved his symptoms.

Initial laboratory results

Test	Result	Reference Interval
Plasma Na	151 mmol/L	135-145 mmol/L
Plasma Osmolality	319 mOsm/Kg	284-295 mOsm/Kg
Urine Osmolality	222 mOsm/Kg	

Laboratory results post-DDAVP treatment:

Test	Result	Reference Interval
Plasma Na	143 mmol/L	135-145 mmol/L
Plasma Osmolality	294 mOsm/Kg	284-295 mOsm/Kg
Urine Osmolality	602 mOsm/Kg	

a. Identify the clinical condition; please be as specific as possible. [2 marks]
b. Describe a water deprivation tests. How is it performed? How is it interpreted? What results would you expect in this patient? [10 marks]
c. Why is the patient initially hypernatremic? Explain the hormonal mechanism that causes hypernatremia in this disorder. [3 marks]

Question 2 [5 marks]
Describe how cut-points are chosen for diagnostic tests. How can this approach also be used to compare the performance of different tests? [5 marks]

Question 3 [20 marks, 5 marks each]
Briefly (but clearly) describe the **indications for use**, **mechanism of action**, including **effect on water**, **electrolyte** and **acid-base homeostasis** for the following classes of diuretic drugs:

1. Carbonic Anhydrase Inhibitors
2. Loop Diuretics
3. Thiazide Diuretics
4. K^+ sparing diuretics

Question 4 [5 marks]
A 25-year old female sought treatment for her constant fatigue, lethargy, and depression. She was small in stature and had previously been diagnosed with attention-deficit disorder. On physical examination she was found to have an enlarged thyroid gland (goiter). Blood tests revealed elevated levels of free T3, free T4, and TSH, yet she did not exhibit symptoms of hyperthyroidism.
Explain her laboratory test results and lack symptoms? Provide a detailed explanation of the hormonal regulatory pathway

Question 5 [10 marks]
a) In a normal, full-term, healthy newborn what is the primary site/organ system for production of blood cells (hematopoiesis)? [2 mark]

b) The Bohr effect is a physiological phenomenon first described in 1904 by the Danish physiologist Christian Bohr, stating that hemoglobin's oxygen binding affinity is inversely related both to acidity [H+] and to the concentration of carbon dioxide [CO_2].

This manifests as a right-ward shift in the Oxygen-Hemoglobin Dissociation Curve described in Oxygen Transport and yields *enhanced unloading* of oxygen by hemoglobin.

Complete the following table by indicating if the corresponding shift of the curve is [LEFT] or [RIGHT]. [4 marks]

Control factors	Change	Shift of curve
Temperature	↑	?
	↓	?
2,3-BPG	↑	?
	↓	?
pCO_2	↑	?
	↓	?
Acidity [H^+]	↑	?
	↓	?

c) Name two (2) nutritional factor deficiencies that are sometimes associated with MACROCYTIC anemia. Also provide 2 biochemistry tests that identifies a true metabolic deficiency of these nutritional factors. [4 marks]