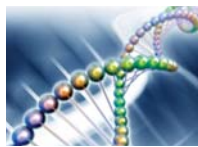


MICHAEL J. DOUGHERTY, PhD



Moving beyond the basics: Teaching the genetics of complex traits

You enter the examination room, where a 28-year-old man waits anxiously. “Should I be worried about this mutation? Am I going to get prostate cancer?” Your patient is holding the results from a personal genetic test that he ordered from a direct-to-consumer testing company. How should you respond?¹ What history do you need to gather?

What if a female patient mentions that her mother has had colon polyps removed? How would you determine whether your patient is at risk for familial adenomatous polyposis, a dominant Mendelian disorder? Should you order a genetic test? Is there other information you need first?

Or consider an African-American patient with high BP. Is the patient’s race relevant to considerations of drug metabolism—making some drug choices better than others—or is race a poor proxy for genetics?²

THE SCIENCE OF WHOLE GENOMES

Increasingly, medical discoveries and their applications to health care (eg, diagnosis, prognosis, treatment, and prediction of future risk) will have their roots in *genomics*, the science of whole genomes. Genomics extends beyond the genetics that is commonly taught in programs that educate health care providers, including PAs. This presents challenges at two levels: Your ability to respond appropriately, and your patients’ ability to understand and benefit from your advice. There is reason for concern at both levels.

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Traditional genetics instruction is built on the conceptual framework of Mendelian inheritance, meiosis, and gene expression—often in that sequence, which tracks the history of discovery in genetics. All these are necessary concepts for complete understanding, but they are not sufficient to meet the needs of modern genetic literacy or health care. Genetic testing has rapidly expanded beyond the detection of individual diagnostic

EDUCATING PATIENTS

The specific genetics information patients need in order to make educated choices and provide informed consent is unclear, but as a clinician, you must be prepared to translate that information at an appropriate level. Researchers in genetics education are investigating various learning models to determine the most effective content and instructional methods. What is clear, however, is that public understanding is well below even

“The American Society of Human Genetics is supporting a curricular approach that teaches students the complex traits first.”

or predictive mutations for single-gene disorders to include screening for thousands of genetic variants associated (often very weakly) with common complex diseases. With time, evidence for those associations will grow stronger and their clinical utility will improve, requiring changes in practice standards.

The proposed core competencies in genetics and genomics recommend that PAs understand Mendelian inheritance and different modes of non-Mendelian inheritance—for example, as when multiple genes and environmental factors contribute to complex diseases, such as heart disease, hypertension, and cancer.³ However, learning the basics in a classroom is not enough. If the practice of medicine is to be informed by genetics, health professionals must learn to apply what they know about inheritance of disease in their clinical training. This goal is complicated by a crowded curriculum, insufficient numbers of genetics professionals, and myriad other challenges.⁴

minimum thresholds required to understand a genetics-based clinical encounter. Many adults in the United States have a “conversational familiarity” with such terms as *genes* and *genetics* but an inability to explain them adequately, and many lack the understanding necessary to cope with the concepts of genetic testing.^{5,6}

We also know that among high school students, misconceptions are common and involve genetic determinism, patterns of inheritance, and the nature of the substances that comprise genetic material.⁷ The National Assessment of Educational Progress reveals that more than 50% of 12th graders have an unsatisfactory understanding of such foundational concepts as genes, mutations, and genetic disease.⁸ Because only one-third of US adults have a bachelor’s degree, we can assume that the average patient has the equivalent of a high school student’s (inadequate) knowledge of genetics.

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CLOSING THE EDUCATIONAL GAP

What can be done to bridge the divide between essential genetics literacy and the status quo for providers and the public? A new conceptual framework and curriculum are needed. Students at all levels currently spend too much time on formulaic approaches to genetics, most notably the analysis of pedigrees and the solution of Mendelian inheritance problems using the familiar Punnett square. Interpretation of pedigrees is an important skill for health professionals, and Punnett squares have been a useful heuristic for more than 50 years. However, an overreliance on algorithms and on examples of single-gene traits (often disorders, such as cystic fibrosis, hemophilia, and Huntington's disease) may help explain why genetic determinism is so common and why students will try to force virtually any trait into a Mendelian pattern. With so much time devoted to single-gene diseases, students also lose sight of the fact that these traits are relatively rare. Little time is spent learning about the genetics of common, multifactorial disorders—those most likely to affect large segments of the patient population. The American Society of Human Genetics is supporting a curricular approach that teaches the genetics of complex traits first and then moves to the rare monogenic traits as a way to restore balance and possibly minimize misconceptions.⁹

What differences should you expect to see in the clinic when viewing disease through the lens of genomics versus the traditional lens of genetics? Several programs from the National Coalition for Health Professional Education in Genetics illustrate contrasting characteristics of complex and single-gene disorders.¹⁰ First, health care professionals will need to move beyond the expectation that genetic disease will manifest only as a familiar Mendelian pattern in a family history. Whereas Mendelian disease will *segregate* in families, following the meiotic movement of chromosomes that carry large-effect, harmful alleles, multifactorial disease will *aggregate* or cluster within families. Why? The reason is that most of the genes contributing to complex disease confer only small increases in risk, and disease manifests only above certain thresholds. Moreover, the environment contributes more substantially to complex disease than to Mendelian disease. Clinically, complex disorders often affect patients when they are older and show greater variation in symptoms, whereas single-gene disorders typically appear at an early age and have less variation in symptoms. Additionally, the risks for relatives of a proband (an individual with a disorder who is the first to be studied) are generally lower for polygenic disease than for monogenic disease.

IMPROVED PATIENT CARE

The hypothetical patients described at the beginning of this article illustrate just some of the challenges that genomics will present to PAs. Although professional training and public education have a long way to go before we can adequately address the changing needs of such patients, we are starting to understand the road we need to travel. The good news is that the journey will improve patient care. **JAAPA**

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