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Title: Fragile X Syndrome: The Place of Molecular Diagnosis and Screening Within an Integrated Service Approach

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Reference: (AÉTMIS 2001-1 RF). Montréal: AÉTMIS, 2001, xxvii-191 p.

Aim:

1) To review the current state of knowledge with regard to the molecular analysis for the diagnosis and carrier identification of the fragile X syndrome.
2) To assess the utility, feasibility, and acceptability of implementing various diagnostic/screening strategies for this syndrome in the Quebec healthcare system.

Results and Conclusions:

- The molecular analysis of the FMR1 gene constitutes a substantial gain over earlier cytogenetic analyses since it clearly establishes the diagnosis in symptomatic individuals and identifies individuals at risk of transmitting the syndrome. It therefore provides an important contribution to genetic counseling, despite residual gaps in current knowledge.
- The reference method for the molecular analysis consists of the Southern blot, followed, if needed, by PCR. None of the alternative approaches has been rigorously and systematically compared with the reference method.
- The analysis of the regional context highlights several shortcomings in the provision of services to affected individuals and their families with respect to diagnosis and management. Consequently, no proactive population screening strategy can be recommended at this time. Such strategies also raise ethical issues and scientific problems which need to be resolved.

Recommendations:

- Molecular tests should be available for: 1) molecular diagnosis of fragile X syndrome in symptomatic individuals, 2) cascade screening of an affected individual's relatives, 3) confirmation of carrier status in a pregnant woman with a family history of signs associated with the syndrome, and 4) prenatal diagnosis if the mother carries a mutation.
- Necessary medical, social, and educational resources should be available to meet the needs of families with fragile X syndrome in a timely and appropriate fashion. Partners in the health, social service, and educational sectors should reinforce intersectorial collaboration to improve the early identification and diagnostic workup of children with signs consistent with fragile X syndrome and the coordination and continuity of available services.

Methods:

Systematic review of published scientific literature; review of administrative and research data regarding regional service provision; consultation with key informants and experts.

Further research required:

Research should be pursued to develop and validate genetic tests better suited to wide-scale use and to further document the epidemiology of the syndrome, the phenotype–genotype correlation, and the psychosocial impact of genetic counseling. Pilot projects need to evaluate any high- or low-risk-population diagnostic/screening strategy that might be considered for implementation.

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