Genetics and Paediatric Health: Section 7

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À l'écoute de notre santé

7.1.1 Genetic Testing and Screening – The Growth in Genetic Testing

There are currently genetic tests for more than 3,500 conditions.

New discoveries are being made at a very rapid rate.

Image credit: Shutterstock. Data from the National Institutes of Health. Genetic Testing Registry. http://www.ncbi.nlm.nih.gov/gtr/ 2012.

The demand for new genetic tests and genetic services is growing exponentially, largely because they are more readily available and affordable than ever before. In addition, genetic testing can now be used for both rare and common conditions.[1] Requests for genetic tests and related services are increasing for chronic conditions, such as cardiovascular diseases, developmental delay, dysmorphic features, neurological disorders (e.g., neonatal seizures), and eye diseases (e.g., retinoblastoma).

In 2012, the Canadian Institutes of Health Research and Genome Canada announced a $65 million program to support research projects in the fields of genomics and personalized medicine. This could result in the development of new genetic tests for Canadians.[2]

Which health professionals are ordering genetic tests is also changing. Once exclusively the job of medical geneticists, now family doctors, oncologists, neurologists, cardiologists, haematologists, ophthalmologists, microbiologists, and pathologists frequently order genetic tests.[1]

[1] McMaster Health Forum. Evidence Brief: Coordinating the Use of Genetic Tests and Related Services in British Columbia. Hamilton, Canada: McMaster Health Forum; 2012.

[2] Canadian Institutes of Health Research. Harper government invests in personalized medicine. Canadian Institutes of Health Research; 2012. http://www.cihr-irsc.gc.ca/e/44825.htm

Implications

These trends in expanding genetic testing capabilities call for greater coordination and streamlined service delivery to determine which tests should be provided, where, and by whom. The increased availability of, and demand for, genetic tests and related services will put increased pressure on current programs and services, especially for common diseases and conditions.[1]

7.1.2 Genetic Screening – Nuchal Translucency Screening in Pregnancy

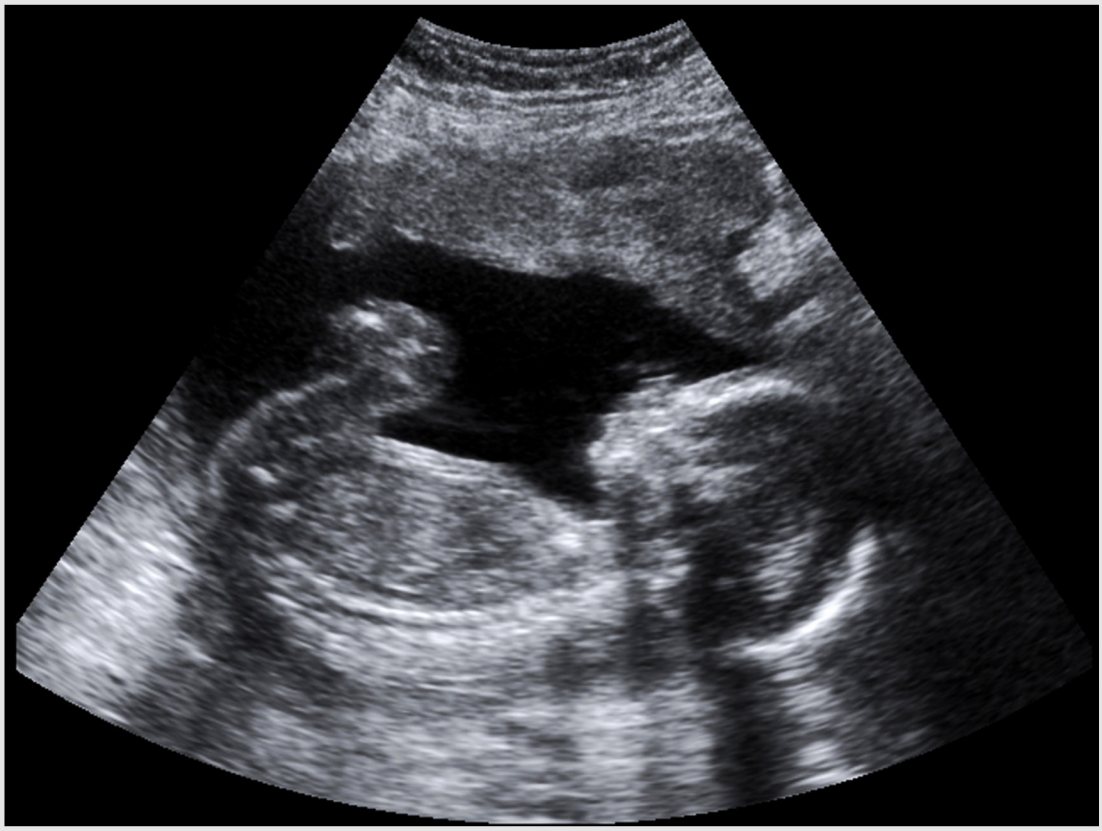

Image credit: Shutterstock

Nuchal translucency screening uses ultrasound to screen for Down syndrome, other conditions caused by an extra chromosome (trisomy 13 and 18), and congenital heart defects. It is performed between 11 and 14 weeks of pregnancy. When nuchal translucency screening is done with blood tests, the results are more accurate. Because nuchal translucency is a screening procedure, it provides a risk estimate for developing one of the conditions. A follow-up diagnostic test – such as chorionic villus sampling or amniocentesis – confirms the diagnosis.

The Society of Obstetricians and Gynaecologists of Canada and the Canadian College of Medical Geneticists recommend that nuchal translucency should only be done where the ultrasound staff is specially trained and accredited to do this procedure. Therefore it is not available in all communities across Canada.[1]

[1] Joint SOGC-CCMG Clinical Practice Guideline. No. 261 (Replaces No. 187, February 2007). Prenatal Screening for Fetal Aneuploidy in Singleton Pregnancies. J Obstet Gynaecol Can. 2011;33(7):736–50. http://www.sogc.org/guidelines/documents/gui261CPG1107E.pdf

7.1.3 Consent and Newborn Genetic Screening

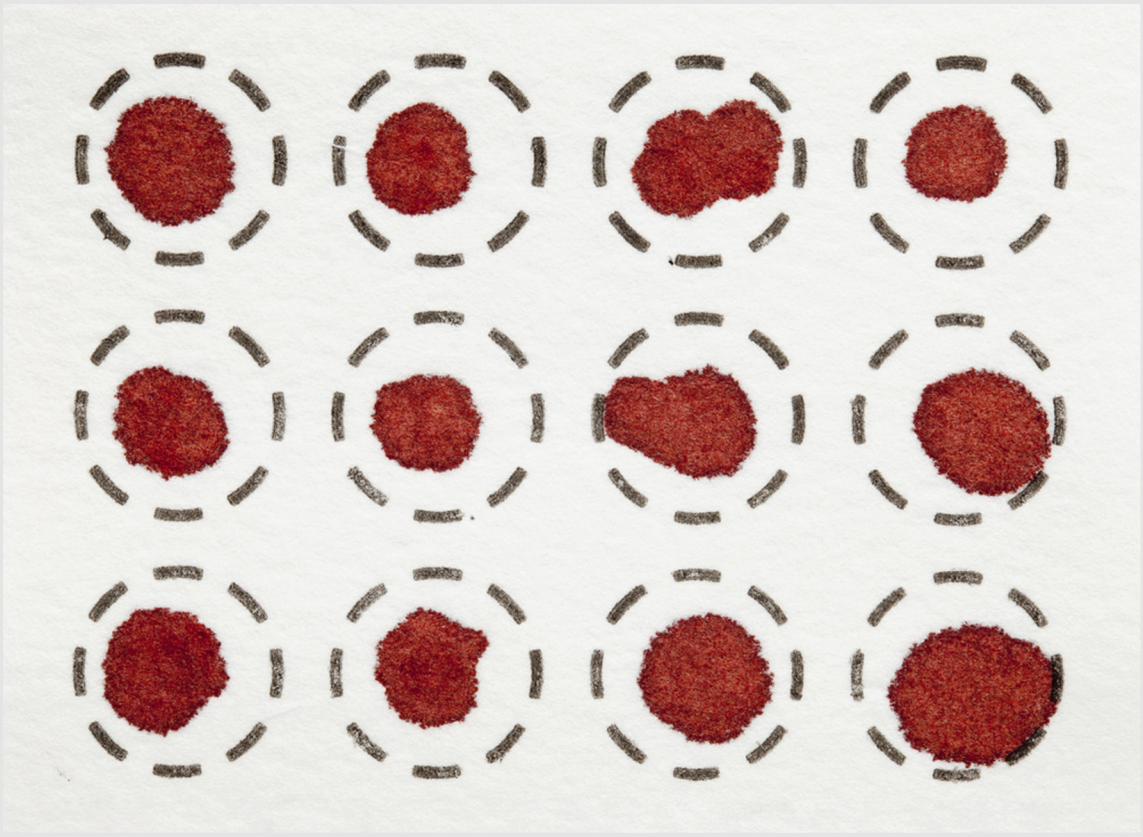

Image credit: Shutterstock

Anecdotal and published evidence about newborn screening programs show that many parents are not aware that babies are offered a screening test. This issue has sparked controversy and debate about the issue of obtaining consent.

Most newborn screening programs do not require explicit consent from parents. Newborn screening is considered part of routine healthcare for children. Newborn screening for treatable and preventable conditions is considered to be in the best interests of the child. In Canada, we have what is called "implied consent," which means parents are not necessarily asked. Doctors assume the parents want screening unless they say otherwise. As a result, although parents are provided with newborn screening pamphlets and the right to decline testing, they may not be aware that newborn screening has been carried out and for which diseases.

Implications

Newborn screening raises a number of legal and ethical issues. Parents may have limited knowledge of the programs and, for this reason, the informed consent process provides an opportunity to educate them on the specifics of the screening procedures. Requiring explicit consent, however, requires additional resources for program implementation. Nevertheless, the timing for giving this information is important.

7.1.4 New Technologies and Newborn Genetic Screening

Image credit: Shutterstock

New technologies are now available that allow screening for a large number of conditions through a single process. One technology that is moving into the clinic to help with diagnosis and treatment is whole genome sequencing (WGS).[1,2] Of note, however, the level and use of new technologies varies from site to site and between jurisdictions. It is not readily available everywhere, therefore it is not accessible to all children and families.

[1] Green RC, Berg JS, Grody WW, Kalia SS, Korf BR, Martin CL, et al. ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing. American College of Medical Genetics and Genomics; 2013. http://www.acmg.net.

[2] Saunders CJ, Miller NA, Soden SE, Dinwiddie DL, Noll A, Alnadi NA, et al. Rapid whole-genome sequencing for genetic disease diagnosis in neonatal intensive care units. Sci Transl Med. 2012;4(154):154ra135

7.1.5 Newborn Screening: Important Questions

Image credit: Shutterstock

As the technological frontier expands, it is possible that whole genome sequencing may supplant newborn screening programs. Before doing so, there are many important questions:

- How will we make decisions about the use of this technology and how will we evaluate its use?
- Who decides which conditions will be screened for?
- What criteria and evidence will be used to decide which conditions to screen for?
- How will these programs be implemented?

7.1.6 Genetic Testing and Screening: Whole Genome Sequencing (WGS)

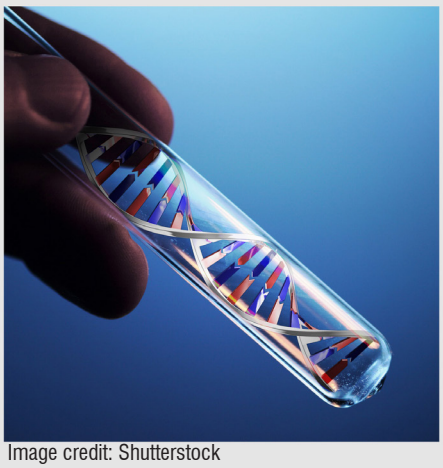

Image credit: Shutterstock

A person's genome is his/her complete set of DNA. Each human genome contains all of the information needed to build and maintain that individual. A copy of the entire genome – which has more than 3 billion DNA base pairs – is contained in all human cells that have a nucleus.

Whole genome sequencing (WGS) compares large amounts of genetic data to identify variations in DNA associated with specific diseases. Once new genetic associations are identified, researchers can use the information to develop better strategies to detect, treat, and prevent disease.[1]

For a more thorough description of whole genome sequencing, click here.

[1] National Genome Research Institute. National Institutes of Health. http://www.genome.gov/20019523

Implications

The use of WGS in the clinic raises a number of questions. Analyzing the entire genome at once can reveal what are called "incidental" findings. Incidental findings are pieces of information learned when conducting genetic testing that do not relate to the clinical problem or concern at hand. Also, there are many genetic mutations that are not adequately understood and cannot be interpreted. This raises debates about WGS: its usefulness in the clinical setting, communicating results to families, informed consent stipulations, and the right to know or not know.

- WGS challenges current policies with regard to the genetic testing of children. Traditional guidance for genetic testing of children recommends that results revealing conditions of adult onset should not be communicated unless disclosure could prevent serious harm to the health of the child's parents or family members.[2]
- WGS raises questions about potential harms, stigmatization, and discrimination. For example, the potential use of this information by insurance companies.
- The rapidly evolving volume of new information is combined presently with a lack of expertise to interpret and communicate this information. It is important that children not be caught up in the current uncertainty surrounding WGS and the communication of genetic research results and incidental findings.

[2] Arbour L. Guidelines for genetic testing of healthy children. A joint statement with the Canadian College of Medical Geneticists Bioethics Committee, Canadian Paediatric Society (CPS) Ethics and Public Policy Committee, Canadian College of Medical Geneticists. Paediatrics & Child Health. 2003;8(1):42–5. Reference No. B03-01. Reaffirmed January 2011. Addendum (April 2008). http://www.cps.ca/english/statements/B/b03-01.htm

7.1.7 Genetic Testing and Screening – Whole Genome Sequencing (WGS) – Questions for Clinicians

Image credit: Shutterstock

Dealing with such a huge amount of data provides a new set of questions for clinicians:

- How do you evaluate the clinical usefulness and the benefit to patients? Should physicians or clinical laboratories provide genomic information that has no medical importance but is of social or personal consequence to the child (e.g., genes associated with athletic or musical ability)?
- Does whole genome sequencing require a different level of consent than other genetic tests or medical assessments?
- Should patients be informed of results that do not have direct implications for them but do for other family members?
- Should other family members be informed of findings that have direct implications for them that were found on analysis of a relative's genome sequence?
- Do physicians or clinical laboratories have a duty to re-contact patients if sequence data that were previously obtained are later found to have serious medical implications?

7.2.1 Pharmacogenetics

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People may react in different ways to drugs based on their genetic makeup. Pharmacogenetics is the study of the how genetic factors influence a person's response to drugs. Testing for certain genetic tendencies before prescribing certain drugs could help avoid harmful drug effects and improve the effectiveness of drug therapy. Pharmacogenetic testing is beginning to revolutionize prescription practices in medicine. The case of codeine is but one example.

Codeine and Breastfeeding: Example of Pharmacogenetic Impact

Some women may produce much more morphine when taking codeine than most people do. In this situation, newborns might be exposed to toxic levels of morphine when breastfeeding.

Health Canada advises the public, especially nursing mothers, about the very rare but serious health risk to breastfed babies posed by codeine use.[1,2] Considering many women receive codeine for post-labour pain, they and their physicians need to be aware of the pharmacogenetic impact of codeine. Options to reduce this risk include discontinuing codeine after 2 to 3 days of use and being aware of symptoms of producing more morphine in both mothers and newborns.

[1] Use of Codeine Products by Nursing Mothers Advisory 2008-164. October 8, 2008. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2008/13255a-eng.php

[2] Madadi P, Moretti M, Djokanovic N, Bozzo P, Nulman I, Ito S, et al. Guidelines for maternal codeine use during breastfeeding. Can Fam Physician. 2009;55(11):1077–8

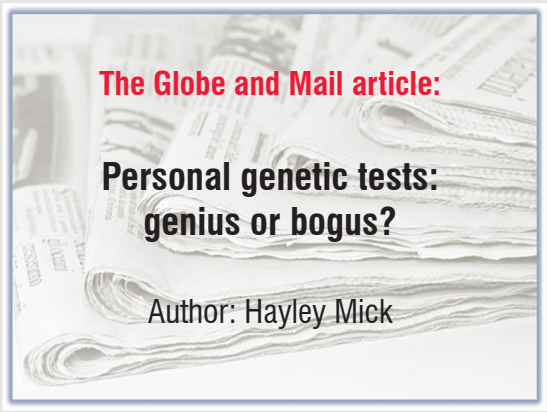
Implications

It will take time for pharmacogenetic testing to enter conventional medical care. Future pharmacogenetic research in children is essential. Children are not small adults. They have unique physiologic differences not only based on their genotype but also on their developmental stage and other factors such as BMI (body mass index). All of these factors will have an effect on their responses to drugs. Therefore adult research is not necessarily transferable to children.

This understanding of pharmacogenetics not only maximizes therapeutic effects but also increases the likelihood that pharmacogenetic differences in children may further complicate clinical trial development for orphan diseases and be a disincentive for drug development targeted to children. As a result, children would not benefit from the promise of pharmacogenetic developments.[3] American and European legislation has put provisions in place in the hope of promoting the development of treatment for children and orphan disease groups. Health professionals, including doctors, nurses, genetic counsellors, and pharmacists, have limited knowledge about pharmacogenetics and will need to receive training to be prepared with the necessary skills for introducing pharmacogenetic testing into their clinical practice.

[3] Joly Y, Sillon G, Silverstein T, Krajinovic M, Avard D. Pharmacogenomics: Don't Forget the Children. Current Pharmacogenomics and Personalized Medicine. 2008;6:77–84

7.2.2 Genetic Tests Sold Directly to Consumers



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To view this article by Hayley Mick, please click **here**.

Private commercial companies are advertising and selling kits via the internet that allow people to send biological samples for DNA analysis. This is called "direct-to-consumer genetic testing." Consumers receive information about their likelihood of developing certain condition(s) linked to particular genes. Many of these companies conduct genetic testing in children and youth,[1] and the tests are often offered without medical supervision.

Companies use promotional statements such as "let your DNA help you plan for the important things in life" or "our goal is to empower you with genetic insights to help motivate you to improve your health."[2]

While some genetic tests are well validated, some have not been validated or are considered inappropriate for the public.

In Canada, Cepmed (Centre for Excellence in Personalized Medicine) and DNA Direct have developed a Personalized Medicine Portal that provides tools to help patients understand how genetic testing can be used in making treatment decisions and promotes communication between patients and healthcare providers. The Portal provides information about access to specific genetic tests in each province.[3]

1 Howard HC, Avard D, Borry P. Are the kids really all right? Direct-to-consumer genetic testing in children: Are company policies for testing minors clashing with professional norms? European Society of Human Genetics. 2011;19(11):1122–6

2 Kolor K, et al. Health care provider and consumer awareness, perceptions, and use of direct-to-consumer personal genomic tests, United States, 2008. Genetics in Medicine. 2009;11:85–95

See, for example, Navigenics' Terms and Conditions: "you should not interpret Your Report or any other Content as recommending any specific treatment plan, product or course of action. You should always consult your physician or other qualified health provider before starting any new treatment."

http://www.navigenics.com/visitor/what_we_offer/our_policies/terms_conditions/ Accessed August 17, 2011

3 Cepmed launches online personalized medicine portal. Marketwire. February 22, 2012. http://finance.yahoo.com/news/cepmed-launches-online-personalized-medicine-204000631.html

Implications

Direct-to-consumer genetic testing for children may provide useful genetic information, though without the benefit of appropriate genetic and clinical counselling. The Canadian College of Medical Genetics and the Canadian Pediatric Society have established professional norms concerning genetic testing of children. They state that for genetic conditions that will not present until adulthood (susceptibility or predictive testing), testing should be deferred until the child is competent to decide whether they want the information. Many argue that testing children using direct-to-consumer services deprives them of the right to decide for themselves whether they want to receive this genetic information. Therefore, it is not in keeping with these norms.