Primary prevention of Down’s syndrome

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Abstract:

Background: Antenatal screening has the capacity to detect more than 90% of Down’s syndrome pregnancies leading to therapeutic abortion. Successes in recent years with such so-called ‘secondary’ prevention have not been matched with progress in primary prevention. Despite considerable research over many decades the principle cause of the disorder is unknown.

Methods: This paper considers three potential primary prevention strategies, (1) avoiding reproduction at advanced maternal age, (2) pre-implantation genetic diagnosis for couples who are at high risk of Down’s syndrome, and (3) folic acid supplementation. The principle aetiological hypotheses are also reviewed. Interpretation: A strategy of completing the family before a maternal age of 30 could more than halve the birth prevalence of this disorder. Women with a high a priori risk should have access to pre-implantation genetic diagnosis, which can lead to a reasonably high pregnancy rate with an extremely low risk of a Down’s syndrome. The evidence suggesting an aetiological role for defective folate and methyl metabolism is not sufficient to justify an active preventative strategy of folic acid supplementation without performing a large clinical trial. Current supplementation policies designed to prevent neural tube defects may incidentally prevent Down’s syndrome, provided a sufficiently high dose of folic acid is used. Further progress in primary prevention is hampered by limited aetiological knowledge and there is an urgent need to refocus research in that direction.

Key Word:
Primary prevention, maternal age, pre-implantation diagnosis, folic acid, aetiology