Precision Medicine is here, but are we ready for it?

Brianna Barsanti-Innes (BSc)

Department of Medicine, University of Toronto, 1 King's College Circle, Toronto, Ontario, Canada, M5S 1A8

Introduction

In 2003, the Human Genome Project was completed, an intensive undertaking that had, for the first time, sequenced the complete human genome. It was a project that took over 10 years to complete and cost over $2.7 billion.1 In the past 16 years, major advancements in this field have changed these figures dramatically. With new next generation sequencing, an individual can have their entire genome sequenced, in less than a week, for increasingly lower prices, recently as low as $599.[1-3] In addition to whole genome sequencing, there has been a boom of other testing modalities over the past decade that are moving genetic testing from its niche use in rare disorders to applications in wide-ranging clinical situations.[4]

The implications of these changes within clinical practice for "precision medicine" are enormous. Increasingly, genetics is playing a role in a physician's ability to properly diagnose disease, aid patients with family planning, correctly predict health risks, and safely prescribe medications.[4] However, for better or worse, testing is rapidly moving out of the clinic and into consumers'/patients' hands.

The Role of Genetics in Medical Practice

In Ontario, genetic testing routinely begins at birth and as of 2008, mutation status for cystic fibrosis was added to the newborn screening panel in the province, aiding physicians with early diagnosis of the disease and determination of carrier status.[5] Pre-symptomatic genetic testing can be used to investigate for treatable diseases like familial hypercholesterolemia or fatal conditions like Huntington's disease and Familial Alzheimer's Disease.[4] These and other testing can help physicians guide patients with respect to their family planning and can help patients prepare for future health concerns.

Advances in pharmacogenomics – the use of genetic characteristics to predict response to therapeutics – are also changing the way physicians prescribe medications to their patients. Genetics is estimated to be responsible for 20-95% of the variation in individual response to drugs.6 Notable examples of this in the treatment of cardiovascular conditions include the discovery of the *VKORC1* gene variant responsible for predicting non-responders to warfarin and the reduced-function variants of *CYP2C19* (its bioactivating enzyme) which result in higher rates of adverse events after stent placement.[7] The use of precision medicine is also increasing in the treatment of cancer. There is great hope in this area that tailoring treatment to the genetic subtype of a patient's tumor will improve response to treatment and overall survival.[8] A notable example of this is the significant increase in disease free survival gained with the addition of targeted therapy trastuzumab in patients with HER2 positive breast cancer.[9]

Despite the many benefits of genetic testing, there are several issues that physicians must consider when ordering and interpreting genetic testing for their patients. Among these are concerns of genetic discrimination, implications for insurance coverage, and the anxiety that may occur from indeterminate and untreatable results.[10]

Discomfort in Current Practice

Despite the fact that there is a dramatic increase in the use of genetics in medical management, several studies have highlighted gaps in physician understanding and limits on their perceived competency of handling genetics in clinical practice.[14-17]

A study of internists at two academic centers in the United States found that 74% and 87% of respondents rated their knowledge of genetics and guidelines for testing, respectively, as somewhat poor or very poor. Furthermore, 41% of the respondents who rated their genetics knowledge as poor had ordered a genetic test in the past 6 months. 82% of internists also felt the need for more training on how to properly counsel patients on genetic testing.[16]

A 2015 study examined the experience amongst neurologists and psychiatrists in the United States of using genetic testing. 70% of respondents felt that compared to current practices, genetic testing should be performed more often, while 84% of respondents felt they needed more training to interpret testing results.[17]

These studies indicate that a lack of proper training is a hindrance for physicians both in being able to take advantage of the vastly increasing knowledge base and tests available in genetics, as well as to properly advise concerned patients who have sought genetic testing outside of physician care.

Genetics in Medical Education

Unsurprisingly, awareness of the gaps in physician knowledge in these areas has led to an interest in understanding how genetics is currently being portrayed in medical education.[18] Several studies have evaluated the extent of genetics teaching in various specialties and levels of training.

In terms of undergraduate medical education, a 2007 study evaluating the genetics curriculums in 149 Canadian and American medical schools found a heavy emphasis was placed on general concepts rather than practical applications.[19] 10 years later, a survey study at one US medical school looking at attitudes of undergraduate medical students towards precision medicine found that while 79% thought that it was important to learn about

Corresponding Author:
Brianna Barsanti-Innes
Brianna.barsanti.innes@mail.utoronto.ca

these genetic tests, only 6% thought that they had been adequately prepared by their medical education.[20]

Residency programs are also noting gaps in medical education surrounding genetics. In the United States, researchers looked at the availability of medical genetics and genomics rotations in obstetrics and gynaecology training and found that, compared to other rotations, there was a great deficiency of opportunities for residents to train in this increasingly important area.[21] A study at the University of Toronto investigating the experiences of family medicine residents found that they felt their genetics education was not clinically relevant or standardized. The authors of the study called for an increased educational focus on common diseases and practical diagnostic, risk assessment, and management issues.[22]

Overall, the research and existing literature into medical education around genetics has shown that there exists a clear disconnect between the reality of what knowledge and testing are currently available, both clinically and on the commercial market, and what is being taught in the classroom. This has left students feeling unprepared to properly apply genetics to treat their patients.

With deficiencies in current educational practices, there is active discussion regarding the expected "genetics competencies" that practicing clinicians should acquire but often lack. Areas of knowledge that have been considered of essential understanding include modes of inheritance, indications for genetic testing, calculation of genetic risk, and awareness of indications for referral to a geneticist. Areas of skill include communicating genetic information, helping patients make informed genetic testing decisions, and managing family dynamics.[23] These elements should inform the development and evaluation of genetics curriculum in medical education. Moving forward, it may be beneficial to incorporate curriculum components such as, i) having students work through genetic case examples using existing online databases such as OMIM to provide a level of comfort with using these resources in practice, ii) adding standardized patient scenarios where medical students can role play counselling a patient about the implications of genetic testing, and iii) incorporating social and legal issues surrounding genetic testing into medical school ethics curriculums.[24]

Conclusion

In 2015, in his state of the union address, President of the United States, Barack Obama announced the launching of the "Precision Medicine Initiative".[25] He called upon researchers and doctors to work towards individualizing healthcare for each patient using their genetic code. He made the bold wish of hoping that soon cancer cures based on one's genome would be as routine as matching their blood for a transfusion. And while clinical and commercial uses of genetic testing and precision medicine are increasing at a rapid pace, there is research to suggest that current physicians practicing in wide-ranging specialties are not equipped to handle the resulting changes to clinical practice. Further research indicates that medical schools are also not keeping pace in terms of providing adequate educational experiences for students including exposures and training in these areas. Precision medicine is no longer a futuristic concept, it is here, and we have to ask ourselves if we, the medical community, are being adequately prepared for it.

References

1. National Institutes of Health. The cost of sequencing a human genome [Internet]. Bethesda MD: National Human Genome Research Institute; 2016. Available from: http://www.genome.gov/27565109/the-cost-of-sequencing-a-human-genome/.
2. Andrews, J. For $600 Veritas Genetics sequences 6.4 billion letters of your DNA [Internet]. Consumer News and Business Channel; 2019. Available from: https://www.cnbc.com/2019/07/01/for-600-veritas-genetics-sequences-6point4-billion-letters-of-your-dna.html
3. Johansen Taber KA, Dickinson BD, Wilson M. The promise and challenges of next-generation genome sequencing for clinical care. JAMA internal medicine. 2014;174(2):275-280.
4. Katsanis SH, Katsanis N. Molecular genetic testing and the future of clinical genomics. Nature Reviews Genetics. 2013;14(6):415-426.
5. Newborn Screening Ontario. Screening History [Internet]. Updated 2019. Available from: http://www.newbornscreening.on.ca/en/about-screening/diseases-screened
6. Evans WE, McLeod HL. Pharmacogenomics--drug disposition, drug targets, and side effects. The New England journal of medicine. 2003;348(6):538-549.
7. Roden DM, Wilke RA, Kroemer HK, et al. Pharmacogenomics: the genetics of variable drug responses. Circulation. 2011;123(15):1661-1670.
8. National Cancer Institute. Precision medicine in cancer treatment [Internet]. 2017. Available from: http://www.cancer.gov/about-cancer/treatment/types/precision-medicine
9. Paik S, Kim C, Wolmark N. HER2 status and benefit from adjuvant trastuzumab in breast cancer. The New England journal of medicine. 2008;358(13):1409-1411.
10. Canadian Medical Association. CMA policy: Direct-to-consumer genetic testing [Internet]. 2017. Available from: http://www.cma.ca/Assets/assets-library/document/en/advocacy/policy-research/cma-policy-direct-to-consumer-genetic-testing-pd17-05-e.pdf
11. The Canadian Medical Protective Association. Direct-to-consumer genetic test results: Be prepared [Internet]. 2017. Available from: http://www.cmpa-acpm.ca/en/advice-publications/browse-articles/2017/direct-to-consumer-genetic-test-results-be-prepared
12. Schmidt S. 9 leading companies in direct-to-consumer genetic testing [Internet]. 2016. Available from: http://blog.marketresearch.com/9-leading-companies-in-direct-to-consumer-genetic-testing
13. 23andMe®. DNA reports list. [Internet]. 2019. Available from: http://www.23andme.com/en-ca/dna-reports-list/.
14. Haga SB, Burke W, Ginsburg GS, et al. Primary care physicians' knowledge of and experience with pharmacogenetic testing. Clinical genetics. 2012;82(4):388-394.
15. Johansen Taber KA, Dickinson BD. Pharmacogenomic knowledge gaps and educational resource needs among physicians in selected specialties. Pharmacogenomics and personalized medicine. 2014;7:145-162.
16. Klitzman R, Chung W, Marder K, et al. Attitudes and practices among internists concerning genetic testing. Journal of genetic counseling. 2013;22(1):90-100.
17. Salm M, Abbate K, Appelbaum P, et al. Use of genetic tests among neurologists and psychiatrists: Knowledge, attitudes, behaviors, and needs for training. Journal of genetic counseling. 2014;23(2):156-163.
18. Salari K. The dawning era of personalized medicine exposes a gap in medical education. PLoS medicine. 2009;6(8):e1000138. doi: 10.1371/journal.pmed.1000138.
19. Thurston VC, Wales PS, Bell MA, et al. The current status of medical genetics instruction in US and Canadian medical schools. Academic medicine : journal of the Association of American Medical Colleges. 2007;82(5):441-445.
20. Eden C, Johnson KW, Gottesman O, et al. Medical student preparedness for an era of personalized medicine: Findings from one US medical school. Personalized medicine. 2016;13(2):129-141.
21. Putra M, Idler J, Dai J, et al. Medical genetics and genomics training in obstetrics and gynecology residencies: Are we ready for the future?. J Matern Fetal Neonatal Med. 2017:1-7.
22. Telner DE, Carroll JC, Talbot Y. Genetics education in medical school: A qualitative study exploring educational experiences and needs. Medical teacher. 2008;30(2):192-198.
23. Guttmacher AE, Porteous ME, McInerney JD. Educating health-care professionals about genetics and genomics. Nature Reviews Genetics. 2007;8(2):151-157.
24. Wolyniak MJ, Bemis LT, Prunuske AJ. Improving medical students' knowledge of genetic disease: A review of current and emerging pedagogical practices. Advances in medical education and practice. 2015;(6):597–607.
25. The Precision Medicine Initiative. The White House Archives. [Internet]. 2015. Available from: https://obamawhitehouse.archives.gov/precision-medicine