The Royal College of Pathologists

MRCPath Part 1 written examination in Clinical Biochemistry

Short Answer Questions

From Autumn 2007, Paper 2 of the Part 1 written examination in Clinical Biochemistry will consist of 20 compulsory Short Answer Questions (SAQs), to be answered in three hours. SAQs are designed to test factual knowledge and understanding across the range of the Curriculum. Each question comprises a stem and six sub-questions. The stem defines the topic of the question and may include a short scenario or vignette. Each sub question is designed to elicit a specific piece of information, or demonstration of understanding of the topic and its context. Unless stated otherwise, the answer required will relate specifically to the material provided in the stem and not to the topic in general.

Points to note:

- SAQs are criterion-marked against an explicit model answer
- Marks are only awarded for information required by the question – no marks are available for additional material
- If a defined number of facts are requested (e.g. State **two** causes of…..), only that number of responses will be marked (e.g. Answer – *correct cause, incorrect cause, correct cause*, will only receive one out of two marks).
- Answers requiring more than single word or phrase responses will be answerable in a single sentence or a small number of sentences.

Examiners will be looking for key concepts in these answers and no marks will awarded for extra information. Candidates should practise writing short, concise answers, which include only the information requested. Good use of English, avoidance of abbreviations, and clear handwriting are, however, essential. Candidates who write unnecessarily long answers are likely to penalise themselves because these answers waste time.

The mark allocation for each sub-question will be stated in brackets in each instance.

Each SAQ paper will undergo a standard setting procedure following which adjusted marks will be aggregated with those from Paper 1, which will comprise four essay questions marked using the College closed marking scheme.

Essay questions

In Autumn 2007, Paper 1 will continue to be a three hour essay paper. The structure of the paper will change slightly in that candidates will be required to write four essays from a choice of six questions set in broad topic areas aligned with the Curriculum.

- Laboratory management competencies
- Analytical techniques and instrumentation
- Analytical methodology
- The chemical pathology of disease – biochemical basis
- The chemical pathology of disease – diagnosis and principles of management
- The chemical pathology basis of metabolic medicine

Example Short Answer Questions with model answers

A 24-year old man with no significant past medical history presents with an episode of mild jaundice. His liver function tests are normal apart from a bilirubin of 45 µmol/L. There is no bilirubinuria. His GP wonders whether this could be due to haemolysis, but you wish to explore an alternative diagnosis of Gilbert's Syndrome

a) Is this patient likely to have likely to have conjugated or unconjugated hyperbilirubinaemia [2]

Unconjugated hyperbilirubinaemia

b) State two routinely available biochemistry tests that are of use in the exclusion of haemolysis [2]

Haptoglobin, LDH

c) What might be seen on blood microscopy indicating increased erythrocyte turnover secondary to haemolysis? [2]

Reticulocytes

d) State two factors that exacerbate the mild hyperbilirubinemia of Gilbert's syndrome [4]

Any two from: *fasting (caloric restriction), intercurrent illness, menstruation, extreme exertion, alcohol*

e) Describe the genetic cause of Gilbert's syndrome [6]

UDP-GAL transferase gene promoter region TATA polymorphism

f) Discuss the diagnostic performance of genetic testing for Gilbert's syndrome [4]

Wild type excludes, but the relatively high prevalence of the abnormal genotype and its incomplete penetrance limits its value in definitive diagnosis and exclusion of other causes

In chronic pancreatitis

a) Destruction of which pancreatic islet cell type causes diabetes mellitus? [2]

Beta cells

b) Are these patients more or less susceptible to insulin-induced hypoglycaemia, and why? [4]

More susceptible because also unable to produce the counter-regulatory hormone, glucagon

c) Name a biomarker that helps to discriminate between chronic pancreatitis and pancreatic carcinoma in patients with a pancreatic mass, if markedly elevated. [2]

CA19-9

d) What other conditions are sometimes associated with increased levels of this biomarker? [4]

Colorectal and other gastrointestinal cancers, breast cancer and benign gastrointestinal disease

e) Name the faecal protein that provides the best discrimintation between chronic pancreatitis and intestinal causes of malabsorption [2]

Elastase

f) List the clinical and nutritional consequences of chronic pancreatitis? [6]

At least three from: *steatorrhoea, iron deficiency, folate and/or vitamin B12 deficiency, osteomalacia (vitamin D deficiency), diabetes, malaise and/or pain, weight loss, diarrhoea, jaundice, vitamin A deficiency*

Measurement of serum creatinine concentration by a spectrophotometric method is the most commonly used test of renal glomerular function, but it suffers from problems of non-specificity, which can partially be overcome by use of a 'kinetic' assay format

a) Name the chromagen used in the Jaffe reaction, and the pH range in which the assay is performed [2]

Alkaline picrate

b) Define the term 'kinetic' [2]

Monitoring of the rate of change of absorbance

c) Explain how the kinetic method overcomes interference [2]

It eliminates interference due to constant background absorbance of reaction mixture

d) Describe an adaptation of the Jaffe assay that is designed to minimise bilirubin interference [4]

Removal of bilirubin with potassium ferricyanide (O'Leary method)

e) Name two mathematical formulae that can be used to estimate glomerular filtration rate (GFR) on the basis of serum creatinine concentration [4]

MDRD, Cockcroft – Gault

f) Discuss the limitations of these methods for estimating GFR [6]

Assumes typical skeletal muscle mass. Not validated in acute renal failure, amputees, pregnancy and malnutrition and limited validation in diabetes. Less valid at extremes of muscle mass. Creatinine method-dependence, including non-specificity and calibration issues. Slight effect of dietary intake.

World Health Organisation guidelines for the diagnosis of diabetes (as adopted in the UK) recommend an oral glucose tolerance test if fasting plasma glucose concentration is in the range 6.1 - 6.9 mmol/L.

a) What is the diagnostic term applied to patients with fasting plasma glucose concentration in this range? [2]

Impaired Fasting Glycaemia (Glucose)

b) Why is an oral glucose tolerance test necessary in this group? [2]

As some will have frank Diabetes Mellitus or Impaired Glucose Tolerance

c) State the dose and composition of the glucose load used in the oral glucose tolerance test, indicating how it should be administered and the timing of the blood samples [4]

75g anhydrous glucose in 250-300mL water over 5 minutes. Blood samples at baseline and two hours.

d) What are the consequences of this state for risk of macrovascular disease and of microvascular disease? [4]

Increased risk of macrovascular but not microvascular disease

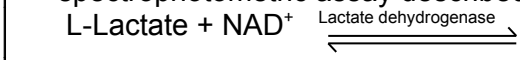
e) What advice should be given regarding the management and follow-up of patients who fall in this category? [4]

Lose weight if overweight (exercise and weight-reducing diet). Repeat test after an interval (e.g 1 year)

f) Comment on the value of HbA1c as a diagnostic test for diabetes in this group. [4]

Low diagnostic sensitivity

Plasma lactate concentration is usually measured by a spectrophotometric assay described by the following formula:



The formation of NADH is monitored, and this is usually configured as an 'end point' assay.

a) At what wavelength is the reaction monitored, and why? [4]

340nm. Absorbance maximum of NADH, which is produced in proportion to the amount of lactate present

b) Which direction must the equilibrium lie in if the assay is to measure lactate concentration? [2]

Right

c) State three ways in which the reaction conditions could be adjusted to ensure that the reaction is optimised to ensure that this is the case [6]

High pH, excess NAD and trap (remove) pyruvate

d) What two factors could you change to enable the reaction to proceed more rapidly? [4]

Temperature, LDH concentration

e) What would constitute a 'reagent blank' for this assay? [2]

Substitute saline or water for sample

f) Why is blanking necessary? [2]

To correct for background absorbance of reagents