1. **Don’t use NIPT as a diagnostic test**

Non-invasive prenatal testing (NIPT) is a method of non-invasive fetal DNA testing done through a maternal blood sample. NIPT testing for common aneuploidies, microdeletions and sex chromosome disorders is clinically available to patients in Canada. NIPT is a highly sensitive and specific screening test, but is not diagnostic. The chance of a positive result being correct is related to the prior risk of a disorder. As aneuploidies and microdeletions are rare amongst the general population, the positive predictive value is not near a diagnostic level. Even in high-risk populations, there are many reasons for a false positive result. Genetic counseling, along with confirmatory testing via amniocentesis or chorionic villus sampling, should be done prior to using the result to impact management of a pregnancy.


2. **Don’t recommend or make medical decisions based on results of direct to consumer genetic testing (DTC-GT) without a clear understanding of the limitations and validity of the test.**

Three types of potentially medically-relevant DTC-GT are available: (1) assessment of risk for common multifactorial diseases (e.g. diabetes, etc), (2) targeted mutation analysis for single gene disorders and
(3) sequencing. Some DTC-GT companies state that they do not guarantee the accuracy or reliability of their tests. Many of the significant genetic risk and protective factors for multifactorial conditions have not been identified. This leads to greatly divergent risk interpretations between companies, even when performed on the same individual\textsuperscript{3,4}. For targeted mutation analysis and sequencing, the specific test may not include all clinically relevant genes or mutations; resulting in false reassurance. Genetic changes which are only weakly associated with disease may be reported, leading to anxiety or inappropriate additional testing. When making medical decisions based on results of genetic testing, the test should meet the recommendations made by the CCMG in 2012. Not all DTC-GT meet these recommendations.

References:


3) I Had My DNA Picture Taken, With Varying Results, NY times, Dec 2013


3. Don’t order a chromosome analysis by karyotype for children with developmental delay of unknown etiology.

Karyotype has a much lower detection rate (3-4\%) compared to microarray (15-20\%) in children presenting with developmental delay. Karyotype remains important in limited clinical situations, where a specific numerical or structural chromosomal syndrome, such as Down syndrome, is suspected.

However, for children with intellectual disability/developmental delay without a recognizable syndrome, microarray is more cost efficient and considered the first-line test. Microarray is also considered a first-line test in other clinical scenarios such as multiple congenital anomalies and autism spectrum disorder.

References:

1) Moeschler JB, Shevell M; Committee on Genetics. Comprehensive evaluation of the child


4. Don’t order whole exome sequencing prior to genetic counseling

Whole exome sequencing (WES) is a powerful test for individuals suspected of having an underlying genetic diagnosis. However, WES increases the likelihood of unexpected findings, which may or may not be clinically significant. Further, due to methodological limitations, WES may not always be the correct test to order as WES will not detect all genetic causes of disease (for example, it will not detect chromosomal structural differences). Both informative and uninformative results can lead to complex patient and family psychosocial repercussions, and could impair future insurability. Genetic counseling facilitates informed decision making. Given complexity of results, WES should only be ordered after counselling by a qualified healthcare provider.

References:


5. Don't order carrier testing in children.

Carrier testing is primarily useful in the reproductive period to determine the risk of an individual having a child affected by the condition for which testing is being considered (Arbour 2003). Knowing that a child is a carrier of a single gene condition usually does not alter their medical care in the pediatric years. The result of carrier testing for X-linked or autosomal recessive conditions typically does not impact health care management of the carrier since most carriers are unaffected. Thus, in most situations, there is not a medical indication for carrier testing in a child. Undertaking carrier testing of a child violates the right of the child to make their own decision about testing and could potentially impair future insurability. An exception could be made for testing in a mature adolescent, after appropriate counselling, to allow them to consider their reproductive choices.


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