LETTERS TO THE EDITOR

Monozygotic twins with 22q11 deletion and discordant phenotypes

I was interested to read the report of Goodship *et al* (J Med Genet 1995;32:746-8) of monozygotic (MZ) twins with a 22q11 deletion who were discordant for cardiac defects. I have recently met a similar family where all the affected members have had a 22q11 deletion detected by FISH.

Twin 1 has a typical facial appearance of the velocardiofacial syndrome (figure) with nasal speech but no cardiac defect detectable clinically or on ECG. Twin 2 required a pharyngoplasty for nasopharyngeal insufficiency and had surgery for an ASD during childhood. She has a very similar facies and both had mild learning difficulties during childhood.

Facial appearance of twin 1.

Twin 1 has a daughter with mild learning difficulties and similar appearance with a normal heart (on clinical and ECG examination) but twin 2 had an affected daughter who died following surgery for Fallot's tetralogy with absent pulmonary valve and hemitruncus. In addition, this child's heart showed severe pulmonary regurgitation and peripheral pulmonary artery stenosis and the left pulmonary artery took its origin from a branch of the aorta. Twin 2 has subsequently had another child with a 22q11 deletion but a normal heart on echocardiography.

DNA studies using six microsatellite polymorphisms on six different chromosomes gives a probability of greater than 99% that the twins are monozygous.

Thus this family supports the observation of Goodship *et al* that cardiac defects can be discordant in MZ twins with 22q11 deletions

and indicates that the intrauterine environment or the twinning process itself may have played a role in the development of a cardiac defect.

This family is also of interest in that both twins have triphalangeal thumbs and twin 1 was also born with postaxial polydactyly. These digital defects also appear to have arisen as a new dominant mutation. Twin 1's child with the 22q11 deletion also has abnormal thumbs which have accessory ossicles visible radiologically. However twin 2's living child has clinically normal thumbs but a 22q11 deletion so the digital anomaly does not appear to be segregating with the deletion.

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CTG repeat length in muscle from patients affected with myotonic dystrophy (DM)

We read with interest the publication of Martorell *et al*¹ "Comparison of CTG repeat length expansion and clinical progression of myotonic dystrophy over a five year period", which appeared in the August issue of this journal. These authors found that the CTG expansion length in peripheral blood cells of DM patients (with varying clinical severity of symptoms and various sizes of repeat amplification) increased over a time span of five years.

They compare their data with a similar follow up study comparing CTG expansion sizes in muscle² in which the authors observed no progression in the size of the CTG length in repeated muscle biopsies from three adult DM patients. According to Martorell *et al*,¹ one possible explanation for this finding would be a negative selection in muscle above a maximum size limit. In this case continued CTG expansions would be seen only in relatively young DM patients.

We have compared the size of the CTG expansion in muscle and lymphocytes in 19 DM patients of different ages (including three children) and varying clinical severity and our data support such a hypothesis.

In accordance with previous publications^{2,3} we have found that the size of the expansion was always greater in muscle than in blood, with no correlation in adults with age at onset or severity of the phenotype.⁴ However, surprisingly, the smallest difference between the size of the expansion in muscle and the size of the expansion in lymphocytes was observed in the affected children (two with congenital DM and in one 11 year old patient with onset in early childhood). In these three young patients, this difference ranged from 2.1 kb to 4.2 kb while in adult patients it ranged from 5.3 kb to 9.0 kb. A significant correlation ($r^2 = 0.64$, $p < 0.05$) was found between patients' age and the difference in the expansion between muscle and lymphocytes.

In summary, although we have not analysed repeated biopsies from the same person (owing to the difficulty of obtaining such samples), we would like to point out that our data suggest that the size of the CTG repeat in muscle increases with age in young DM affected patients, apparently reaching a plateau in adulthood. Moreover, in young DM cases, it seems that the progression in the size

of the CTG expansion in muscle may be greater than that observed in peripheral blood. It would be interesting to observe if this finding is confirmed in other studies.

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- 2 Anvret M, Grandell U, Ahlberg G, *et al*. Larger expansions of the CTG repeat in muscle than in lymphocytes from patients with myotonic dystrophy. *Hum Molec Genet* 1993;2:1397-400.
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- 4 Zatz M, Passos-Bueno MR, Cerqueira A, *et al*. Analysis of the CTG repeat in skeletal muscle of young and adult myotonic dystrophy patients: when does the expansion occur? *Hum Molec Genet* 1995;4:401-6.

Selection for presymptomatic testing for Huntington's disease: who decides?

With the transfer of presymptomatic testing for Huntington's disease from research to clinical service, the conflict between making judgements about the candidate's eligibility to receive a test result and the non-directive ethos of clinical genetics has been felt by many of us. Evidence for adherence to eligibility criteria, rather than reliance on self-selection among at risk subjects, is apparent in published reports. In a survey of all centres offering presymptomatic testing in the United States,¹ the majority of the centres (18 out of 26) had postponed or denied testing at least once. Reasons for this included "inappropriate requests" for testing (eg, to confirm a diagnosis of possible HD), as well as decisions based on personal or situational factors affecting the individual that indicate that more caution should be exercised².

The practice of withholding testing from applicants is clearly at odds with the psychotherapeutic model of genetic counselling, as discussed by Sharpe²: "the geneticist must explicitly acknowledge that at all times decision making remains under the control of the patient; that the geneticist must act in accordance with a patient's decisions irrespective of how the geneticist may perceive their rationality or competence". It also contradicts the notion of providing information in response to the counsellee's specific questions: an applicant for predictive testing who is suspected to be symptomatic may want to know whether (s)he carries the gene for HD, rather than whether (s)he is currently affected.

There are clearly occasions when the clinician's concern to "do no harm" is perceived

* It is unclear whether these requests came from clinicians or individual people.