



UNIVERSITY OF
BIRMINGHAM

STUDENT BOOKLET

Name: _____

ID No: _____

MSc in Clinical Biochemistry
Course Code 5602
Year 1&2

SHORT ANSWER PAPER
Friday 3rd July 2009

Room WF15
Medical School
University of Birmingham

Answer all Questions

Time Allowed 2 hours (1315 – 1515)

You will need to pass each module

Please write final answers to calculations in the boxes provided below the question

Module 3

1. 65 year old man presented with fever, dyspnoea and oliguria. Biochemical investigation revealed:

Serum	Sodium	132 mmol/L
	Potassium	6.9 mmol/L
	Urea	42 mmol/L
	Glucose	12 mmol/L
	Creatinine	608 μ mol/L
Urine	Osmolality	290 mmol/kg
	Sodium	55 mmol/L
	Urea	101 mmol/L

- a) Does the patient have pre-renal or established renal failure? (4 marks)

Established renal failure

- b) Give three reasons to support your answer. (2 marks each)

Urine Na 55 mmol/L (>40 renal, <20 pre renal)

Urine:serum urea 2.4 (<3:1)

Urine:serum osmolality 0.87 (<1.1:1)

or Urine osmolality <600mOsm/kg

(Give 1 mark for calculating serum osmolality)

2. A two year old boy was admitted to Accident and Emergency unconscious and hyperventilating. He had been perfectly well until 2 hours previously when he started vomiting. He had the following biochemistry results:

Serum	Sodium	130 mmol/L
	Potassium	3.3 mmol/L
	Chloride	94 mmol/L
	Urea	3.1 mmol/L
	Glucose	9.0 mmol/L
	Creatinine	40 μ mol/L
	Arterial Blood	pH
H ⁺		63 nmol/L
pO ₂		14.0 kPa
pCO ₂		2.0 kPa
HCO ₃ ⁻		10 mmol/L
Urine	glucose +	
Ketones	trace	

- a) What is the acid base disturbance? (4 marks)

Uncompensated metabolic acidosis

- b) What is the likeliest cause? (4 marks)

Salicylate poisoning

- c) What further investigation is required? (2 marks)

Measurement of serum salicylate

3. Table 2 gives the cortisol results from a batch of samples. The assay has been performed using a new lot of calibrators. The tube number corresponds to the position of the sample in the run. Patients A, C and D had short Synacthen tests performed and cortisol collected 0, 30 and 60 minutes post synacthen, the times given in the table were those recorded on the samples. Patient B had an overnight Dexamethasone suppression test. No clinical details were provided on the request form for Patients E, F and G . Table 1 gives the target mean and standard deviation (sd) for the internal quality control (IQC) samples.

Table 1

IQC Level	Mean	1 sd
Low	15	0.8
Medium	300	8.9
High	750	15

Table 2

Tube	Name	Sample number	Cortisol
1	LOW QC		13.5
2	MEDIUM QC		310
3	HIGH QC		778
4	Patient A 0	1	335
5	Patient A 30	2	642
6	Patient A 60	3	753
7	Patient B	1	<0.5
8	Patient C 0	1	>1750
9	Patient C 30	2	>1750
10	Patient C 60	3	>1750
11	Patient D 0	1	563
12	Patient D 30	2	210
13	Patient D 60	3	798
14	Patient E	1	370
15	Patient E	2	712
16	Patient F	1	12
17	Patient G	1	500
18	LOW QC		12.1
19	MEDIUM QC		294
20	HIGH QC		745

- a) Assuming that acceptable limits for the IQC were mean \pm 2SD state, giving your reasons, which samples if any should be authorised.

Samples with concentrations between the middle and high IQC are safe to pass for authorisation. Patients A, C E, G meet this criteria.

- b) How would you deal with the remaining samples?

Assuming sufficient sample remaining, re calibrate and re-run the analysis.

Check that the results obtained fit with the clinical information.

May wish to try fresh IQC sample

Patient F - ?dex suppression test or adrenal insufficiency prudent to call clinician for more information due to delay in results.

- c) What would you like to know in order to optimise the quality control in this assay?

What was the IQC performance using the old calibrators particularly at the lower end?

Is there a problem with the IQC material?

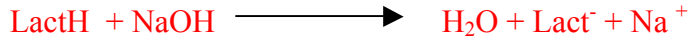
What has the EQA performance been like?

Difficult to comment on only one run using new calibrators, however could run samples (particularly low results) using the old calibrators with IQC material used in dodgy batch and with fresh IQC to check if there is a problem with IQC/Calibration.

- d) Comment on the results from patient D assuming the analysis has been performed correctly.

Results from patient D suggest that sample 1 and 2 have been incorrectly labelled. It is likely that the patient has adequate adrenal reserve.

4. Calculate the number of grams of lactic acid that must be added to 5g of sodium hydroxide to give a litre of solution with a pH of 5.0 (pKa of lactic acid = 3.86. molecular weight of sodium hydroxide = 40 and molecular weight of lactic acid = 90). (10 marks)



$$\text{pH} = \text{pKa} + \log_{10}[\text{salt}]/[\text{acid}]$$

Assuming

NaLact completely dissociated
Negligible contribution of lactic acid to Lact^-

$$\text{pH} = \text{pKa} + \log_{10}[\text{Lact}^-]/[\text{LactH}]$$

Calculate Molar contribution of sodium hydroxide and use in place of $[\text{Lact}^-]$:

$$\text{Molar concentration of NaOH} = \text{Concentration (g/L)}/\text{Molecular weight} = 5/40 = 0.125 \text{ mol/L}$$

Reaction of sodium hydroxide with lactic acid yields approximately equal amount of Lact^-

$$5.0 = 3.86 + \log_{10}0.125/[\text{LactH}]$$

$$1.14 = \log_{10}0.125/[\text{LactH}]$$

Antilog:

$$13.8 = 0.125/[\text{LactH}]$$

$$[\text{LactH}] = 0.125/13.8 = 9.06 \times 10^{-3} \text{ mol/L}$$

$$\text{Wt lactic acid} = \text{concentration (mol/L)} \times \text{MW} = 90 \times 9.06 \times 10^{-3} \text{ mol/L} =$$

Weight of lactic acid required

0.81g

5. Calculate the Creatinine Clearance in a 65 year old man with the following results:

Serum Creatinine 150 μ mol/L

24 hour Urine Creatinine 10 mmol/L
 Volume 2010mL

(10 marks)

Creatinine Clearance (mL/min) = UV/ST

where U = urine cre mmol/L
V = urine volume mL
S = serum cre mmol/L
T = time min

= $10 \times 2010 / 0.15 \times 60 \times 24 =$

Creatinine Clearance

93 mL/min

Module 7

1. List five components that contribute to the cost of a laboratory test. (2 marks each)

Costs for Staff, Reagents, Consumables, Transport, External Quality Assurance, Service, Equipment, Overheads (heat, light & rent)

2. List five advantages and five disadvantages of Point of Care Testing. (1 mark each)

Advantages

Improved Turnaround Time
Better Monitoring of Certain Conditions
Less Clinically Invasive
Useful where access to laboratory is limited
Testing at locations more convenient for patients e.g in PCT
More convenient for clinician
Reduced anxiety for patient e.g. less time to wait for results in HIV testing
Reduced workload for lab e.g. blood gas analysis
Rapid analysis equates to more rapid diagnosis, treatment and triage

Disadvantages

Less control of inappropriate testing
Duplication of equipment
Staff with non analytical background
Issues of result recording in patient record
Incompatibility with lab method
Probably more expensive
More scope for incorrect use e.g. lack QC incorrect calibration chips, failure to EQA
Use of device outside of intended use e.g. inappropriate sample type
Accuracy and precision may be inferior to lab method
Incomplete or non existent clinical protocols resulting in problems with result interpretation
Potential for use by untrained staff if not connected
Duplication of testing if results have to be checked in lab

3. List five causes of hyperammonaemia in neonates (2 marks each)

- Delay in analysis/ Haemolysis
- Specimen contamination
- Sick baby – asphyxia, infection
- Liver disease
- Parenteral nutrition
- Drugs affecting mitochondrial function e.g. valproate
- Urea cycle defects
- Organic acid disorders
- Transient hyperammonaemia of the newborn
- 3H syndrome
- Lysinuric protein intolerance
- Hyperinsulinism (glutamate dehydrogenase deficiency)

4. Calculate the probability that medium chain CoA dehydrogenase deficiency is present when the test for it is positive, if the sensitivity is 0.95 and the specificity is 0.98 and the prevalence of disease is 1 in 10000. (10 marks)

$$\text{Sensitivity} = \frac{TP}{TP + FN}$$

TP = true positives
FN= false negatives

$$\text{Specificity} = \frac{TN}{TN+FP}$$

TN=true negative
FP=false positives

Assuming 1,000,000 people tested

	+ve test	-ve test	total
Disease	95	5	100

No Disease	19998	979902	999900
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Predictive value of positive result = $TP/(TP+FP) * 100$

Probability of disease if positive test = $95/(95 + 19998) * 100 = 0.473\%$

Predictive value of a positive result = 0.473%
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5. A child is receiving 10g nitrogen per day as amino acids. Urinary urea excretion is 500 mmol/24 hours. Calculate whether he is in positive or negative nitrogen balance. State what assumptions you make (10 marks)

Urea has the formula $CO(NH_2)_2$ so each molecule contain two atoms of nitrogen.
 Each mmol of urea contain 2 mmol of nitrogen
 Atomic weight of nitrogen = 14 so each mmol of urea contains $2 * 14 = 28$ mg nitrogen
 Division by 1000 converts this figure to g nitrogen

Urinary nitrogen excretion (g/24hr) = (Urinary urea excretion (mmol/24h)/1000) * 28

$(500/1000) * 28 = 14g/24 h$

Nitrogen balance (g/24h) = Nitrogen intake (g/24h) – Nitrogen excretion (g/24h)
 $= 10 - 14 = -4g/24h$

Other urinary losses of nitrogen add an additional 20% to nitrogen excretion and nitrogen excretion through other routes is around 2g

Corrected nitrogen excretion = $(14 * 120/100) + 2 = 18.8 g/24hr$

Corrected nitrogen balance = $10 - 18.8 = -8.8g/24h$

Nitrogen balance
-4g/24hr uncorrected
-8.8g/24hr corrected

Module 8

1. Match the following disease states with the most likely biochemical/clinical characteristics
(2 marks each)

- a) Neuroblastoma
- b) Insulinoma
- c) Glucagonoma
- d) Carcinoid Disease
- e) Somatostatinoma

- i. Elevated urine 5-hydroxyindole acetic acid (5HIAA) output and raised plasma chromogranin A in a 65 year old man.
- ii. Abdominal distension and raised urine 3-hydroxy 4 methoxy mandelic acid (HMMA) output in an 18 month old child.
- iii. 61 year old man with a history of headaches and confusion with plasma glucose <2.0 mmol/L.
- iv. 55 year old woman with necrolytic migratory erythema and diabetes mellitus
- v. Fasting blood sugar > 9mmol/L on two occasions with steatorrhea

- a & ii
- b & iii
- c & iv
- d & i
- e & v

2. An 84 year old man with progressive weakness has difficulty in walking. His serum biochemistry results are:

Calcium	1.81 mmol/L	
Phosphate	0.80 mmol/L	
Alkaline Phosphatase	900 IU/ L	(30 –130)
Albumin	40 g/L	
Creatinine	80 μ mol/L	

- a) What's the diagnosis? (4 marks)

Osteomalacia
(Accept hypovitaminosis D)

- b) Give two other biochemical investigations which may help in the management of the patient. (4 marks)

Serum Vitamin D
Malabsorption studies:
Tissue transglutaminase antibodies
Faecal elastase

- c) Why does the patient have difficulty walking? (2 marks)

Proximal myopathy secondary to vitamin D deficiency
(Accept bone pain)

3. A patient on the Intensive Care Unit has the following results:

Serum	Sodium	132	mmol/L
	Potassium	7.2	mmol/L
	Urea	8.4	mmol/L
	Creatinine	95	$\mu\text{mol/L}$
	Calcium	1.12	mmol/L
	Bilirubin	19	$\mu\text{mol/L}$
	Alkaline Phosphatase	20	IU/L
	Alanine aminotransferase	101	IU/L
	Protein	80	g/L
	Albumin	29	g/L

a) Why is the serum potassium raised? (4 marks)

K-EDTA contamination

b) Give other two reasons to support your explanation (4 marks)

**“Hypocalcaemia”
Low serum alkaline phosphatase activity**

c) What would tell the clinician? (2 marks)

Send a fresh sample for analysis

4. Prostate Specific Antigen (PSA) has a physiological half life of 3 days in serum. What serum level would you expect 1 week after radical prostatectomy if the pre op concentration was 12 $\mu\text{g/L}$. (10marks)

$$I = I_0 e^{-kt}$$

where I_0 = PTH conc initially
 I = PTH conc now
 k = decay constant
 t = time

$$I = I_0/2 \text{ at } t_{1/2}$$

$$I_0/2/I_0 = e^{-kt}$$

$$1/2 = e^{-kt}$$

$$\ln 1/2 = -kt$$

$$-0.6931 = -kt$$

$$t_{1/2} = 3 \text{ days}$$

$$0.693/3 = k$$

$$0.231 \text{ days}^{-1} = k$$

PSA concentration at 1 week post op

$$\ln I = \ln I_0 - kt$$

$$\ln I = \ln 12 - (0.231 * 7)$$

$$I = 2.38 \mu\text{g/L}$$

PSA concentration =
2.38 µg/L

5. A HPLC assay of an extract of a catecholamine standard mixture and an extract of an identical volume of a 24 hour urine collection, each containing an equivalent mass of DHBA as internal standard, gave the following detector responses in peak height units:

Standard	Noradrenaline (300 nmol/L)	60
	Adrenaline (50 nmol/L)	25
	DHBA	100
	Dopamine (1500 nmol/L)	150
Urine	Noradrenaline	15
	Adrenaline	39
	DHBA	110
	Dopamine	55

Given that the volume of the urine collection was 1500 mL, calculate the patient's 24h urinary output of noradrenaline, adrenaline and dopamine. (10 marks)

Use the peak height ratio(PHR) method:-

$$\text{a) Peak Height Ratio (PHR)} = \frac{\text{Peak Height urinary Catecholamine}}{\text{Peak Height Internal Standard (DHBA)}}$$

$$\text{b) Concentration of Unknown} = \text{PHR urine} \times \text{Standard Value}$$

PHR standard

$$c) \text{ Urinary Output/24hr} = \frac{\text{PHR urine}}{\text{PHR standard}} \times \text{Standard Value} \times \text{Urine Volume (L)}$$

PHR standard

	Concentration nmol/L	Peak Height Ratios
Standard		
Noradrenaline	300	60/100 = 0.6
Adrenaline	50	25/100 = 0.25
Dopamine	1500	150/100 = 1.50
Urine		
Noradrenaline		15/110 = 0.14
Adrenaline		39/110 = 0.35
Dopamine		55/110 = 0.5

Substituting PHR values, appropriate standard values and the urine volume of 1.5 L into equation the following outputs are obtained:-

Urinary Noradrenaline	105 nmol/24h
Urinary Adrenaline	105 nmol/24h
Urinary Dopamine	750 nmol/24h

24 hr urine output:

Noradrenaline 105 nmol/24h

Adrenaline 105 nmol/24h

Dopamine 750 nmol/24h

Module 9

1. A 16 year old girl with increasing weight and thinning hair has a 3 month history of amenorrhoea. Her serum biochemistry shows:

Prolactin	2,520 mU/L	(25-625)
FSH	<1.0 IU/L	
LH	<2.0 IU/L	
Testosterone	5.7 nmol/L	(0.22 – 2.9)
TSH	0.93 mU/L	(0.27 – 4.2)

- a) Give one explanation for the clinical and biochemical features (5 marks)

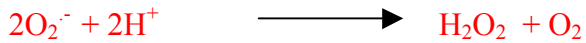
Pregnancy

- b) Give one diagnostic test. (5 marks)

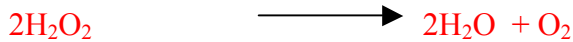
Pregnancy Test

2. a) Give three enzymes that protect against free radical damage and outline the reactions that they catalyse. (3 marks each)

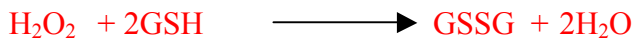
Superoxide Dismutase



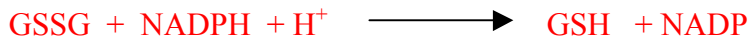
Catalase



Glutathione Peroxidase



Glutathione Reductase



GSH is an important cellular antioxidant

b) Which free radical is formed by the Fenton reaction (1 mark)

Hydroxyl radical

3. A 26 year old obese woman visits her GP with a 5 month history of oligomenorrhoea. The results of the biochemical investigations performed by the GP are:

Prolactin	600	mU/L	(25-625)
FSH	4.8	IU/L	
LH	12.0	IU/L	
Testosterone	3.5	nmol/L	(0.22 – 2.9)
TSH	2.7	mU/L	(0.27 – 4.2)

What is the most likely diagnosis? (2 marks)

Polycystic ovarian syndrome

What are the diagnostic criteria for this disorder? (8 marks)

Rotterdam Criteria (2003) [2 out of 3]

- Oligo-ovulation or anovulation
- Clinical or biochemical signs of hyperandrogenism

- Polycystic ovaries: at least 12 follicular cysts measuring 2-9 mm or increased ovarian volume >10 cm³ or both (TVUS)
After exclusion of other endocrinopathies, e.g. Cushing's syndrome, hypothyroidism, late-onset congenital adrenal hyperplasia

4. A paper on ectopic pregnancy from the USA gives serum progesterone results in $\mu\text{g/L}$. If the conversion factor for progesterone is $\text{nmol/L} \times 0.314 = \text{ng/mL}$. What is a progesterone concentration of $8\mu\text{g/L}$ when expressed in SI units. (10 marks)

$$\mu\text{g/L} \equiv \text{ng/mL}$$

$$\text{ng/mL}/0.314 = \text{nmol/L}$$

$$8/0.314 = 25.5 \text{ nmol/L}$$

Progesterone concentration

25.5 nmol/L

5. A point of care testing analyser with one channel for human chorionic gonadotrophin (hCG) fails on average once in every 100 working days. More tests on different channels are added to the repertoire of the analyser. Assuming the same failure rate for the other channels, what is the probability that all channels will work on any one working day :

- a. on a five channel analyser? (5 marks)
- b. on a ten channel analyser? (5 marks)

The probability that all channels will work on a multi-channel on any one working day is given by the cumulative probability of each. Therefore:-

a) 5 channels = $0.99^5 = 0.95$

b) 10 channels = $0.99^{10} = 0.90$

Probability

On a five channel analyser 0.95

On a ten channel analyser 0.90