

The role of genetic assessment in determining a patient's disease risk

When it comes to the integration of genetics into daily patient care, some among us have sounded a bit like Paul Revere—ready to give the signal from the light tower: one if by Internet, two if by continuing medical education. Even as the PA community awaits the signal that will tell us where to watch for the latest information, the question demanding our attention is this: How will genomics change the way we practice medicine today?

Like any good treatment plan, the answer to this critical question does not come in the form of a simple drug prescription. Instead, future treatment plans will involve a complex regimen of knowledge and a change in clinical practice methodology that incorporates the understanding that your patient's medical condition may have a genetic root cause as opposed to simply an environmental one. (In fact, the cause of the condition is usually a combination of the two.)

You have all heard this before, but it is worth repeating: We are now on the leading edge of personalized medicine, a revolution that is just getting under way. Over the course of the next decade, the provision of personalized care will have a profound impact on the way we practice medicine. As PAs, we can position ourselves to play a leading role—if we are willing to increase our knowledge base of personalized medicine; familiarize ourselves with the ABCs of genetic testing and pharmacogenomics; form relationships with genetic counselors; and prepare to inte-

grate existing genomics tools, such as family history, into our daily practice.

First we need to understand how genetics can affect a diagnosis and treatment plan which is based on information that we should already know. According to a 2006 AMA monograph entitled *Risk Assessment for Hereditary Cancer Syndromes—A Physician's Guide to Clinical Genetic Testing and Medical Management (An AMA Continuing Medical Education Program for Primary Care Physicians)*, identifying and managing patients at risk for hereditary cancer syndromes can have a significant impact on their future health and the health of their families.¹ Identification of an increased cancer risk should prompt education, counseling, referral to genetic counselors when appropri-

A PA who does not know that genetic testing for HNPCC is available and does not understand all the increased risk factors faced by patients whose test result is positive is missing an entire piece of the picture. That missing piece will hamper the PA's ability to provide preventive health care for the patient and may have significant long-term morbidity and mortality implications for both the patient and his or her family members.

The hereditary cancer syndrome example is just the tip of the iceberg. The field of genetic testing began by focusing on single-gene disorders with full or complete penetrance (ie, everyone or almost everyone with the genetic mutation will get the disease). Later, the field evolved to include single-gene disorders

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ate, and the recommendation and management of various approaches to minimize the risk for patients and their family members.

Next comes the tricky part: How much do we as clinicians really know about identifying hereditary cancers? An abstract on *Genetic Testing for Colorectal Cancer Among Primary Care Providers* released by the American Society of Clinical Oncology, also in 2006, stated that none of 245 primary care providers who were asked to complete a self-administered questionnaire were able to correctly identify a single case of hereditary nonpolyposis colorectal cancer (HNPCC).² In fact, only 55% of respondents had ever heard of genetic susceptibility testing for patients with a family history of colon cancer.

with incomplete penetrance (eg, hereditary cancer syndromes). Now, genomic testing is on the brink of using one test to look for variants in tens to hundreds of genes that have small incremental effects on complex diseases. To help imagine this burgeoning world of genomic testing, let us consider a clinical situation. Recently a patient consulted me about the results of a saliva-based DNA analysis from one of three direct-to-consumer companies. Before he came to the office, he also completed an online family history at www.progenygenetics.com, which generated a three-generation genetic pedigree (see Figure 1, page 67). A similar program called “My Family Health Portrait” is available from the US Surgeon General's Office.

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GENOMICS IN PA PRACTICE

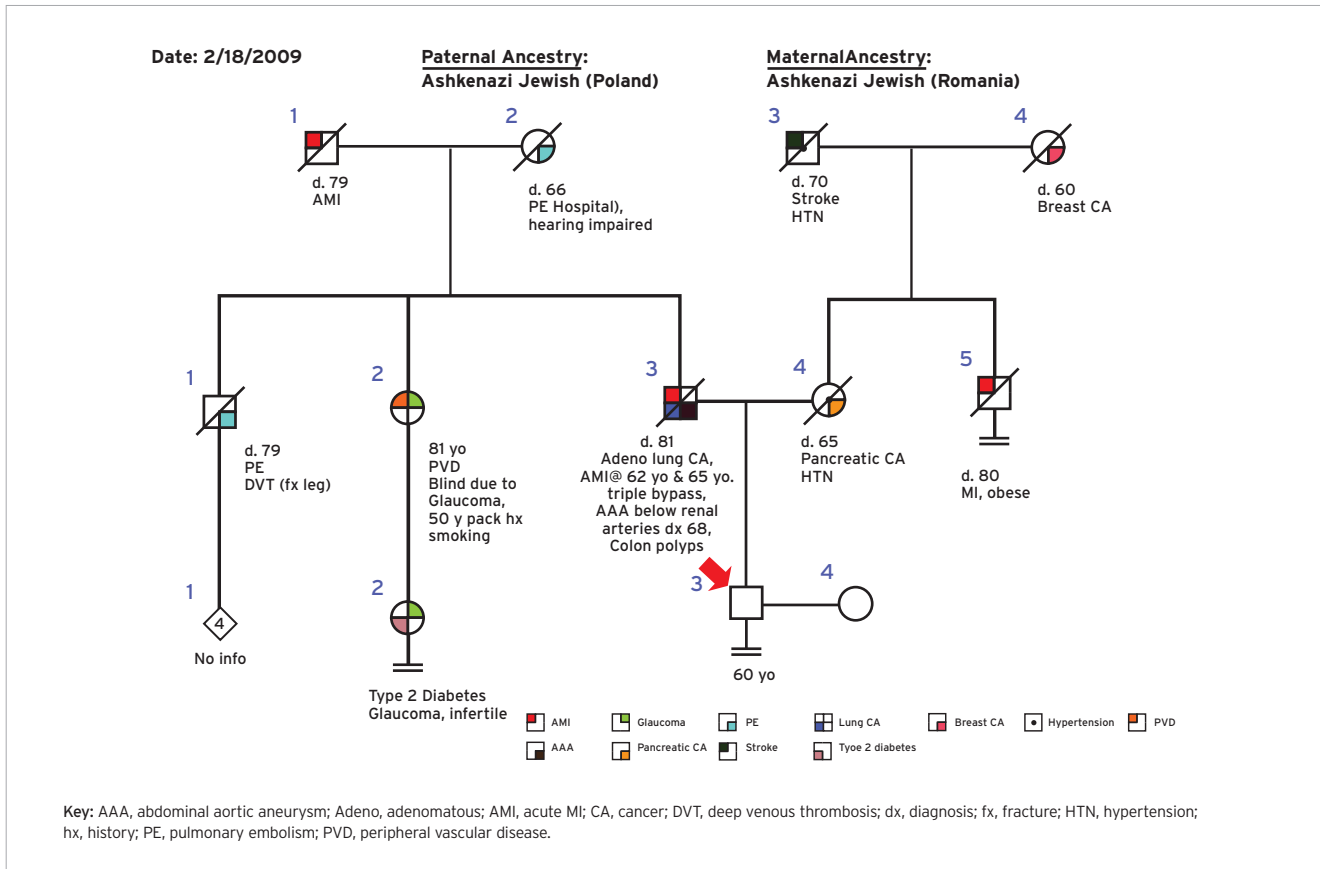


FIGURE 1. The patient's three-generation genetic pedigree

The completed family history showed that the patient is a 61-year-old white male with a medical history of Gilbert syndrome, obesity, and infertility of unknown cause. He is otherwise presumed healthy. Childhood illnesses include mumps, chickenpox, and measles. Adult conditions are allergic rhinitis and irritable bowel syndrome, both of which were diagnosed about 15 years ago. In addition to the vaccinations he received while serving in the US Air Force, he has been immunized against hepatitis A/B and, more recently (2000), tetanus. At this office visit, his BP was 126/80 mm Hg. His body mass index of 30 kg/m² classified him as obese.

The patient has a family history of cancer, hypertension, peripheral vascular disease, stroke, pulmonary embolism, abdominal aortic aneurysm, and glaucoma. (Ages at diagnosis are

documented on the pedigree.) His personal lipid profile and his biochemical and thyroid studies are within normal limits. He is not taking any medication.

The results of DNA testing show that the patient has multiple gene variants that increase his risk for a number of common complex diseases. More specifically, he is homozygous for the *LOXL1* gene, which puts him at higher risk for glaucoma (3.4% lifetime risk versus an average population risk of 1.1%). But wait, the story does not stop here. He also has six of eight markers that increase his risk for prostate cancer, although his prostate-specific antigen level has been stable at 2.5 ng/mL. The information on the report about prostate cancer states that the patient's lifetime risk is 31% compared with an average risk of 17%.

The challenge: How would you counsel this patient, given the information outlined? We look forward to your comments, which we will post on the JAAPA Web site (www.jaapa.com) along with an evaluation from a genetic counselor.

Please send your comments to jaapa@haymarketmedia.com. JAAPA

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REFERENCES

- Dold C. *Risk Assessment for Hereditary Cancer Syndromes—A Physician's Guide to Clinical Genetic Testing and Medical Management (An AMA Continuing Medical Education Program for Primary Care Physicians)*. Chicago, IL: American Medical Association; 2006.
- Sheinfeld Gorin S, Honda K, Heck JE, et al. Genetic testing for colorectal cancer among primary care providers. Paper presented at: 2006 Gastrointestinal Cancers Symposium; January 26-28, 2006; San Francisco, CA. Abstract 313.