



Family Name	
Given Names	
Student Number	
Teaching Period	Semester 1, 2016

<b>FINAL EXAMINATION</b>	<b>DURATION</b>				
<b>MLS245 – Medical Biochemistry</b>	<table border="1"> <tr> <td>Reading Time:</td> <td><b>10</b> minutes</td> </tr> <tr> <td>Writing Time:</td> <td><b>120</b> minutes</td> </tr> </table>	Reading Time:	<b>10</b> minutes	Writing Time:	<b>120</b> minutes
Reading Time:	<b>10</b> minutes				
Writing Time:	<b>120</b> minutes				

**INSTRUCTIONS TO CANDIDATES**

The examination has TWO (A and B) Sections:

Section A contains Multiple Choice Questions: Answer All questions. Total marks allocated: Sixty (60). Suggested time allocation: Sixty (60) minutes

Section B contains Short Answer Questions: Answer All questions. Total marks allocated: Sixty (60). Suggested time allocation: Sixty (60) minutes

**EXAM CONDITIONS**

**You may begin writing from the commencement of the examination session.** The reading time indicated above is provided as a guide only.

This is a RESTRICTED OPEN BOOK examination

Any non-programmable calculator is permitted

One A4 sheet of handwritten double-sided notes permitted

No dictionaries are permitted

ADDITIONAL AUTHORISED MATERIALS	EXAMINATION MATERIALS TO BE SUPPLIED
No additional printed material is permitted	1 x 16 Page Book 1 x 5-Multiple Choice Answer Sheet 1 x Scrap Paper

**THIS EXAMINATION IS PRINTED  
DOUBLE-SIDED.**

**THIS PAGE HAS BEEN INTENTIONALLY LEFT  
BLANK.**

**Section A**  
**Multiple Choice Questions**  
**Total Number of Marks for this section: 60 Marks**

This section should be answered in the Multiple Choice Answering Sheet provided.

Marks for each question are indicated.  
Suggested Time allocation for Section A: **60 minutes**

---

**Section B**  
**Case Study Based Questions**  
**Total Number of Marks for this section: 60 Marks**

This section should be answered in the Answer Booklet provided.

Marks for each question are indicated.  
Suggested Time allocation for Section B: **60 minutes**

---

**Question B-1**

Arsenic is a natural toxin; it can inhibit the activity of pyruvate dehydrogenase. When a person is exposed to arsenic poisoning, how will the cellular level of following compounds be affected?

(Note: Pyruvate dehydrogenase catalyze the pyruvate decarboxylation reaction which transform pyruvate into acetyl-CoA)

- i. pyruvate
- ii. acetyl coA
- iii. NADH
- iv. ATP

**(2+2+2+2 = 8 Marks)**

**Question B-2**

- i. What is micronutrient?
- ii. Briefly describe the function of Vitamin A, Vitamin C, and Vitamin E.
- iii. Name one disease that is the consequence due to deficiency of each of the vitamins in Question B-2 (ii)?

**(3+6+3 = 12 Marks)**

### Question B-3

In a biochemistry experiment, *Student A* investigates the enzyme kinetic reaction of lactate dehydrogenase (LDH). He extracts the LDH from chicken breast fillet he bought at supermarket, and uses lactate as the substrate for this experiment. After preparing various concentration of substrate with the same amount of enzyme, he determines the initial rate of the reactions as displayed in following table:

(Note: LDH is a group of enzymes that catalyze the reaction which interconvert lactate and pyruvate, and found abundance in animal tissues.)

Substrate concentration (mM)	Initial velocity ( $V_0$ ) $\mu\text{M sec}^{-1}$
2	4.6
4	13.0
6	16.0
8	17.0
10	17.3

*Student A* is told that the LDH he extracted from chicken breast may contain compound(s) that interfere with the enzyme. He repeats the experiment using the same amount of LDH, but with purified laboratory graded enzyme. The result he recorded is displayed as follow:

Substrate concentration (mM)	Initial velocity ( $V_0$ ) $\mu\text{M sec}^{-1}$
2	7.5
4	18.2
6	23.0
8	25.0
10	25.5

Answer the following questions:

- What is the  $V_{\text{max}}$  and  $K_m$  for each of the enzymatic reaction?
- How would you explain the two different set of results, considering that *Student A* has used the exact same amount of LDH enzyme?
- If this reaction is to occur within a living chicken (Note: chicken has normal body temperature of  $\sim 41^\circ\text{C}$ ), how would this reaction rate different?

**(8+4+2 = 14 Marks)**

## Question B-4

The following is a monograph from American Liver Foundation webpage (January 14th, 2015), describing a rare genetic condition called Type 1 Glycogen Storage Disease:

*“Type 1 glycogen storage disease (GSD I), also known as von Gierke’s disease, is the most common form of glycogen storage disease, accounting for 25% of all cases. It is an inherited disorder that affects the metabolism - the way the body breaks food down into energy.*

*After we eat, excess glucose is stored in the liver as glycogen to maintain normal glucose levels in our body. In GSD I, the enzyme needed to release glucose from glycogen (Glucose-6-phosphatase) is missing. When this occurs, a person cannot maintain his or her blood glucose levels and will develop hypoglycemia (low blood sugar) within a few hours after eating. The low levels of glucose in the blood of these individuals often result in chronic hunger, fatigue, and irritability. These symptoms are especially noticeable in infants.*

*Since people with GSD I are able to store glucose as glycogen but unable to release it normally, stores of glycogen build up in the liver over time and cause it to swell. The liver is able to perform many of its other functions normally, and there is no evidence of liver failure. The kidneys also become enlarged because of increased glycogen storage.”*

Based on the information provided and your knowledge in biochemistry, examine each of the following statement and determine if it is correct. Give your reasoning and explanation of your decision

- i. Given that people with GSD 1 cannot breakdown glycogen, the body would use fat as primary source as fuel.
- ii. Without Glucose-6-phosphatase, the cells would not be able to conduct glycolysis (break down of glucose to pyruvate) and subsequently unable to provide acetyl CoA for the Citric-Acid-Cycle.

**(6+6 = 12 Marks)**

## Question B-5

The following is the beginning paragraph of one of the recent articles from the Journal of Hepatology (Ref: Tilg H., et al. Pathways of liver injury in alcoholic liver disease; *Journal of Hepatology*. 2011;55(5):1159-1161):

*“Oxidative stress: a driving force in alcoholic liver injury*

*The development of ethanol-induced liver injury including liver cirrhosis and severe alcoholic steatohepatitis (ASH) is a complex process involving various liver cell types and mainly factors released under the control of the innate immune system. Chronic ethanol consumption induces oxidative stress and production of reactive oxygen species (ROS), cytokine release, mitochondrial dysfunction, endoplasmic reticulum stress, and others. ROS initiate lipid peroxidation that directly damages plasma and intracellular membranes and leads to the production of reactive aldehydes with potent pro-inflammatory and pro-fibrotic properties. Oxidative stress and ROS are predominantly generated through the induction of cytochrome P450-2E1 (CYP2E1). A key role for this enzyme in ethanol-induced liver injury has been demonstrated by its inhibition through chlormethiazole and by the finding that CYP2E1 knock-out (KO) mice do not show evidence of ethanol-induced liver disease. Furthermore, transgenic overexpression of human CYP2E1 in a mouse model results in more severe liver disease. Both the hydroxyethyl radical and acetaldehyde, the first products of ethanol metabolism, can bind glutathione (GSH), a tripeptide that acts as a direct free radical scavenger. The transcription factor nuclear factor (erythroid-derived 2)-like 2 (Nrf2) protects cells against xenobiotic and oxidative stress. Nrf2 KO mice exhibit a dramatically increased mortality after ethanol feeding, highlighting the important role of oxidative stress in ethanol-induced injury.”*

Using the knowledge you have, examine the following statement and determine if it is correct. Give your reasoning and explanation of your decision as well.

- i. The damage done by alcohol is not alcohol itself, it is its metabolite. If I can somehow stop the activity of CYP2E1 enzyme, I should be able to drink as much as I want without injuring my liver.
- ii. Grape fruit juice is apparently a good CYP450 enzyme inhibitor. I should just have a big glass of those before going out for drink, and I will be all right.

**(7+7 = 14 Marks)**

**(END OF EXAM PAPER)**