HUMAN GENETICS SOCIETY OF AUSTRALASIA:

TESTS, TREATMENTS AND PROCEDURES HEALTH PROFESSIONALS AND CONSUMERS SHOULD QUESTION.

The Human Genetics Society of Australasia was formed in 1977 to provide a forum for the various disciplines collected under the title of Human Genetics. The HGSA is a full member of the International Federation of Human Genetics Societies and domestically we work closely with the Royal Australasian College of Physicians and Royal College of Pathologists of Australasia as well as other groups through the Pathology Associations Council.

1. Don't use brain magnetic resonance imagery (MRI) for routine surveillance of asymptomatic neurofibromatosis type 1

Neurofibromatosis type I (NF-1) is a tumour disorder caused by the mutation of a gene on chromosome 17 that is responsible for control of cell division. It causes tumours along the nervous system that can grow anywhere in the body. Routine screening investigations are not recommended for the detection of the majority of complications associated with the condition. Baseline brain and spine MRI, and routine imaging of the chest and abdomen to identify asymptomatic tumours, do not influence management and should not be undertaken.

Supporting Evidence

- Ferner RE, Huson SM, Thomas N, et al. Guidelines for the diagnosis and management of individuals with neurofibromatosis 1. Journal of Medical Genetics 2007;44:81-8.

2. Don't undertake sequential testing for heterogeneous genetic disorders when targeted next generation sequencing (NGS) is available.

A heterogeneous genetic disorder is one where the same disease or condition can be caused, or contributed to, by a number of different genes. The traditional strategy for genetic testing involves sequential sequencing of individual genes, selected according to the patient's clinical presentation and family history. By contrast, next generation sequencing (NGS) involves the sequencing of millions of small fragments of DNA at the same time. Reductions in the cost of NGS now make it a more attractive solution for clinical diagnostic testing to identify the disease-causing mutation(s) in patients with genetically heterogeneous disorders than traditional sequential testing. In particular, the targeted NGS approach which restricts analysis to genes known to be implicated in a particular phenotype has been also successfully applied to heterogeneous disorders such as inherited peripheral neuropathy (IP).

Supporting Evidence

- Antoniadi T, Buxton C, Dennis G, et al. Application of targeted multi-gene panel testing for the diagnosis of inherited peripheral neuropathy provides a high diagnostic yield with unexpected phenotype-genotype variability. BMC Medical Genetics 2015;16:84.
- Ellard S, Lindsay H, Camm N, et al. Practice guidelines for targeted next generation sequencing analysis and interpretation. Association for Clinical Genetic Science, 2014.

3. Don't undertake genetic testing for methylenetetrahydrofolate reductase (MTHFR), apolipoprotein E (APOE) and other such tests where the clinical utility for diagnostic purposes is extremely low.

While genetic testing can help indicate susceptibility to particular genetic conditions, there are some conditions where the presence of particular alleles is neither necessary nor sufficient to cause the condition or where the alleles have a higher prevalence in the general population than the condition itself. This is the case for instance with apolipoprotein E as a genetic marker for Alzheimer's disease and methylenetetrahydrofolate as a marker for venous thromboembolism.

Supporting Evidence

- Goldman JS, Hahn SE, Catania JW, et al. Genetic counseling and testing for Alzheimer disease: joint practice guidelines of the American College of Medical Genetics and the National Society of Genetic Counselors. Genetics in Medicine 2011;13(6): 597-605.
- Hickey SE, Curry CJ, Toriello HV. ACMG Practice Guideline: lack of evidence for MTHFR polymorphism testing. Genetics in Medicine 2013;15(2):153-6.

4. Don't undertake carrier state testing for rare recessive disorders where a partner has a family history, the couple is non-consanguineous and there are no common causative mutations.

With a rare recessive disorder, although the individual with the family history will have an increased risk of being a carrier, their unrelated partner will have a low general population risk. Therefore, their a priori combined risk of having a child with this rare recessive condition will generally be less than 1%. If the gene has no known common disease causative mutations then testing the unrelated partner for carrier status has low sensitivity and specificity.

Supporting evidence

- Meikle PJ, Hopwood JJ, Clague AE, Carey WF. Prevalence of lysosomal storage disorders. JAMA 1999;281(3):249-54.

5. Don't undertake genetic testing when clinical diagnostic criteria exist and there are no reproductive or predictive testing implications.

Like other screening or diagnostic tests, genetic tests do not have inherent utility. It is the adoption of therapeutic or preventive interventions that influences health outcomes. If clinical diagnostic criteria already exist for the condition in question and there are no reproductive or other predictive testing implications as a result of definitively identifying a genetic cause for the condition, then this renders genetic testing unnecessary.

Supporting evidence

- Ferner RE, Huson SM, Thomas N, et al. Guidelines for the diagnosis and management of individuals with neurofibromatosis 1. Journal of Medical Genetics 2007;44:81-88.

How was this list created?

A preliminary list was developed by the Lead Fellow which was then distributed to all the clinical geneticists in Australia who are all members of the Australasian Association of Clinical Geneticists (AACG), a special interest group of the HGSA. Following feedback the topic was revisited at a meeting of this group during the annual scientific conference of the HGSA, after which the list was finalised.