

DNA Testing for Fragile X Syndrome in 255 Males from Special Schools in Singapore

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Abstract

Introduction: Fragile X syndrome, the most common cause of inherited mental retardation, results from unstable expansion of a trinucleotide (CGG)_n repeat in the FMRI gene. Phenotypic expression is variable making clinical diagnosis difficult, while diagnosis by Southern blotting is relatively expensive and labour intensive. The prevalence in Singapore has not been studied. **Materials and Methods:** We developed a rapid screening test using a PCR analysis. We studied 255 males with unexplained cause for learning difficulties from 8 special schools. A clinical scoring system based on characteristic features described was devised. **Results:** PCR analysis showed absence of the band for the normal allele in 11 samples, 6 of which were confirmed by Southern blotting to be positive for FMRI expansion, giving a 2% false-positive rate with PCR. Sensitivity of the PCR test was evaluated by performing Southern blotting in all PCR-normal samples; all of which were confirmed to be normal. This PCR test was shown to be highly reproducible. Clinical criteria were not predictive. **Conclusions:** Six (2.4%) new cases of fragile X syndrome were detected. There is a need to incorporate fragile X testing in routine screening of patients with developmental delay and learning difficulties. The use of PCR could eliminate the need for Southern blotting in up to 95% of cases. PCR analysis provides a simple, reliable and rapid tool for screening.

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