General Comments

We have noted made up DOBs in some reports. This is poor practice as DOB is used as a patient identifier. Perhaps in some labs this is a mandatory field in the patient database and therefore a fake DOB has been entered. It was on oversight on our part to send out the cases this time with a patient age rather than DOB given, and we will avoid this in the future.

HGVS: We have documented all labs not including full and/or correct HGVS nomenclature, and noted anything that does not include a mutation and matching ref seq. This may be pedantic when a nucleotide sequence clearly indicates a protein amino acid sequence. In some other EQA schemes in molecular genetics, laboratories would be penalised for less than full and correct HGVS. Pragmatically, everyone understands C282Y and H63D. Some clinicians don't like HGVS nomenclature, but this is not a reason to shy away from including it.

Scenario 1

This is a predictive referral of a mother whose husband is a C282Y homozygote to assess any risk of haemochromatosis for the couple's children. The question asked relates to the risk to the children, and that must be answered.

The other consideration is there is an incidental finding of a possible small risk to the patient of iron overload, based on her genotype, and this should be commented upon.

Any children of the patient and her C282Y-homozygous husband will be compound heterozygotes for HFE C282Y and H63D: this genotype is associated with type 1 haemochromatosis. These children, once they are over 16 should be advised to seek a consultation and may be offered confirmatory genetic testing. Children below 16 are not at risk and genetic testing and monitoring is not advised. Monitoring of adult compound heterozygote's iron status by testing serum ferritin and fasting transferrin saturation at 3 year intervals should be advised.

Some reports seemed to overplay the risk of HH for the H63D homozygote, and the emphasis in these reports was for the risk to Maria. Some of these reports read more like a diagnostic referral rather than focusing on the question in hand which was to clarify the risk to offspring.

Scenario 2

The patient is a C282Y and H63D as compound heterozygote. This genotype is associated with increased risk for type 1 haemochromatosis. However, the risk of developing haemochromatosis in patients with this genotype is quite low, particularly in women.

The patient has abnormal biochemical iron indices. However the current normal tfsat suggests that the patient may not be iron overloaded, and that the raised serum ferritin may be due to something else. Not all reports recognised this.

The combination of a low penetrance genotype and an incidental borderline tfsat (which might be after a high iron meal for example) could create a smokescreen that means the real problem is missed.

A repeat test of fasting transferrin saturation should be suggested as it might further reduce the suspicion of iron overload. Investigation of other possible causes of the elevated ferritin and ALT should be advised.

Notwithstanding any of the above, the patient still has a risk of developing haemochromatosis and monitoring of iron status by testing ferritin and fasting transferrin saturation at 3 year intervals should be advised.

The patient should also be informed that genetic testing for first-degree relatives is available, and in this regard the report should state that testing of children under 16 is not advised.