Past Papers (Non-medical Candidates)

This file contains 6 laboratory scenarios which have been presented to candidates for the Part 2 MRCPath oral examination in Clinical Biochemistry. Candidates are given half an hour to prepare their answers to this laboratory scenario and a management case.

After each case, the notes for the examiners have been provided by the examiner who set the question. These are not intended to be exhaustive but provide some background for the case. More importantly, they provide some insight for candidates into what the examiners are looking for.

Note that the examiners may provide results to be interpreted and expect candidates to be reasonably proactive in suggesting additional tests that may be necessary.

Note also that examiners are more interested in candidates showing a logical progression from the diagnosis of the problem to the management of it than a list of causes, whether the problem is clinical interpretation, sorting out an EQA problem or a laboratory error.

In most scenarios, some issues need attention before others. Failure to recognise the importance of those that immediately affect patient management as the first matter requiring attention will count against candidates as the examiners are looking for evidence of safe practice.

Note that some cases are incomplete and in the ideal scenario, with candidates who are on top of the problem, the discussion should end up as a dialogue with the examiners who may also be looking for help with a difficult problem!

In preparing for this part of the examination, there is no substitute for regular discussion about laboratory issues with senior consultant staff and, if possible, trying to arrange “mock” oral examinations with senior colleagues.

T.A. Gray
Chairman of the Panel of Examiners in Clinical Biochemistry
January 2005

Question 1

‘What action would you take when you discover that, due to a mechanical failure on a large automated analyser involving specimen sequencing, 100 sets of general clinical biochemistry results have been reported against the incorrect patient identities?’

The results had left the laboratory 36 hours previously and were from patients on medical and surgical wards, and patients seen in outpatients, renal clinics and by general practitioners.

Question 1: Notes for Examiners

The suggested action might be along the following lines:

1. Inform all staff receiving requests for results over the phone, of the extent of the problem, including the specimen accession numbers involved, and instruct them to explain that these results are being rechecked. Where urgent clarification is need recommend specimen recollection.
2. Identify correct results either by reanalysis or, where possible, reliable correction of mismatched specimen and patient identity.
3. For each patient, compare correct with erroneous results, any previous results and the source of the request.
4. Based on this information, 'triage' reports into those requiring immediate action because of patient status and the magnitude or significance of the discrepancy. (eg. preop/post op, time taken for report to reach user, such as computer report or hard copy).
5. Attempt to contact medical staff and nursing staff concerned for high priority patients identified above.
6. Amend computer database (both Lab and Hospital) with correct results. There is an issue of transparency here so that accusations of a 'cover up' cannot be laid.
7. Issue amended hard copy reports with an explanatory comment regarding previous erroneous results.
8. Investigate and document the circumstances of the incident following the local policy for 'Incident reporting'.
9. In addition to reviewing the mechanical failure and taking steps to prevent a repetition, investigate how procedures for analytical validation and clinical credibility failed to identify the error earlier.

Question 2

After many years of using a traditional wet chemistry analyser to provide the bulk of your analyses, you are about to replace this with a modern discretionary analyser. The old analyser required very frequent calibration; the manufacturers claim that each assay which is run on the new analyser will only require calibration at intervals of 3 to 6 months.

Outline the internal quality control system you think appropriate to maintain the quality of analyses on the new analyser.

Question 2: Notes for Examiners

Every candidate should know that classical internal QC techniques are designed to detect unacceptably large changes in bias caused by calibration or reagent changes. In essence, such techniques rely on deciding whether a QC signal (usually the result given by a QC sample) lies within or outside a pre-set limit, which is usually a line drawn on a 'QC chart' (at for example 3 SD away from the mean), often refined by further rules such as those proposed by Westgard. The response to a result lying outside the limit is to re-calibrate and possibly to change the reagents.

Every candidate should realise that the QC problems with modern analysers are different. They are not about sudden stepwise changes in bias. They are about very slow changes in bias with time (drift), about periods of deteriorating precision associated with less than optimal analyser performance, and about occasional fliers. Candidates should realise that classical QC techniques are inappropriate to these problems.

A more appropriate QC system must include:

1. Checking whether bias is acceptable after calibration (eg. by comparison of QC results or patient sample results before and after calibration).

2. Monitoring very small bias changes over time, to decide the point at which re-calibration is necessary.

A good candidate should point out that it is difficult to detect fliers, and this can usually only be done by comparing results with previous results on that patient (delta checks) or by comparing results with clinical information and/or with that is credible. The appropriate response is of course to repeat the analysis.

An extremely good candidate may mention the problem of periods of increased imprecision. There are several ways to look at this – the number of patient results falling outside the reference range is often a good guide. The appropriate response to worsening imprecision is to check instrument maintenance; and if necessary call the manufacturers in.

It may also be possible to push a good candidate into a discussion of what constitutes acceptable performance, both for bias (particularly for hormone analyses) and for imprecision (should be based on biological variation). Classical QC tends to be directed towards technical achievability, not biochemical desirability.

Question 3

You are telephoned at home at 11.45 pm by a House Officer in the Accident and Emergency Department, who would like an urgent blood ethanol measured on a 17 year old boy. He has been involved in a road traffic accident, and the House Officer explains that the boy's parents are anxious to know the result.

What do you do?

Question 3: Notes for Examiners

This is a difficult real-life problem, and there are three distinct issues.

1. Medical
   In my view, the only medical justification for measuring ethanol in this case would be if the patient had an altered state of consciousness, which could be related to ethanol or could be related to a head injury. Knowledge of the ethanol concentration could therefore affect subsequent medical assessment and treatment. If so, this is a justified demand which could well be urgent. Without an altered state of consciousness, there is no justification for measuring ethanol for medical reasons in this case.

2. Legal

   I think there are two main legal issues.

   a. Confidentiality
      1. The Victoria Gillick case established that even children of 15 have the right to medical confidentiality. The House Officer must be told that any results, particularly an ethanol result, should only be given to the parents if the patient agrees. Where there is reason to believe that a crime has been committed, the police may obtain authorisation to see medical records or seize samples – authorisation may be given by for example a Coroner, a Judge, etc.

   b. Assault
      A blood sample which is potentially to be used for non-medical purposes can only be taken from a patient if the patient agrees (or if unconsciousness, his next of kin or other representative). I am unsure to what extent the parents of a minor can give consent if the minor himself disagrees.

3. Ethical

   This is particularly difficult.

   I personally believe that we should neither help nor hinder the police. However, where there is reason to believe that a crime may have been committed, then there is a public duty to ensure that as far as possible any relevant evidence is retained. In this case, there are three main scenarios.

   a. The patient is the driver of a motor vehicle. Potentially, a sample for blood ethanol measurement could be instrumental in showing if he had driven while over the statutory limit.

   b. The patient is a pedestrian who was hit by a motor vehicle. The sample could then be important evidence in a charge of dangerous driving by the driver of the vehicle.

   c. The patient was a passenger in a motor vehicle. In this case, his blood ethanol is likely to be irrelevant to any crime which may have been committed.

   My own feeling is that if (a) or (b) apply, one should make an effort to obtain an appropriate sample for blood ethanol measurement (although probably not to measure it). However, to stay within the law, consent for this sample must be obtained from the patient or his representative. It will be necessary to point out that in the event of a crime, the result could help the prosecution or help the defence.

Question 4

You are contacted by a GP who wants to discuss the creatinine result on a full biochemical profile on a 53 year old lady, and would like advice on further tests.

Na	141	mmol/L	Alkaline phosphatase	148	U/L (RR<150)
K	3.9	mmol/L	Total Protein	69	g/L
Urea	6.8	mmol/L	Albumin	39	g/L
Creatinine	250	umol/L	Bilirubin	7	umol/L
Calcium	2.20	mmol/L	AST	27	U/L (RR<50)
Phosphate	0.69	mmol/L			

The clinical details given at the time were “Routine screen”. You note a previous creatinine one month ago was 213 umol/L and that haematinics taken at that time were normal. In his introduction the GP reveals that the lady had non-specific malaise with vague back and loin pain but had no previous medical problems and had rarely bothered the surgery. One month ago a haemoglobin of 9.7 g/dL with normochronic normocytic picture and ESR of 62 mm/h had prompted the haematinic request and three faecal occult bloods were normal.

What information do you require from the GP and what further tests would you undertake on this sample or suggest in the future?

Question 4: Notes for Examiners

This is a real case from last year. The lady obviously had some nephropathy but the absence of a raised urea in the face of quite abnormal creatinine was very odd. The first things I checked with the GP were that they had checked her BP and urinalysis – ie. was this diabetic or hypertensive nephropathy. Her BP was normal and he thought urinalysis was negative.

I then asked about drugs, concerned about a drug induced nephritis – she was using an NSAID (I forget which) but not regularly. However I would want to try and draw out the association of NSAID with nephritis and raised creatinine.

I was concerned at the time about some fliers on our creatinine method (Vitros dry slide) and sent it for analysis a different way (Olympus – Jaffe). It came back identical.

I think it would be reasonable to suggest asking for a urine protein and MSU in view of her symptoms in order to eliminate chronic nephritis but we never got to that stage as we got the diagnosis on the sample we had.

I was then left with endogenous causes of nephropathy of which there are 3 easily eliminated ones – myoglobin (no muscle symptoms except the vague back pain which could have been renal), uric acid (but urea is usually elevated and no joint pains) and myeloma proteins. I asked for a CK, forgot about uric acid, and despite the normal protein requested an electrophoresis.

Electrophoresis showed a strong band which typed as free kappa light chains only with immune paresis. This explains the lack of dipstick proteinuria and normal globulins. The normal calcium was a good prognostic point (but the only one – her low urea was actually a bad sign as it indicated massive anabolic activity and aggressive low grade disease). Had we got round to measuring urine protein she had grams of pure Bence Jones protein in her urine when worked up elsewhere by the haematologists.

This lady has an aggressive Bence Jones myeloma. She has had marrow ablation and a transplant but has a very poor prognosis of less than 5 years survival.

Question 5

You have received a letter from NEQAS pointing out your poor performance in your plasma urate assay. The letter states that your results have been very variable, with major biases being seen either side of your method mean on different samples. Some recent NEQAS returns are included in the following table.

Return Number	Method Mean	Your Result
101	105	133
102	257	265
103	98	129
104	555	434
105	200	211
106	425	357

Can you think of some possible explanations for these differences and explain how you would investigate further?

Question 5: Notes for Examiners

From the NEQAS data it could be supposed that there may be a calibration problem, with either the method group or your particular assay. It appears for high results your laboratory is reporting results that are too low, and for low results your laboratory is reporting results that are too high. At concentrations of urate of approximately 240-260 umol/L your laboratory agrees with the consensus mean.

Possible actions:

- Establish whether the correct results had been sent in.
- Establish whether the laboratory has been put into the correct method group.
- Establish from the NEQAS return whether the method mean is different to the other reported method means.
- Check your internal QC charts to check the precision, to see the amount of acceptable variation you may expect for a serum urate assay (CV's ~ 1-3%), ie. can the results be explained by analytical variation. Do the charts show any variation over the measuring range for urate?
- Establish whether your laboratory performs the assay as per protocol, or whether you use different calibrators, single-, multi-point, force-, do not force through zero.
- The outcomes of these questions could lead you to think whether your laboratory is "right" or "wrong". It would be wrong to presume that the method mean is actually the correct answer. Further action could range from doing some simple experiments to contacting the company and NEQAS to discuss the problem.
- Simple experiments could include "spiking" a sample with a known concentration of urate (the candidates should think about how they would spike a sample with a high concentration of urate), double diluting serum/control with saline (once again what effects could this have, eg. matrix problems).
- Time and money permitting you could check your method against an authenticated standard, or get your friendly expert to measure some sample by isotope dilution MS.

You never know sometimes you can be right and they can be wrong!

Question 6

How would you assess a Laboratory’s performance?

Question 6: Notes for Examiners

Candidates should be able to come up with a range of answers, those sticking just to QC and EQA should be encouraged to think wider.

EQA performance
- Analytical
- Clinical Comments

CPA

Error rates - Types of error (is it even measured?)
- Clerical
- Analytical
- Clinical Authorisation

Good risk management with follow up of mistakes and near-misses

Turnaround times

Clinical Audit participation

How many calls to the duty biochemist are made per day
(Personal opinion is that if high indicates good use of Lab expertise, but open to argument)

Laboratory initiated and collaborative research
- Publications
- Research funding

Teaching
- Biomedical Scientists
- Clinical Scientists
- Junior medical staff/medical students (if teaching hospital)

Feedback from users (CPA are particularly interested in this)

Others?