UNIVERSITY OF BIRMINGHAM

STUDENT BOOKLET

ID No: _____

College of Medical and Dental Sciences

MSc in Clinical Biochemistry
Course Code 5602
Module 5 & 6
Friday 2nd July 2010

Room WF15, Medical School
University of Birmingham

Enter your student ID number in the space provided on this answer booklet.
For the Essay Questions please answer ONE question for each module in the answer booklets provided. One answer per booklet.
For the Short Answer Questions please answer all questions using this booklet. Please write final answers to calculations in the boxes provided below the question.

Time Allowed: 2 hour 30 minutes (1245 – 1515). For each module allow 45 minutes for the essay question and 30 minutes for the short answer questions.

For examiners use only

	Module 5			Module 6		
Question	Mark 1	Mark 2	Final	Mark 1	Mark 2	Final
1						
2						
3						
4						
5						

Essay Questions

Module 5

1. Critically discuss the methods for the measurement of alkaline phosphatase isoenzymes.

OR

2. Write short notes on all of the following:
   The Aldosterone to Renin Ratio (ARR)
   Apparent mineralocorticoid excess
   Glucocorticoid suppressible primary hyperaldosteronism

Module 6

1. Discuss the role of biochemical investigations in the diagnosis and management of acute pancreatitis.

OR

2. Define the terms imprecision, and bias (or inaccuracy). How can these be assessed when initiating an assay and how can they be monitored long term?

Short Answer Questions

Module 5

1. Define the pharmacokinetic term bioavailability. **2 marks**

Bioavailability is the ratio of the dose reaching circulation to the dose administered. For intravenous administration the bioavailability is one

The bioavailability of a drug is 0.9. Calculate the theoretical maximum plasma concentration if 270 mg of the monosodium salt of a drug is administered to a 70 kg male. The molecular weight of the parent drug is 300 Da and its sodium salt is 322 Da. Assume the drug is only distributed throughout the extracellular fluid (the volume of which is 20% of body weight). **8 marks**

First calculate the salt conversion factor (S)

S = MW parent drug/MW sodium salt of drug = 300/322 = 0.93

Dose reaching circulation = F*S*Dose administered where F = bioavailability

Dose reaching circulation = 0.9*0.93*270 = 226 mg

The volume of distribution (Vd) is the ECF volume = 20% of body weight (70kg) assuming an ECF density = 1

Vd = 70*20/100 = 14L

Vd = amount of drug in body/plasma concentration

Plasma concentration = 226/14 = 16mg/L

2. A subject was infused with a drug at the rate of 50µmol/min until a steady state plasma concentration of 200 µmol/L was reached. What is the clearance of the drug? **10 marks**

Clearance (mL/min) = Rate of excretion (µmol/min) /C(µmol/mL)

Where C = plasma concentration

Under steady state conditions:

Rate of excretion = Rate of infusion = 50µmol/min

Clnce (mL/min) = Rate infusion (µmol/min)/Plasma concentration (µmol/mL)

Plasma concentration = 200µmol/L = 200/1000 = 0.2 µmol/mL

Clearance = 50/0.2 = 250 ml/min

3. An overweight and hypertensive 65yr old woman presents to her GP with shortness of breath on exertion. He considers heart failure and requests a serum NT-BNP (B-type natriuretic peptide).

What is the main clinical utility of NT-BNP (or BNP)? **3 marks**

The main clinical utility is that when normal (especially with normal ECG), in drug naive subjects, heart failure is virtually ruled out.

What test is considered the gold standard for diagnosing heart failure? **2 marks**

Echocardiography

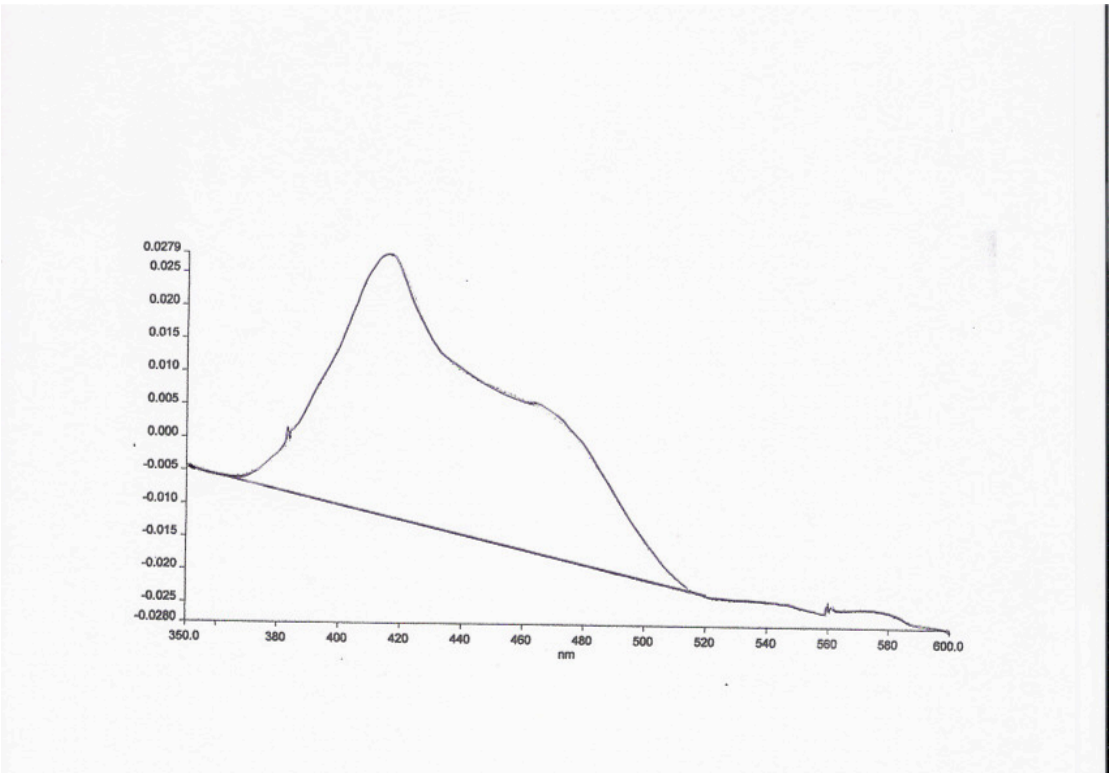
Give five causes of an elevated NT-BNP (BNP) **5 marks**

Heart failure
High sodium diet
Exercise prior to sampling
Renal failure
Myocardial infarction
Acute coronary syndrome
Pulmonary embolism
Hyperthyroidism
Tachyarrhythmias
Cirrhosis
(Do not accept age or gender)

4. List five factors that affect the measured activity of enzymes **2 marks each**

Temperature
pH/buffer
Substrate
Substrate concentration
Cofactors/activators
Assay direction

5. The scan of a sample of cerebrospinal fluid (CSF) collected from a 33 year old woman with a 2 day history of sudden onset of headache is given below.



The protein concentration in the CSF sample was 0.33g/L and the bilirubin in a serum sample collected on the same day was 9 µmol/L.

Calculate the net bilirubin and net oxyhaemoglobin absorbance and indicate what interpretation you would include. **6 marks**

To calculate net oxyhaemoglobin absorbance (NOA)

(Ht from baseline to peak absorbance at 415nm/Ht of axis) * Absorbance range of axis

(3.5cm / 5.0cm) * 0.0559 = 0.0391

To calculate net bilirubin absorbance (NBA)

(Ht from baseline to peak absorbance at 476nm/Ht of axis) * Absorbance range of axis

(1.7cm / 5.0cm)*0.0559 = 0.0190

NBA > 0.007 and oxyhaemoglobin present but NOA<0.1

Increased CSF bilirubin consistent with sub arachnoid haemorrhage

List four CSF sample requirements for xanthochromia investigation **4 marks**

The specimen for spectrophotometry should be the least blood stained fraction of CSF, usually the last and preferably at least the fourth

The volume must be sufficient to allow the analysis to be conducted without dilution

The specimen should be protected from light

Use of the pneumatic tube system to transport the sample is best avoided but the overriding consideration is rapid transport to the laboratory

If immediate analysis of the sample is not possible then the sample should be centrifuged upon receipt

The sample must be collected at least 12 hours post the onset of symptoms

The sample must only be collected if negative CT scan

Module 6

1. A 32 year old man with persistently elevated liver enzymes is being investigated for hereditary copper overload:

What is the disorder affecting the liver as a result of copper overload? **2 marks**

Wilson's disease

List four biochemical abnormalities that may assist in the diagnosis of hereditary copper overload **4 marks**

Low serum copper
Low serum caeruloplasmin
High urine copper
Increased D-penicillamine-induced copper excretion
High liver copper
Increased serum free copper

List four non-hepatic clinical features of hereditary copper overload **4 marks**

Kayser-Fleischer rings
Parkinsonian (extrapyramidal) features
Behavioural problems
Renal tubular dysfunction
Haemolytic anaemia

2. Peptic ulceration

Give two factors which stimulate gastric acid secretion **2 marks**

Gastrin
Vagus (histamine)
Hypercalcaemia

Outline the principles of the urea breath test in the management of *Helicobacter pylori* infection **6 marks**

H Pylori contains urease

$^{13 \text{ or } 14}$C-Urea $\xrightarrow{\text{Urease}}$ $NH_3 + {}^{13 \text{ or } 14}CO_2$

Administer oral urea

Infection indicated by increased breath $^{14}CO_2$

What are the two biochemical hallmarks of Zollinger-Ellison syndrome? **2 marks**

Increased gastric acid output (gastric hyperacidity)

Inappropriate hypergastrinaemia

3. External Quality Assurance (EQA)

List four potential uses of EQA schemes **4 marks**

Assessment of analytical performance of individual laboratory assays
Assessment of analytical performance of an individual method
Assessment of interpretation of analytical results
Education
Samples for method evaluation
Samples to investigate lot to lot variation

True or False

Proportional bias of a sodium method on an EQA scheme means that when the laboratory results (y axis) are plotted against the target results (x axis) the distance of the data points from the 45 degree line increases with the magnitude of the measured value and is negligible at zero. **2 marks**

True

The UK NEQAS B score is a trimmed SD of percentage biases **2 marks**

False

The higher the A score on UK NEQAS the better the performance **2 marks**

False

4. Over a period of 24 hours a liver patient excretes 1L of urine with a pH of 5.0. Calculate the amount of free hydrogen ion excreted. **10 marks**

$pH = -\log_{10}[H^+]$

$[H^+]$ = antilog (-pH) = antilog (-5) = 1.0×10^{-5} mol/L = 10 µmol/L

5. A test for coeliac disease gave a 9% false positive rate and a 4% false negative rate. What are the sensitivity and specificity of the test? **10 marks**

If the false negative rate is 4%, for every 100 patients with disease, 4 false negatives will be obtained.

FN = 4 and TP = 96

FN false negatives
TP true positives

So sensitivity = TP/TP+FN = 96/100 = 0.96

If the false positive rate is 9 then for every 100 patients without disease 9 false positive results will be obtained

FP = 9 and TN = 91

FP false positives
TN true negatives

So specificity = TN/TN+FP + 91/100 = 0.91