and there is little evidence of somatic mosaicism. The authors account for the drastically reduced mRNA levels of the X25 gene in FRDA patients by proposing that the intronic GAA expansion interferes with RNA processing or transcription. These results are important for a number of reasons. Firstly, the triplet repeats will provide a direct means for the diagnosis and prenatal testing of the majority of FRDA families. Secondly, they show for the first time that triplet repeat expansion is a mutational mechanism that can lead to a recessive condition, that GAA triplets as opposed to CCG, CAG, or CTG triplets can be involved, and that the expansion can have an intronic location. Thirdly, they suggest that the phenomenon of anticipation need not invariably be associated with triplet repeat mutations. It will also be possible to consider whether repeat length is correlated with age of onset or the expression of the less common FRDA complications and whether alterations of the FRDA gene and its protein product frataxin might have a wider role in the aetiology of heart disease or diabetes.

JOHN C K BARBER

Prenatal screening for cystic fibrosis: 5 years' experience reviewed

Brock DJH, *Lancet* 1995;347:148-50.

Professor Brock reviews his five years' experience of offering cystic fibrosis (CF) testing to couples who present to the antenatal clinic. Two models of testing were used, either a two stage process, where the mother was tested first and testing only offered to her partner if she was shown to be a carrier, or a couple procedure where both partners were

tested simultaneously. A total of 25 000 couples were screened over the five year period. Uptake was similar in both models at about 70%. Twenty two couples were identified with both partners detected as being carriers; 20 of these opted for prenatal diagnosis and termination of eight affected fetuses was carried out. No information is available as to whether any affected babies were born whose parents were not detected as being at risk, either through the technical limitations of screening for selected mutations, or through late presentation in pregnancy, or through a decision not to participate in the programme. Professor Brock concludes from the results that couple testing has proved the better option for prenatal screening for CF. Although in the two stage model testing can be offered to relatives of all those women identified as carriers, in practice the uptake of this has been low. The couple testing method reduces the number of counselling sessions needed and raises anxiety only in those couples with a 25% risk of an affected fetus. The study has shown consistent high levels of take up of screening with both models, even when research has moved to service provision, and confirms the interest of the population in genetic testing when directly related to their own reproduction.

ANGELA BARNICOAT

Non-Mendelian transmission in dentatorubral-pallidoluysian atrophy and Machado-Joseph disease: the mutant allele is preferentially transmitted in male meiosis

Ikeuchi T, Igarashi S, Takiyama Y, *et al. Am J Hum Genet* 1996;58:730-3.

Over the last 10 years geneticists have come to terms with several patterns of inheritance

which do not follow a simple mendelian pattern. In this report, from Niigata University in Japan, the authors report a skewed form of autosomal dominant inheritance with preferential transmission of the mutant allele in male meiosis. Two CAG triplet repeat disorders, dentatorubral-pallidoluysian atrophy (DRPLA) and Machado-Joseph disease (MJD), have been studied. As expected, there was an inverse correlation of age at onset with the length of the expanded CAG trinucleotide repeats, and the intergenerational instability of the length of the CAG repeat was more prominent in paternal transmissions (these factors appear to explain clinical evidence of anticipation). The segregation patterns were studied in 211 transmissions in 24 DRPLA pedigrees, and 80 transmissions in seven MJD pedigrees. Significant distortions in favour of transmission of the mutant allele were found in male meiosis, where the mutant alleles were transmitted to 62% of offspring in DRPLA, and 73% in MJD (both reaching statistical significance). The authors suggest that the results are consistent with meiotic drive in DRPLA and MJD in male meiosis, and since more prominent meiotic instability of the length of the CAG repeat is observed in male meiosis as well, the authors postulate that a common molecular mechanism may underlie both phenomena. Studies of this kind may be subject to ascertainment bias, but from a practical point of view, if these findings are confirmed elsewhere, clinicians may have to increase the risk quoted to offspring of inheriting DRPLA or MJD if the affected parent is the father. A prior risk of greater than 50% of inheriting an autosomal dominant disease is likely to have a significant impact on genetic counselling.

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