Genetic testing in cardiovascular disease

To the Editor: We read with interest the review by Gray and colleagues on genetic testing in cardiovascular disease, in particular familial hypercholesterolaemia.[1] As they highlight, familial hypercholesterolaemia is common and when undetected and untreated, leads to premature coronary artery disease (CAD). There are more than 100 000 individuals with familial hypercholesterolaemia in Australia, with 20 000 of them children under 16 years, with an additional three children born with familial hypercholesterolaemia every day.[2] Similar to other countries, more than 95% of children with familial hypercholesterolaemia across Australia are currently undiagnosed, and on a trajectory to develop premature CAD.[3]

Unfortunately, Gray and colleagues failed to draw attention to the crucial fact that familial hypercholesterolaemia is a treatable paediatric disorder and that by detecting and treating familial hypercholesterolaemia from childhood, CAD is preventable and individuals can expect a normal life expectancy.[4] National paediatric familial hypercholesterolaemia guidelines have been published and include guidance on the diagnosis and management of familial hypercholesterolaemia in children.[2] A phenotypic diagnosis of probable familial hypercholesterolaemia is made with one of the following:

- a low-density lipoprotein (LDL) cholesterol level higher than 5 mmol/L in the absence of a parental history of hypercholesterolaemia or premature CAD;
- a LDL-cholesterol level of 4–5 mmol/L with parental history of hypercholesterolaemia or premature CAD; or
- a LDL-cholesterol level higher than 3.5 mmol/L with a parent with a pathogenic gene variant.

Genetic testing should be offered to confirm the diagnosis in children with probable familial hypercholesterolaemia.

Currently, the diagnosis of familial hypercholesterolaemia in childhood usually follows cascade screening after detection of a parent with familial hypercholesterolaemia. However, several opportunities to detect familial hypercholesterolaemia in childhood have been proposed, including child–parent screening at the time of an immunisation.[5] Universal screening of children and genomic newborn screening, combined with reverse cascade screening of parents, have great potential for improving outcomes of both children and adults with familial hypercholesterolaemia.

Once the diagnosis of familial hypercholesterolaemia has been made in a child, the management is relatively straightforward, with education on a healthy lifestyle and the initiation of lipid lowering therapy by the age of 8 to 10 years in heterozygous familial hypercholesterolaemia, to achieve an LDL-cholesterol level less than 3.5 mmol/L (95th percentile) or a 40–50% reduction. Treatment in homozygous familial hypercholesterolaemia should ideally be started by the age of 2 to 5 years.

"Prevention is better than cure". It is time that we redefine familial hypercholesterolaemia as a treatable paediatric disorder, transforming the perspectives of our adult colleagues so that together we can change the natural history of this condition from childhood, thus avoiding the development of CAD and improving cardiovascular outcomes at a national level.

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