Genetics and Genomics

An oncology nurse’s journey in practice

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BACKGROUND: Cancer genetics and genomics are now an integral component of oncology care. Genetics and genomics guide recommendations not only for cancer prevention and early detection, but also for cancer treatment.

OBJECTIVES: This article documents the personal experiences of an oncology nurse who has worked in cancer prevention and early detection since the 1990s and describes the many changes that have occurred in cancer-related genetic and genomic care during that time.

METHODS: This is a personal account of genetic practice in the past 30 years.

FINDINGS: Nurses can no longer ignore cancer genetics and genomics in oncology care. Some aspects of care have changed dramatically, including the number of genetic tests and potential uses for genomic information; however, some remain the same, particularly the human component of care. Patients and families need comprehensive education and support to understand the role that genetics and genomics play in cancer care. Oncology nurses are well suited to provide this care.

KEYWORDS
genetics; genomics; cancer prevention; early detection

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IN HIS 1980 COMMENCEMENT SPEECH at Connecticut College, actor Alan Alda encouraged graduating students to do the following: “Begin challenging your own assumptions. Your assumptions are your windows on the world. Scrub them off every once in a while, or the light won’t come in” (para. 18). If I had not challenged my assumptions about what encompasses oncology care, I would have missed a most amazing professional journey. In 1988, I accepted a position to direct a cancer screening program that included risk assessment and management of individuals with suspected hereditary risk for developing cancer. I had held positions on busy academic medical oncology, gynecologic oncology, and bone marrow transplantation inpatient units, but this opportunity turned out to be a completely unexpected and life-changing professional experience for me.

Shortly after I began my new role, a respected oncology nurse and colleague approached me at an Oncology Nursing Society (ONS) chapter meeting and told me she was so sorry I had given up oncology nursing practice. I was surprised, discouraged, and saddened by her comment. I was settling into my new role. I had traveled to take additional classes in other states and engaged in mentorship with a well-known genetics expert to develop the skills and knowledge base I was going to need for my new position. After only a few months, I was awed, amazed, and more clinically challenged than I had ever been in my career. Almost 30 years later, I realize that, at the time, I could not have imagined or predicted how genetics (the study of hereditary and single genes) and genomics (the study of the entire organism’s genes) would revolutionize oncology care and how privileged I would be to have one of the best possible oncology nursing positions to observe and be a part of the implementation of this exciting science, which is transforming oncology care.

The age of genomic and precision medicine has arrived. In the less than three decades since the Human Genome Project was initiated, the impact and magnitude of the information gleaned from this project continues to expand exponentially and directly affects oncology practice (see Table 1). This era in health care presents many exciting and unforeseen challenges and opportunities because genetics and genomics intersect with all aspects of oncology care.

The Early Years

When I first began working in this area, genetic assessment was confined to collecting family histories and drawing pedigrees on large pieces of paper.
using rulers, plastic templates to create circles and squares, and colored pencils, all the while employing standardized pedigree nomenclature (Bennett et al., 1995). Now, I construct pedigrees using sophisticated software that creates visually appealing pedigrees and often simultaneously calculates an individual’s risk for developing various malignancies or having a germline mutation. These pedigrees can be updated with a few keystrokes. Families are always surprised that I spend so much time asking many questions about family history and constructing detailed pedigrees, whether with paper and pencil or with software. Even though the technology by which genetic testing is done is sophisticated, the pedigree, which is a relatively low-tech visual representation, has not really changed much and remains the critical starting point for risk assessment and a discussion about genetic testing (Mahon, 2016). I remind every family that the completeness and accuracy of the pedigree is important to select the best genetic test(s), as well as that the pedigree, along with the genetic test results, provides valuable information to guide recommendations for cancer prevention and detection (Mahon, 2016). I review the completed pedigree with the families at regular intervals; families I have followed for decades have pedigrees that have been updated multiple times as more information about family history or genetic test results becomes available.

Early in my career, we could look at pedigrees and discuss with the patient and his or her family why we thought the risk for a particular disease was elevated, and then recommend increased screening and provide education about leading a healthy lifestyle. However, no means existed to determine if someone in the family carried increased risk because of a genetic susceptibility mutation (or who that individual was). As a result, many individuals were undoubtedly subjected to unnecessary screening. Our methods were limited, and true cancer prevention was still a dream.

The Promise of Genetic Testing
Genetic testing for hereditary risk held the promise that individuals could be evaluated to determine if they carried a germline mutation conferring increased risk. Consequently, aggressive screening and prevention measures would be reserved for those with known risk, sparing unnecessary worry for those who did not inherit the risk and saving valuable healthcare dollars.

The real promise of genetic testing is not just identifying those with hereditary risk for developing cancer—it is in its potential for true cancer prevention (Rahman, 2014). A classic example is the woman with a BRCA1/2 mutation—which has an associated 85% lifetime risk for developing breast cancer and a 50% risk for developing ovarian cancer—who chooses risk-reducing mastectomies and oophorectomies (National Comprehensive Cancer Network [NCCN], 2017). Prevention of cancer became a plausible option and reality for families affected in this way if a germline mutation being passed from generation to generation could be identified. For the first time, members of such families had the potential to exert some control over their health risks, but this came with a significant price. Risk-reducing mastectomies and oophorectomies are drastic surgeries that come with physical and emotional costs (Razdan, Patel, Jewell, & McCarthy, 2016). With the promise of true cancer prevention came many new challenges.

Changing Roles
When genetic testing for germline mutations known to increase cancer risk became commercially available in the late 1990s, my role changed in what seemed like a blink of an eye. Like many new technologies and healthcare innovations, the initial uptake was slow. Families were understandably concerned about genetic discrimination. No federal protections were in place to prevent job and health insurance discrimination (Hudson, Holohan, & Collins, 2008). However, a number of brave families stepped up and embraced the potential risks and benefits that accompany genetic testing. When I disclosed to women who already had a diagnosis of breast cancer that they also carried a susceptibility gene, they often told me that the diagnosis of hereditary risk was as devastating as the diagnosis of breast cancer itself. The diagnosis of a germline mutation had a direct impact on siblings, offspring, and other relatives. These families taught me much, and I learned about the complex psychosocial and ethical considerations that accompany the courageous decision to engage in cancer genetic testing. As a nurse, I was challenged to find ways to deliver education about complex technological and biologic concepts in understandable terms so patients and families had enough information to make an informed decision about genetic testing that was consistent with their values and needs. Still another challenge is in coordinating care for other family members who are potentially at risk for having a germline mutation once a germline mutation is identified in a family (Sharaf, Myer, Stave, Diamond, & Ladabaum, 2013). Families may not live in the same geographic area and may need help finding a genetics professional in another region. Even more
challenging is helping individuals in families who are estranged share information that a germline mutation has been identified; these families must not only cope with fractured relationships but also the possibility that they are at substantially increased risk for having a diagnosis of cancer. I also had to learn how to best provide psychosocial care and support to enable these families to adjust to the diagnosis and make difficult decisions, as well as cope with uncertainty (Mahon, 2014b). For those families in which a germline mutation is detected, they trade the uncertainty of whether they have a hereditary risk for developing cancer for the uncertainty of how high the risk is, when or where the cancer may occur, and the effectiveness of the recommended cancer prevention and early detection strategies (including their limitations) (Hall, Forman, 2012).
Pilarski, Wiesner, & Giri, 2014). For example, the woman who does not have a diagnosis of cancer but learns that she has a deleterious BRCA mutation must confront the uncertainty of how soon she may develop melanoma or breast, ovarian, or pancreatic cancer and which cancer(s) she may develop (Hampel, Bennett, Buchanan, Pearlman, & Wiesner, 2013). Will it be in her right breast or her left ovary? Will it happen next year or in 15 years? Many do not realize that increased risk for developing pancreatic cancer is associated with mutations in the BRCA gene (NCCN, 2017). Little is known about pancreatic cancer screening, and no evidence-based guidelines are available (NCCN, 2017). This creates another area of uncertainty. Helping patients and families cope with uncertainty is an important, time-consuming, and difficult component of the genetic testing process that often goes unnoticed (Mahon, 2013a).

The early days of genetic testing for hereditary susceptibility also brought a lot of frustration. Insurance coverage was variable and required composition of detailed letters of medical necessity from the provider ordering the test. Probably even more frustrating were the many families who had overwhelming family histories of malignancy who tested negative for deleterious germline BRCA1/2 mutations. I was able to enroll some families in research studies that did not provide quick answers, but families at least felt that they were contributing to advancement of the science. For those families with histories highly suggestive of hereditary risk who tested negative or had a variant of unknown clinical significance, we continued to manage them just as we had early in my career. Recommendations were still based on personal and family history and were largely limited to increased screening and health promotion behaviors (Mahon, 2015).

### Changes to Practice

#### Political Influences

In 2008, the federal government passed the Genetic Information Nondiscrimination Act (GINA), which made employer discrimination against employees or applicants because of genetic and genomic information illegal, and it prohibited group health plans and health insurers from denying coverage to a healthy individual or charging that person higher premiums based solely on a genetic predisposition for developing a disease in the future (Hudson et al., 2008). Many families who had previously been reluctant to engage in genetic testing for hereditary risk moved forward because they no longer had to worry about losing their health insurance or being trapped in a job because of employment discrimination fears. GINA changed the way I educated patients about discrimination. However, I continue to discuss with patients how GINA does not provide protection when purchasing life or disability insurance. I feel pressure to be a good patient advocate and make sure patients and families understand this potential risk as part of the informed consent process. Families are understandably worried about discrimination.

#### Technological Influences

The question of what to do for patients who had previously tested negative when more genetic testing becomes available occurred for the first time when large rearrangement testing in the BRCA1/2 genes became available (such testing uses alternative laboratory testing methods because sequencing will not detect large duplications and deletions in genetic material, which may result in altered gene function). In October 2012, Medicare approved coverage for BRCA1/2 large rearrangement testing, and soon after, it was covered by most commercial insurance companies (Mahon, 2013b). I had many patients who had not undergone the large rearrangement testing and had undergone incomplete testing by 2012 standards. I was faced with the dilemma of how to let patients know about the updated testing. I sent a letter to patients who could benefit from testing; although some patients could not be found because their provided addresses and telephone numbers were no longer current, many came back for additional testing. In a small percentage of these patients, a germline mutation was identified, and they were able to engage in more appropriate cancer prevention and early detection; other family members were able to have the opportunity and option to undergo testing as well. Many genetics professionals, including myself, learned that recontacting patients is difficult and extremely labor intensive. Now, I spend a lot more time during the pretest phase of counseling and during disclosure instructing patients to call me back every year to determine if recommendations have changed or if more testing has become available that may be helpful. I also include a statement about this in every letter of recommendations I send to patients I see, as well as in the letter I send to the provider (this letter summarizes the risk assessment, results of genetic testing when done, and recommendations for cancer prevention and early detection). I have educated many providers about the importance of continually reviewing recommendations for cancer prevention and early detection and the possibility of more testing as the science of genetics and genomics evolves. I have many more patients and providers checking back than I did even three years ago. This helps to ensure more current and appropriate care.

#### Social Influences

In 2013, actress Angelina Jolie publicly announced that she carried a genetic mutation associated with a greatly increased risk for developing breast and ovarian cancer and had undergone risk-reducing mastectomies and breast reconstruction. In the early years of my clinical practice, when genetic testing was just beginning, most families shared such information among themselves but not with others because of fears of discrimination and lack of public understanding about why a woman may choose to undergo a risk-reducing surgery, which was often considered to be extreme (Borzekowski, Guan, Smith, Erby, & Roter, 2013). Jolie made families’ once-private discussions of their journey and their fears more socially acceptable. I did many TV, print, and radio interviews following the revelation that Jolie had undergone risk-reducing testing; although some patients could not be found because their provided addresses and telephone numbers were no longer current, many came back for additional testing. In a small percentage of these patients, a germline mutation was identified, and they were able to engage in more appropriate cancer prevention and early detection; other family members were able to have the opportunity and option to undergo testing as well. Many genetics professionals, including myself, learned that recontacting patients is difficult and extremely labor intensive. Now, I spend a lot more time during the pretest phase of counseling and during disclosure instructing patients to call me back every year to determine if recommendations have changed or if more testing has become available that may be helpful. I also include a statement about this in every letter of recommendations I send to patients I see, as well as in the letter I send to the provider (this letter summarizes the risk assessment, results of genetic testing when done, and recommendations for cancer prevention and early detection). I have educated many providers about the importance of continually reviewing recommendations for cancer prevention and early detection and the possibility of more testing as the science of genetics and genomics evolves. I have many more patients and providers checking back than I did even three years ago. This helps to ensure more current and appropriate care.
bilateral mastectomies, as well as after she underwent bilateral salpingo-oophorectomy in 2015. I was repeatedly asked if this was too drastic of a procedure. In response, I discussed how this decision is a personal one and noted that I have had the privilege of working with many families, most of whom had far fewer financial and social resources, who made similar complicated decisions and had difficult days. However, in time, and with social support, most have adjusted to the diagnosis and to the consequences of the decisions they have made about cancer prevention and early detection. Jolie did much to raise awareness about the potential benefits of genetic testing; in fact, the number of patients I saw after Jolie’s 2013 announcement more than doubled.

Other Influencers of Change
My practice changed again drastically in 2013 when next-generation testing became available and the U.S. Supreme Court ruled that naturally occurring DNA cannot be patented. Next-generation genetic testing uses a technology known as massively parallel sequencing, which enables the evaluation of multiple genes simultaneously at a lower cost (Hall et al., 2014). Suddenly, ordering testing involved choosing among a number of laboratories and multiple panels of genes. The question of recontacting patients also surfaced in a much bigger way. I expended a lot of effort learning about the many newly identified genetic mutations, management of individuals who have newly identified gene mutations, and the scientific techniques used in laboratories to analyze the genes and reclassify variants of unknown clinical significance—all of which is much more complicated than it appears. Counseling families about a panel of genes is a very different process than counseling them about a single gene or syndrome. Great variation exists among management strategies for genes on a single panel (Hampel et al., 2014). Patients need to understand the range of possible management strategies based on the genes on the panel, and they, along with their families, must grasp the rationale for why a particular panel was selected (Hall et al., 2014).

Humans have genetic variation. Each nucleotide in a gene is evaluated and classified into categories including pathogenic, likely pathogenic, likely benign, or no mutation detected (negative) (Evans, Powell, & Berg, 2017). Sometimes the meaning of the genetic variant is not clear, and it is classified as a genetic variant of unknown clinical significance. Many variants of unknown clinical significance are detected on panels of genes because multiple genes are tested, and many genes have been identified only recently, with less known about the clinical significance of a particular genetic variant (NCCN, 2017). Patients need to understand that their results may include the identification of one or more variants of unknown clinical significance (Mahon, 2015). I spend a lot of time telling patients that a variant of unknown clinical significance means that not enough data are available to determine if it is a harmful or harmless change in the genetic material. Many will eventually be reclassified, and most will be harmless, but a variant of unknown clinical significance is not clinically actionable (Richards et al., 2015). Recommendations are based on family and personal history, not the variant. Other family members will not be offered testing for the variant, except in the context of a clinical variant reclassification program. It is a frustrating result for families.

In 2014, the U.S. Food and Drug Administration approved the use of poly (ADP-ribose) polymerase (PARP) inhibitor therapy for the treatment of ovarian cancer in BRCA1/2 mutation–positive women (Scott, Swisher, & Kaufmann, 2015). Suddenly, many women with a previous diagnosis of ovarian cancer, along with gynecologic oncologists, were referring all their patients with ovarian cancer for genetic testing. Genetic testing for germline mutations was being used not only to understand risk and develop a plan for prevention, but also to select effective therapies (Scott et al., 2015). Similarly, microsatellite instability testing on colon cancer tissue is used to determine colon cancer therapies, but microsatellite instability can also be an indicator of genetic risk (Mahon, 2014a). More recently, tumor testing, particularly in ovarian and colon cancer, often identifies genetic changes; this information can be used to select better targeted therapies (Cheng et al., 2017). Most of these pathogenic genetic changes will be somatic genetic changes that are occurring in the tumor and will not be passed genetically to subsequent offspring. Some of these are germline changes; additional testing is required to determine if the change is germline and has implications for other family members (Cheng et al., 2017). Somatic tumor genetic testing is also used to predict whether chemotherapy may be beneficial in breast cancer (Schmidt, 2016). Patients may have difficulty understanding the difference between germline and somatic tumor testing, particularly when overlap exists. I spend a great deal of time educating patients about this difference.

The Nursing Component
Over the years, I have enrolled many families in various genetic and genomic studies. These often were families with a significant history of cancer who tested negative on the commercially available genetic tests. They enrolled in studies with the hope of finding a less common gene for which they could not obtain testing or for more expert care recommendations to manage risk from national and international experts. With the advent of next-generation sequencing and panel testing, many families have been enrolled in variant reclassification studies to better understand if the variant is harmful or harmless (Richards et al., 2015). These families are motivated not only to help themselves, but also to help future generations. Genetic and genomic research is complicated and
filled with many ethical conundrums (Ormond & Cho, 2014). I was encouraged when the National Cancer Moonshot Initiative Task Force was launched in 2016 and an oncology nurse was on the team (Oncology Nursing Society, 2016). The goal of the Cancer Moonshot is to accelerate cancer research, including genetic and genomic research, to improve prevention and treatment modalities in oncology care (Singer, Jacks, & Jaffee, 2016).

I am constantly confronted with the need to stay current in genetics and genomics. Finding quality education programs remains challenging, and being informed requires continually reading many journal articles and carefully researching newly identified pathogenic gene mutations and the management of associated disease risk prior to making recommendations. I did not have any formal training in cancer prevention, cancer screening, or genetics and genomics in my undergraduate or graduate studies. Formal training in these areas was available on a limited basis when I began my professional adventure in the world of prevention, detection, and genetics 30 years ago. In 2001, I was in the first group of 13 advanced practice nurses credentialed in genetics by the Genetic Nursing Credentialing Commission. In early 2016, many insurance companies began requiring patients to be evaluated by a credentialed genetics professional for coverage of genetic testing (Wang, Beattie, Ponce, & Phillips, 2011). Credentialed genetics professionals include physicians who are board certified in genetics, master’s-prepared genetic counselors, and advanced practice genetic nurses who are credentialed (advanced genetics nurse–board certified, or AGN-BC) through the American Nurses Credentialing Center. I could have never anticipated that the skill set I honed when I accepted that position in a cancer screening center would be so valuable.

I am frequently asked to provide education to healthcare professionals (e.g., physicians, residents, medical students, nurses, nursing students, allied health professionals, allied health students) so they will better understand cancer genetics and genomics; many times, the goal is for these professionals to be able to order a genetic test or panel of genetic tests after an hour or two of this education. I always feel overwhelmed by this request because I know we need to do a much better job of educating students and healthcare professionals about genetics and genomics and the importance of interprofessional care that includes a credentialed genetics professional on the team. Far more than a continuing education program is required for a healthcare professional to have the knowledge and expertise to order and interpret a genetic test, which is more complex than a simple blood test.

**Conclusion**

Today, we know that genetics and genomics directly affect the care of patients with cancer and their families and that the field is constantly evolving (Offit, 2016). Enormous challenges exist in regard to managing data in an ethical manner that efficiently and effectively advances genetic and genomic research, as outlined by the Cancer Moonshot (which seeks to accelerate cancer research to make more cancer therapies available to more patients, while also improving the ability to prevent cancer and detect it at an earlier stage by using genomic information and streamlining the management and accessibility of genomic data) (Hsu, Klemm, Kerlavage, Kusnezev, & Kibbe, 2017). I never could have anticipated the amazing explosion of developments in genetics and genomics during the past 30 years or the true potential for cancer prevention and more targeted effective treatments that have resulted. My colleague was wrong; I did not abandon oncology nursing practice. Oncology nurses need to be knowledgeable about genetics and genomics. It is exciting to think of the promise and potential for the next 30 years.

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