Feedback of the FRCPath Part 1 examinations in Genetics, Clinical Cytogenetics and Molecular Genetics 2017.

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There were a total of 24 candidates who sat the Part 1 FRCPath written papers for genetics which were held on 21st March 2017. As for the last 2 years, there were three papers; 8 candidates sat the Clinical Cytogenetics examination, 13 sat the Molecular Genetics examination and 3 sat the combined Genetics examination. The pass rates were 50%, 69% and 100% respectively. The examination consisted of two papers; Paper 1 (am) essay questions and Paper 2 (pm) short answer questions.

Scientists planning to sit FRCPath Part 1 examinations in the future are reminded that Spring 2017 was the final sitting of the Clinical Cytogenetics and Molecular Genetics papers. From Autumn 2017 onwards, all candidates will sit the Combined Genetics examination.

Paper 1: The essay paper was shared across all examinations and required answers to 4 out of the 5 questions set.

Question 1: Define mosaicism and use four clinical examples to illustrate four different genetic mechanisms by which mosaicism can arise. Show, in each example, how the detection of mosaicism impacts on diagnosis and management and describe the choice and limitations of the test repertoire to detect mosaicism in the diagnostics laboratory.
Emerging technologies are likely to increase the prevalence of detected mosaicism. Comment on the challenges that this is likely to bring.

This question was answered by all 8 candidates sitting the cytogenetics exam, 8/13 candidates sitting the molecular genetics exam and all 3 candidates sitting the combined genetics exam.
Candidates were expected to describe four clinical examples with clear reference to the clinical significance of mosaicism and the limitations of the tests employed. In addition, candidates were expected to demonstrate an understanding of the likely impact of NGS in the detection of mosaicism. There was a spread of quality of answers, with some candidates failing to provide four clear examples and/or discuss the implications of NGS for mosaicism detection. This question was generally answered less well than the other questions.

Question 2: Classification of variant pathogenicity is a critical aspect of genetics laboratory services. Briefly summarise the current processes for classifying variants. Discuss how you think this will change over the next 5 years. Why is there a need for change and what will the benefits be?

This question was answered by all candidates across all exams.
Variant classification processes are very topical in the UK and worldwide. Candidates were expected to provide a clear summary of current processes followed by a discussion of the need for change and what changes may happen over the next 5 years. The examiners were looking for the discussion to include standardisation, bioinformatic tools and data sharing, as

well as other relevant points. Again, there was a range in the quality of answers, with poorer answers generally only including a limited discussion about future changes. Several candidates spent too long summarising current processes which the question asked to be "briefly" summarised.

Question 3: You have been asked by your local neurologists to give a presentation on current diagnostic genetic testing for neurological disorders and what will impact on service provision over the next 5 years. Include current and future testing options, including the techniques, their advantages and disadvantages.

This question was answered by 4/8 candidates sitting the cytogenetics exam, 11/13 candidates sitting the molecular genetics exam and 2/3 candidates sitting the combined genetics exam.
As a minimum, the examiners were expecting answers to include:

- A summary of current testing to include a wide range of mendelian disorders, and current testing methodologies to include at least array CGH and sequencing.
- Impact on service provision over the next 5 years including at least technological developments such as WES and WGS.
- Discussion of the advantages & disadvantages of current testing options compared with future testing options.

Question 3 was generally well answered with very few candidates failing this question. The best answers also included discussion of susceptibility genes/factors, as well as the impact of bioinformatic developments and increased knowledge of disease pathogenesis on service provision.

Question 4: Discuss the role of stratified medicine in chronic myeloid leukaemia (CML) and lung cancer and compare the relative merits of rapid targeted versus panel based tests.

This question was answered by 6/8 candidates sitting the cytogenetics exam, 7/13 candidates sitting the molecular genetics exam and 2/3 candidates sitting the combined genetics exam.
Candidates were expected to include types of genetic changes and their relevance in both tumour types. The examiners were looking foranswers with a clear rationale around stratification and panels vs rapid targeted tests.
For CML, candidates were expected to cover imatinib and one other TKI in CML, and to provide an overview of the use of cytogenetics and RT-qPCR for monitoring in CML, ideally also including resistance mutations.
For lung cancer, candidates were expected to cover the genes in which the main driver mutations are found, as well as resistance and sensitising mutations, different treatments, and the use of ctDNA.
This question was generally satisfactorily answered, but some candidates lost marks for omitting key examples outlined above and/or for not including a clear discussion of the merits of rapid targeted vs panel tests for each cancer type.

Question 5: Analysis of cell-free DNA from blood is widely used to provide genetic information in pregnancies due to the presence of fetal DNA (cffDNA) and in cancer patients due to the presence of circulating tumour DNA (ctDNA). For both cffDNA and ctDNA, describe the scientific basis of the available tests and compare the advantages and disadvantages with non cell-free DNA methods.

This question was answered by 6/8 candidates sitting the cytogenetics exam, all 13 candidates sitting the molecular genetics exam and 2/3 candidates sitting the combined genetics exam.

The examiners were looking for answers to include:

- A description of the clinical, scientific and technical basis of a range of tests, in the context of clinical examples for both cffDNA and ctDNA (i.e. both descriptions of the techniques and explanations of how they are used to answer specific clinical questions).
- A discussion of the advantages and disadvantages of cffDNA and ctDNA testing.

Some candidates answered this question very well whereas others answered poorly. Good answers included a wide range of examples and a clear discussion of advantages/disadvantages. Poor answers contained insufficient detail and/or inaccurate material.

Paper 2: The Short Answer Questions (SAQ) paper consisted of 20 questions containing a stem question and 6 sub-questions worth a total of 20 marks. Ten SAQs were common across the three examinations.

Most candidates provided an answer for all questions; however, candidates are reminded that on average each question should take no longer than 9 minutes to complete. For the majority of questions there was a wide variation in marks across the candidates from poor answers to very good answers. In general, the unsuccessful candidates scored significantly lower on the SAQ paper than their peers.