Preface

Genetics for the Generalist: Yes, This Is Important for Your Patient

This issue of *Medical Clinics of North America* is about genetics. Unlike an organ system-focused or other specialty-based topic, the field of genetics truly touches on every specialty and every aspect of health and disease. There are hundreds of individually rare (but collectively common) single-gene Mendelian disorders, affecting every system, organ, tissue, and cell in the human body. But even more prevalent is the effect of multiple different genetic variants on predisposition to complex multifactorial diseases and the interaction between genetic variants and the environment. This includes not only what patients are exposed to in their day-to-day lives but also the various medications, radiation, and other factors we inflict upon them in an effort to diagnose, prevent, or treat disease. When considering this broadly, it is clear that genetics is too large topic for a single issue of any journal. Even selected highlights for the generalist will fail to adequately cover the field.

You will absolutely find authoritative and helpful information about many specific genetic conditions in the pages (or pixels) of this issue, and I encourage you to read each article herein. I also encourage you to look for common themes among and between these expert reviews.

Family history has always been the first, best, and least expensive genetic test. Obtaining, updating, and qualitatively interpreting the family medical history do not take much effort and can really help to inform your differential diagnosis, risk assessment, and preventive counseling. Even if there isn’t a dominant, recessive, or x-linked condition in your patient’s family, recognizing that the same or related disorders occur multiple times among family members will help you and your patient to identify the complex multifactorial conditions for which she or he is most at risk and possibly help you to disentangle the next confusing set of signs and symptoms she or he manifests.
Selecting, ordering and understanding genetic tests are also practical for generalists, once some basic principles are understood. Like all other tests, genetic tests are often clearly normal, sometimes clearly abnormal, and frequently somewhere in between. Variants of uncertain significance (VUS) are still quite common today. They will gradually become less common as we learn more about the genome, but for the next several years, it is important for all providers and patients to understand that a VUS is neither normal (benign) nor abnormal (pathogenic). If the differential diagnosis is very narrow, one should test only the one or few genes of interest in order to minimize the likelihood of finding a VUS that is unlikely related to the clinical question at hand. When the question is broader, sequencing of large panels of genes (or even the entire exome or genome) is reasonable but comes with more uncertainty.

Our genes do not define us and, with rare exception, the presence or absence of a pathogenic variant does not guarantee disease or lack thereof. Rather, our genetic makeup increases or decreases our risk of certain diseases (or, in the case of pharmacogenetics, of responding well to and tolerating a particular medication). Identifying disease-predisposing variants can help inform lifestyle modification for risk reduction, screening for earlier disease detection, and targeted therapeutic interventions.

If you've come here looking for information about a specific condition covered among these articles, I'm confident you'll find what you seek. I hope you'll also come away with more confidence incorporating the principles of genetics into your general or specialty practice.

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