LETTER

Diagnosis of Hb-pathies

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I would like to praise the *EJHG* and the authors Villard and Fontes¹ for the concise and practical updating on X-linked alpha thalassaemia/mental retardation syndrome.

I would also like to place an additional remark on the paragraph 'Diagnosis'. The authors state correctly that the X-linked alpha thalassaemia phenotype in affected males can be detected by haemoglobin electrophoresis or by the presence of HbH inclusion bodies in peripheral blood smears.

However, only the $--/\alpha$ (HbH disease) and $--/--$ (Hb-Bart's Hydrops Foetalis) genotypes result in an abnormal electrophoresis which is otherwise normal in alpha thalassaemia. Hence, one may expect in X-linked alpha thalassaemia females, but depending on the lack of α expression also in males, that the HbH fraction could be below detection level on electrophoresis or could have disappeared because of the typical instability of this non-functional tetramer.

The same can happen looking at the HbH inclusion bodies in the peripheral blood. Moreover, this test is working well in skilled hands but may easily produce false

positive or false negative interpretations in most (inexperienced) labs.

Probably because of the concise character of their publication the authors did not mention the parameters that may give the most reliable diagnostic indications, which are: (1) The simple observation of the haematological indices (thalassaemic patients are microcytic and hypochromic without iron deficiency); and (2) The measurement of the β/α expression rate at the mRNA or at the protein level (globine chains synthesis), which is always unbalanced in thalassaemias, globin gene related or not.

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Reference

- 1 Villard L, Fontes M: Diagnosis of Hb-pathies. *Eur J Hum Genet* 2002; 10: 223–225.