Examples of New Style Paper 1 Questions

Background
In both the October and November 2019 editions of the Biomedical Scientist, and also on the IBMS website there has been information about a major review of the Higher Specialist Diploma examination that the Institute’s Education and Professional Standards Committee (E&PSC) has undertaken. This as part of its responsibility for ensuring that its qualifications are fit for purpose and meet the needs of both its members and the wider profession.

The HSD review group was led by the IBMS Deputy Chief Executive and included the IBMS Executive Head of Education, the IBMS Head of Examinations, representatives from each of the HSD disciplines and a representative of the E&PSC. As part of this work the review group recommended changes to the nature of Paper 1 to ensure that the questions were more appropriate for an M-level qualification and that they enabled candidates to demonstrate their ability to operate at a senior level.

It has been agreed that from the 2020 exam series onwards that for each discipline Paper 1 will consist of four (rather than ten) mandatory questions to be answered in an hour. These questions will have a focus on problem-solving, operational scenarios, analysis of results or quality control issues.

The following are examples of the new style questions and the indicative answers developed by the examiners for these questions. It must be stressed that the examiners would expect answers to be written in full sentences (rather than the bullet point that have been put forward in some of the indicative answers) and would accept other relevant points beyond those that are shown here.

It should also be noted that these are only examples and that the scenarios, quality control issues or analysis of results presented in the exams may differ from those shown in these examples. They do however provide a good indication of the type of questions that may arise in the exam.
Cellular Pathology

A pathologist asks you to investigate the possible presence of Hepatitis B in a liver biopsy. Explain your approach, which tests would you use and why? Outline some of the potential findings.

The answer ought to indicate that a standard set of liver special stains would usually include an orcein. Orcein would demonstrate copper associate protein, linked to Hep B – but that this is not specific. This might also be investigated using IHC for Hep B surface antigen or Hep B core antigen. The answer ought to describe how Hep B is indicated in orcein and the IHC staining patterns see in surface and core antigen positivity.

When embedding you note that some of the tissues are quite fragile and fragment under mild pressure. What will you do in this situation?

The first priority is to ensure that the processed tissue is preserved as much as possible. Ensure any other embedding staff are aware of this issue to minimise tissue damage, also ensure any microtomists are aware that tissue may be brittle when sectioning. The blocks may need to be trimmed / faced / rough cut more gently than usual and may need time on wet ice to soften before cutting.

The cause of this must be investigated, the instrument / reagents involved should be identified. Where multiple processors are used, if block tracking is in place, it should be possible to identify whether an individual instrument is involved.

Investigations such as when the instrument was last changed, noting reagent batch numbers, any fault warnings, power fail events etc. should all be reviewed. If more than one instrument is involved, note any similarities.

Note if there is any consistency in the type / size of tissues involved – are these small biopsies that have been placed on a “large” processing programme? The underlying reason for the over processing should be identified, and measures put in place to prevent a repeat occurrence.
Clinical Chemistry

A student asks you what is the difference between ionised and total calcium and how they are measured, how would you answer this question?

Mention of Reference range difference: (adults): 2.20–2.60 mmol/L (total, adjusted), 1.15–1.34 mmol/L (ionized). Other points to include:
Explanation of the different forms of calcium - ionized calcium, calcium bound to other minerals (anions), and calcium bound to proteins like albumin, which includes:
1. Ionized calcium, also known as free calcium, is the most active form.
2. A total calcium test usually checks the total amount of calcium (free and bound combined)
3. Mention of ‘adjusted [calcium]’ and the frequently used formula: adjusted [calcium] = (measured [calcium] + 0.02(40 – [albumin]))

Measurement methods include:
Total - Colourimetric methods: either o-cresolphthalein (Alkaline conditions 570-580 nm) or arsenazo III (acid conditions 650 nm). Atomic absorption spectrophotometry (although accurate and precise, this method is not suited to automation and is rarely used)
Ionised - Indirect potentiometry using a calcium-selective electrode. NB need for arterial samples.

Exceptional answers would mention that adjusted formulae are unreliable with [albumin] <25 g/L, with abnormal concentrations of globulins (which also bind calcium), jaundice, high [free fatty acids] or abnormal blood [H+]. They may also include mention of Ionized calcium levels importance if there are abnormal levels of proteins, such as albumin, or immunoglobins and that changes in plasma [albumin] and any mention of when Ionized calcium is relevant such as kidney disease, certain kinds of cancers, or problems with your parathyroid gland. Patients who are critically ill and on intravenous (IV) fluids, receiving blood transfusions and after major surgery

Following the release of results from a patient which are significantly different to those seen 24 hours previously you decide to provide a tutorial to assist in spotting erroneous results.
What information could you give in a tutorial?

Answer should include:
Describe the process of technical validation and clinical validation
The use of ‘delta checking’
Discussion of analytes which don’t change which can be key indicators of mismatch (Creatinine etc)
Highlight analytes susceptible to contamination and suggest causes eg Drip contamination - Raised glucose, Sodium and Chloride, decreased protein, albumin and other analytes due to dilution.
Collection tube contamination
EDTA – abnormal Potassium, Calcium, Mg and ALP explaining why and how they are affected.
Fluoride Oxalate – NA, K Calcium, Mg and ALP (How and why)
Etc.
Haematology
A laboratory wants to introduce a method for measuring plasma fibrinogen levels. They want to know what tests are available, which they should use and why and how to establish the assay. What advice would you give?

2. Speed, cost, use On-Call, sensitivity, ease-of-use, automation etc.
3. Guidelines
4. Comparison Clauss methods and derived-fibrinogen
5. Sample collection and pre-test variables
6. How to set up the Assay: buffers, thrombin, machine carry-over, end-point detection, Validation/verification. Use of stored calibration curves, temporal drift, dilution ranges and reflex-testing
7. Standardisation: reference preparations, standards and controls. QA/QC.
8. Sensitivity and specificity
9. Reference ranges and disease states – low-end of normal
10. Limitations and costs
11. Conclusions/recommendations

A blood sample arrives in the lab, from a patient with a clinical and travel history suggesting malaria infection.

Rapid diagnostic test result: Control line visible, *P. falciparum* line detectable, but faint suggesting low positive, pan-*Plasmodium* line – no visible line.

Microscopy of fixed, stained thin blood film: no malaria parasites observed.

How would you proceed to investigate this case?

(Candidates are not expected to provide all the points stated below in the 15 minutes that they would have to answer this question in the exam. The indicative answer below provides a detailed explanation of all the areas that answers may be covered)

Consider other infectious diseases due to travel history. If travelling to Africa consider VHF.

Competency of individual performing RDT – have they been deemed competent?

2nd individual to repeat test to confirm result. If result remains the same:

a. If one off then consider false positive and causes
b. Discussion of advantages and disadvantages of RDTs as outlined below and include HRPII vs pLDH

Recognized disadvantages of RDTs are:

(i) occasional false positives occur
(ii) they are less sensitive than reference microscopy
(iii) persisting histidine-rich protein 2 (HRP2) anti-genaemia can give a positive test when no viable parasites are present
(iv) except in the case of *P. falciparum* or *P. vivax* infection, the species cannot be determined
(v) quantification is not possible
(vi) operator misunderstanding or misinterpretation of test line patterns may lead to apparent discrepancy between RDT and blood film results
(vii) rarely, a prozone effect may occur with HRP2 based RDTs.

Candidate should mention if this is a persisting issue and what they would consider:
c. **Batch acceptance**
   - Performance of batch accepted
   - Storage of RDTs correct
   - Expiry date

d. **NEQAS performance**
   Review previous returns – any issues highlighted, any outwith consensus, false positives, false negatives, if so at what level parasitaemia

e. **Selection of RDT**
   Know about the WHO Malaria Rapid Diagnostic Test Performance: Results of WHO product testing of malaria RDTs:
   - Specificity and sensitivity and test limitations
   - Are they aware of the different types of RDT and their target antigens (HRPII, pLDH and Aldolase) and what species they detect
   - Be able to name a HRPII test and a pLDH test
   - Detection of *P. knowlesi*

   Also consider very low parasite levels (barely detectable in RDT) and scanty parasites not found in thin film. Would also like to see if they have liaised with Infectious Disease team if ‘no parasites observed’ and be aware that if there is a high clinical suspicion then treatment should be started.

f. **Retesting interval** (repeat 12-24 hrs later)

g. **Referral to LSHTM for PCR if microscope remains as no parasites detected**

h. **Thin films:**
   - pH of stain – choose pH7.2 and extended staining time
   - Inverted slide is helpful as prevents Giemsa precipitate so easier to identify parasites
   - Extended viewing if high clinical suspicion of malaria determining species present and further tests. If species *P. vivax* or *P. ovale* knowledge of needing a G6PD prior to primaquine treatment for hypnozoites due to risk of haemolysis
   - Remember to review the film using x10 to exclude other parasites such as microfilaria and trypanosomiasis remember to review pH6.8 for other abnormalities. Potential to miss other significant morphology if concentrating on excluding malaria

i. **Thick films**
   - More helpful to identify parasites at low levels
   - Needs very skilled reviewer
   - Consider stain – Field’s vs. Giemsa
   - Quality of smear
   - Able to read print through it
   - No pavement cracks
   - Size is big enough to view 200 fields minimum
Leadership and Management

You are called into the laboratory because two staff are having a loud and heated argument including name calling. One staff member says they will take out a grievance against the other for bullying and harassment. Explain what your immediate actions would be and how you manage this situation going forwards.

- The immediate action that would be taken to calm the situation down, separate the staff and ensure that other staff are put at their ease and then seek advice from HR.
- Locate and read the Trust / organisation policy on bullying and harassment (or local equivalent policy document)
- Speak to staff members involved
- Consider working arrangements i.e. rotas, shifts, weekends
- May need to consider suspension depending on reasons for angst between them
- Work with HR to find investigating manager
- Inform your superior / line manager - in case it goes to hearing

Heavy rain has caused a leaking roof to collapse above Pathology and rainwater is running through the ceiling. Staff have placed large containers to catch the water, but the flow is fast, and the containers soon fill up.

Describe how you would manage this situation and explain the rationale for your decisions.

- Make area safe
- Assess for electric points - risk and hazard assess
- Inform Estates and Facilities
- Inform senior manager in Pathology or in organisation if appropriate
- Assess damage to estate and / or analysers / kit
- Assess whether relocation of work is required
- Manual handling issues whilst using temporary large containers
- Check future weather report
- Complete an incident report
Medical Microbiology

Your departmental H&S Lead asks you to conduct a mock ‘spill’ exercise in the category 3 laboratory. Explain why this is required, how you would undertake the task and how you would audit the actions of the staff working in that area.

Spillage drills in the CL3 environment are integral to the CL3 Code of Practice. Each member of staff who works in CL3 must be able to demonstrate the correct evacuation procedure in the event of a spill. This can be achieved through written learning and observation of known evacuation skills. Biannual drills are usually scheduled as part of the laboratory quality management system.

Only the H&S Lead and the chosen individual should be aware of when the event will take place to make as realistic as possible. The candidate should be able to describe how the drill is initiated using a simulated sample (usually water). The sample could be either dropped in the CL3 lab or spilt inside the safety cabinet. They should then describe the audit actions which would include observation of the following:

- Clear warning to other staff in the room instructing an immediate evacuation
- Staff ceased tasks as quickly and as safely practicable before proceeding to evacuate
- Staff evacuated the CL3 room in a calm orderly manner by the nearest safe route
- Staff removed PPE (where practicable before leaving the CL3 suite)
- Staff avoided moving through the area of spillage unnecessarily
- Access to the CL3 suite bared by locking door
- Biological incident sign erected
- Appropriate staff member(s) informed as per SOP
- CL3 evacuation and response checklist completed

There should be an immediate debrief with the team. Any non-conformities, lessons learnt and positive findings should be documented and tracked through the laboratory quality management system. All findings should be reviewed at departmental H&S meeting.

Your laboratory is considering changing to low fill volume MRSA plates. Describe the processes required to ensure the necessary validation and verification standards are meet.

A change control request should be completed and submitted to the laboratory Clinical Governance group or equivalent departmental review panel. The change request should described the reason for change, the associated risk for remaining ‘as-in’, give consideration of any new risks related to the change, outline the validation and verification plan, lists training requirements and provide references to support the change.

The candidate should be aware that low fill volume plates (15mls instead of 25mls) are generally only for used for culture requiring 18-24hrs incubation. Longer culture would dry out the media making it unsuitable for bacterial detection.

The candidate should be able to describe the specifics of the media validation process. There must be a comparison with existing methods using patient samples, a selection of known strains of MRSA and EQA samples to determine the sensitivity and specificity of the new media. Higher scores would be awarded to candidates who demonstrate knowledge of creating inoculum variance when assessing the media with the known strains, how to calculate positive/negative predicative values and the use of P value to determine any statistical difference between the methods.
Transfusion Science
You serologically crossmatch 4 units of red cells by IAT for a 46-year-old male patient undergoing major abdominal surgery. The patient has a previous anti-E. You selected E negative red cells. Theatres retrieve all 4 units urgently (before the compatibility testing is complete). Upon completion of your crossmatch you discover 1 of the units has a positive reaction (2+).

Describe the steps you would take and explain the possible causes for the positive reaction.

- Contact theatres to recall the unit or stop the transfusion if possible
- Inform Haem Consultant
- Repeat the XM - there could be carry over/contamination
- Check the unit group is compatible
- Check the unit is E negative
- Check the patient for antibody history/panel results
- Check the results from the most recent antibody panel and screen, is there more than 1 antibody present, put a panel up (IAT and enzyme) if not already performed.
- DAT the unit
- Check that the consumables are all within their expiration date and in good condition
- Serologically crossmatch (4) more units until your investigations are complete
- Explain that there might be an unidentified antibody present leading to a delay in the blood
- Issue the compatible units as a concessionary release until you have identified the problem

Your blood group analyser has held two results back for authorisation. Interpret the results below and explain why the reactions might have occurred.

<table>
<thead>
<tr>
<th>Anti-A</th>
<th>Anti-B</th>
<th>Anti-D (VI-)</th>
<th>Control</th>
<th>A₁ Red Cells</th>
<th>B Red Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>MF</td>
<td>0</td>
<td>4+</td>
<td>0</td>
<td>0</td>
<td>4+</td>
</tr>
</tbody>
</table>

- Mixed-field reactions are most commonly seen following a transfusion of ABO compatible, but not ABO identical blood, such as group O into a group A individual.
- Mixed field in A well - could be a subgroup of A e.g.: A3 phenotype will appear as a mixed-field reaction with anti-A and anti-A, B
- Certain antigens are weakened during disease states. This is true of the A antigen in leukaemia, but it would be unusual to see a strong anti-B in the plasma.
- Mixed-field reactions will also be seen for some time after an ABO mis-matched bone marrow transplant.

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- These results cannot be validated as the control well is 4+.
- This could indicate a patient with strong cold antibodies (cold agglutinin disease) which has affected every well
- This could be a damaged blood group card
- The reagents should be checked to see if they are fit for purpose, expired, temperature controlled
- The analyser may have an error and may have pipetted incorrectly
- Check the patient history they may have started on monoclonal therapy
Virology
A student on placement in your laboratory asks you “Can you explain how antivirals work?”. Using a named example, provide an answer to this question.

The chosen example should be clearly stated with a rationale for the choice. Discussion of biological reasons why it is harder to find effective and clinically useful antivirals than antimicrobials (lack of selective toxicity). Outline of the virology of the virus groups the drug works on.

Explanation (involving diagrams) of how the drug interacts with the viral processes and inhibits replication. Side effects of the drug (and reasons for them – e.g. drugs which target fast replicating cells also toxic to developing blood cells in bone marrow)

Discussion of extent of resistance to chosen drug and if relevant possible measures to minimise development of resistance

Explain what you would include in an information leaflet outlining the introduction of a screening programme for Hepatitis C virus in prisoners. This should include what prison governors and staff (prison officers, medical officers, support workers) and prisoners need to know and how they should work with the laboratory team.

Leaflet should be succinct with key details only (e.g. no background virology). It should outline sample collection and which specimen containers to use. Initial screen would probably be using a point of care saliva test, but then any positives would have to be followed up with blood tests in the main lab. Give expected turnaround times and what the format of the result will be. Provide contact details of the laboratory for queries about samples and the medical team for clinical questions.