



UNIVERSITY OF
BIRMINGHAM

STUDENT BOOKLET

ID No: _____

College of Medical and Dental Sciences

MSc in Clinical Biochemistry

Course Code 5602

Module 1 & 4

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 (0930 – 1200). For each module allow 45 minutes for the essay question and 30 minutes for the short answer questions.

For examiners use only

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

Essay Questions

Module 1

1. Critically evaluate the methods for the measurement of calcium in serum and urine.

OR

2. Discuss the differential diagnosis and investigation of an eight year old child below the third centile for height.

Module 4

1. Discuss human iron homeostasis in health.

OR

2. Discuss with examples the factors that are important in optimising an assay using HPLC.

Short Answer Questions

Module 1

1. 20 day post operatively a patient has a thyroglobulin = 4 µg/L. Immediately pre operatively the thyroglobulin was 100 µg/L. The surgeon rings to ask if he has completely removed the tumour. Assuming a half life for thyroglobulin of 2 days calculate the expected thyroglobulin concentration at 20 days post operatively. **8 marks**

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

I_0 = Initial concentration

I = Concentration at time t

k = elimination rate constant

t = time

To calculate k

$$t_{1/2} = 0.693/k$$

$$k = 0.693/t_{1/2}$$

$$k = 0.693/2$$

$$k = 0.347 \text{ day}^{-1}$$

$$I = 100 * e^{(-0.347 * 20)}$$

$$I = 0.098 \text{ µg/L}$$

Concentration 0.098 µg/L

What advice would you give to the surgeon? State any assumptions that you make. **2 marks**

The measured thyroglobulin concentration is more than the expected concentration indicating that residual thyroid tissue remains. Assumes no interference in the assay from thyroglobulin antibodies

2. A 70kg patient with severe hypomagnesaemia requires 32 mmoles of magnesium intravenously.
What volume of solution containing 0.48g/2mL of anhydrous magnesium sulphate would be needed? (Atomic weights: Mg = 24, S = 32, O = 16, Na = 23, Cl = 35) **5 marks**

32 mmols magnesium are required

The stock solution contains 0.48g/2mL of MgSO_4

Molecular Weight of $\text{MgSO}_4 = 24 + 32 + (4 \times 16) = 120$

Molar concentration of stock solution = $0.48/120 = 0.004 \text{ mol/2mL}$

Volume containing 32 mmol of magnesium = $32/4 \times 2 \text{ mL} = 16 \text{ mL}$

Volume 16 mL

What is the final calculated osmolality if this volume of this magnesium sulphate solution is added to 500mL of 0.9% w/v sodium chloride solution?
5 marks

Final volume of solution = 516 mL

500mL of 0.9% w/v saline contains 4.5g of NaCl = $4.5/(23+35) = 0.0775$ mols

Or 77.5 mmol sodium chloride

16mL of magnesium sulphate contains 32 mmol

Therefore, 516 mL solution contains 32 mmol of magnesium sulphate and 77.5 mmol of sodium chloride.

Concentration of NaCl/L = $(77.5/516)*1000 = 150$ mmol/L

Concentration of MgSO₄ = $(32/516)*1000 = 62.0$ mmol/L

Both compounds dissociate in solution therefore, the osmolality of the solution

$2*(150+62) = 424$ mmol/kg

Osmolality 424 mmol/kg

3. A 33 year old woman with hypertension was investigated by her GP for possible Cushing's syndrome. The woman had normal renal function and was taking anticonvulsants and the combined oral contraceptive pill. The following results were obtained:

Overnight dexamethasone suppression test (1mg dexamethasone at 2300)

Serum cortisol (at 9am following morning) 123nmol/L

24 hour urinary free cortisol (on a different day) 250 nmol/day
(Reference range <350 nmol/day)

Comment on the results

3 marks

Serum cortisol <50 nmol/L at 9am post overnight dexamethasone suppression test usually taken as a normal response. Therefore, serum cortisol of 123 nmol/L does not exclude Cushing's syndrome. However, the 24 hour urinary free cortisol is not consistent with Cushing's syndrome.

Give three possible reasons to explain the result

3 marks

False +ve overnight dexamethasone suppression test could be due to:

- i. increased cortisol binding globulin due to the oral contraceptive pill giving rise to increased serum cortisol.
- ii. increased metabolism of dexamethasone due to induction by the anticonvulsants. Lower concentration of dexamethasone means less suppression of cortisol.
- iii. assay interference
- iv. Patient did not take (or vomited) dexamethasone

False -ve 24 hour urinary free cortisol could be due to:

- v. incomplete urine collection
- vi. assay interference

Give four further laboratory investigations that may help to explain the result

4 marks

Repeat overnight dexamethasone suppression test increasing dose to 2mg

Repeat overnight dexamethasone suppression test but measure either free cortisol or salivary cortisol (surrogate for free cortisol)

9am and midnight salivary (or serum) cortisol

Measure cortisol binding globulin

Measure serum dexamethasone

Investigate assay interference:

- i. Measure using different assay
- ii. Use blocking tubes

4. List five causes of a low serum phosphate

2 marks each

Decreased Absorption

Malnutrition

Alcoholism

Vitamin D deficiency

Phosphate binding antacids

Malabsorption syndrome: short bowel syndrome, tropical sprue, celiac disease, Crohn's disease

Phosphaturia

Hyperparathyroidism

Diuretics

Proximal tubular disorders

Phosphaturic rickets

Redistribution :shift from serum into cells

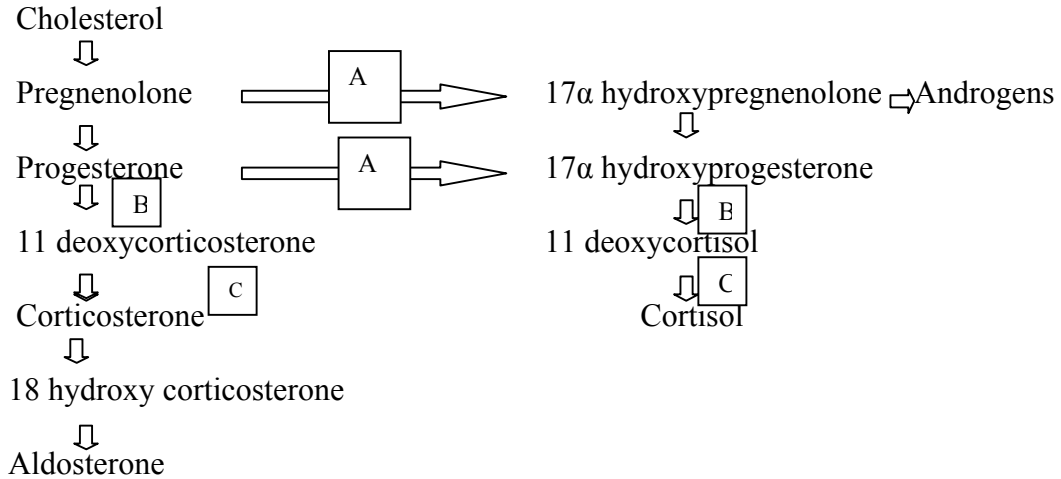
Carbohydrate infusions

Hormone effects (Catecholamines & Insulin)

Respiratory alkalosis (hyperventilation, salicylate poisoning)

Rapid cellular uptake (Refeeding syndrome, Lymphoma, Hungry Bone Syndrome)

5. The pathway for the biosynthesis of adrenal steroid hormones is:



Possible Clinical Presentations

- E. Virilization in females, precocious puberty in males and presentation as a life threatening salt losing state shortly after birth in males.
- F. Hypertension, hypokalaemia, precocious puberty in males and virilization in females.
- G. Hypertension, hypokalaemia with lack of sexual development in girls and pseudohermaphroditism in boys.

Match the enzymes given below with the letters on the pathway and the clinical presentation **6 marks**

- 17 α hydroxylase **A & G**
- 21 hydroxylase **B & E**
- 11 β hydroxylase **C & F**

List four actions of cortisol

4 marks

Increases blood glucose

Fat is broken down to fatty acids

Breakdown of muscle protein to release amino acids

Immunosuppression

Permissive actions

With glucagon and growth hormone breaks down liver glycogen

Required for catecholamines to produce vasoconstriction

Renal clearance of water

Module 4

1. Define the following genetics terms **2 marks each**

a. Heteroplasmy

The presence of a mixture of more than one type of mitochondrial DNA within a cell or individual

b. Expressivity

The degree to which a phenotype is expressed among individuals with the same genotype

c. Heritability

The proportion of phenotypic variance attributable to genetic factors

d. Haplotype

A variant sequence which comprises more than one closely linked base changes that are inherited together

e. Co-dominance

The situation in which a heterozygote shows the phenotypic effects of both alleles fully and equally

2. A 50yr old woman presents with chronic shortness of breath. Initial laboratory investigations are:

Hb	7.3 g/L	(11.5 -16.0)
MCV	125 fl	(80.0-100)
WCC	3.4×10^9	(4 -11)
Platelets	90×10^9	(150-450)
Reticulocytes	2.0%	(0.2-2.0)

Serum:

Folate	7.5 ng/mL	(2.5 -11.9)
Ferritin	150 ng/mL	(15 -300)
Lactate Dehydrogenase	1200 IU/L	(300-650)

a. Her anaemia is due to a dietary deficiency of what compound? **2 marks**

Vitamin B12

b. Where is the precise site of absorption of this compound? **2 marks**

Terminal ileum (do not accept ileum or small bowel)

c. List four causes which may give rise to this deficiency. **4 marks**

Dietary deficiency: Strict Vegans

Gastric disorders: Gastrectomy

Atrophic Gastritis: Pernicious anaemia

Accept Hypochlorhydria (elderly)

Small Bowel disorders: Bacterial overgrowth and tapeworm infestations

Ileal disease: Inflammatory bowel disease (Crohns)

TB ileitis

Ileal Resection

d. Give two non-haematological effects of the deficiency? **2marks**

Peripheral Neuropathy

Subacute combined degeneration of the spinal cord

Cerebral degeneration (accept: dementia)

Optic atrophy

3. A group of 192 blood donors are tested for a polymorphism in the rhabarbin gene. 121 are found to have the RR genotype and 12 the rr genotype.

Calculate:

- a. The expected allele frequencies for the R & r alleles

3 marks

Observed genotypes:

RR	Rr	rr	Total
121	59	12	192

Calculate allele frequencies:

$$R \text{ alleles} = (2 \times 121) + 59 = 301/384 = 0.784$$

$$r \text{ alleles} = (2 \times 12) + 59 = 83/384 = 0.216$$

- b. The expected number of blood donors with each of the two possible phenotypes if “R” is completely dominant over “r”

3 marks

Expected genotypes

$$RR = (0.784)^2 = 0.6147 \times 192 = 118$$

$$Rr = 2 \times 0.784 \times 0.216 = 0.3387 \times 192 = 65$$

$$rr = (0.216)^2 = 0.0467 \times 192 = 9$$

$$\text{Phenotype 1} = RR + Rr = 118 + 65 = 183$$

$$\text{Phenotype 2} = rr = 9$$

Based on these data, comment on the conformity to the Hardy-Weinberg equilibrium.

2 marks

Observed similar to expected. Likely to conform to H-W equilibrium

If a patient population with rhabarbitis shows that 22% are rr homozygotes, comment on these findings compared with those in the population above.

2 marks

22% in patients with rhabarbitis much higher than expected 4.7% in general population (blood donors) with rr genotype. Therefore, rhabarbin is associated with increased risk of rhabarbitis.

4. 4. An HPLC assay for the measurement of plasma phenylalanine uses N-methyl 1-phenylalanine (NMP) as an internal standard. 200 μL NMP has been added to 200 μL aliquots of standard or sample prior to analysis. The following peak areas were obtained:

Sample	Peak area	
	NMP	Phenylalanine
Standard (350 $\mu\text{mol / L}$)	15000	60000
Patient	12000	3000

Calculate the phenylalanine concentration in the patient's sample

10 marks

First calculate the peak area ratio (PAR) of the phenylalanine peak to that of the internal standard (NMP) for the standard and the patient

$$\text{PAR (Standard)} = 60000/15000 = 4$$

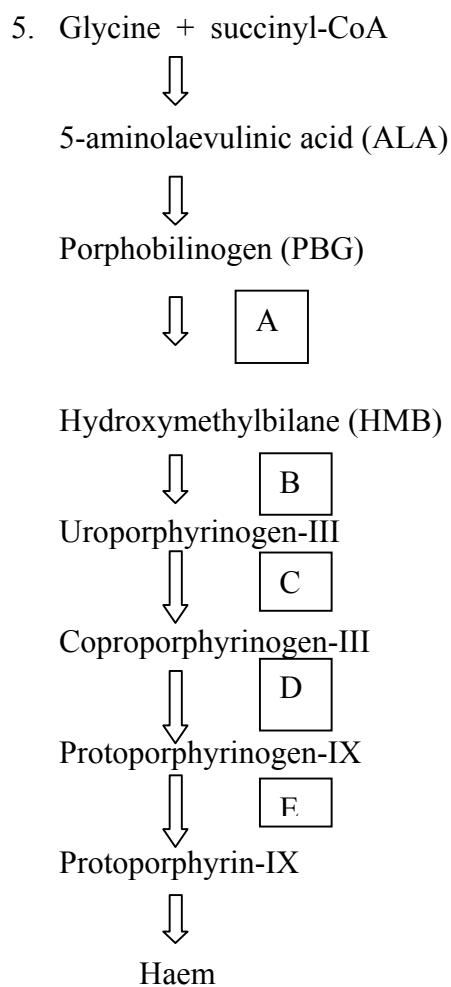
$$\text{PAR (Patient)} = 3000/12000 = 0.25$$

Assuming that PAR is proportional to concentration

$$\text{PAR (standard)/Conc(standard)} = \text{PAR(unknown)/Conc (unknown)}$$

$$\text{Conc (unknown)} = (\text{PAR(unknown)* Standard Conc})/\text{PAR(standard)}$$

$$\text{Conc (unknown)} = (0.25*350)/4 = 21.9 \mu\text{mol / L}$$



For the steps indicated with the letters A to E give the enzyme deficiency and the type of porphyria that this deficiency causes **2 marks each**

- | | | |
|---|--------------------------------|-------------------------------------|
| A | Hydroxymethylbilane synthase | Acute intermittent porphyria |
| B | Uroporphyrinogen III synthase | Congenital erythropoietic porphyria |
| C | Uroporphyrinogen decarboxylase | Porphyria cutanea tarda |
| D | Coproporphyrinogen oxidase | Hereditary coproporphyria |
| E | Protoporphyrinogen oxidase | Variegate porphyria |