Patient care in the dawn of the genomic age

New scientific developments come with new nursing considerations.

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**APPLICATION** of genetics and genomic science to health care is emerging in full force and having a powerful effect on nursing practice. Genomic medicine—using an individual's genomic information to help guide diagnosis and treatment—is taking off as a healthcare discipline. (See *What’s in a name: Genetic vs. genomic and other basic terms.*)

This new era is characterized by its emphasis on addressing individual genetic makeup as part of care, which has profound implications for nurses. You may need to take into account patients' specific genetic characteristics when assessing them, managing their care, and providing education. Be ready for change:

- New genetic tests are expanding healthcare choices and treatment options.
- Advances in pharmacogenomics—the study of how genes affect a person's response to drugs—are taking off. Expect one day to administer medications based on your patients' specific genetic makeup, if you aren't doing so already.
- New ethical and legal questions are emerging and will undoubtedly affect nursing practice.

This article offers a crash course to get ready for nursing in the genomic age. We focus on three key areas: genetic testing, pharmacogenomics, and ethical and legal implications of genomic-based nursing practice. (See *Genetics: Back to basics.*)

**Genetic analysis**

Genetic tests identify changes in chromosomes, genes, and proteins. These tests can confirm or rule out a suspected genetic condition or help determine an individual’s likelihood of developing or passing on a genetic disorder.

Different methods are used to obtain genetic information about patients:

- **Molecular genetic tests** (or gene tests) study single genes or short lengths of DNA to identify variations or mutations that lead to disorders. (See *Understanding the role of genetic mutations.*)
- **Chromosomal tests** analyze whole chromosomes or long lengths of DNA to identify large genetic changes that could cause a genetic condition, such as an extra copy of a chromosome.
- **Biochemical tests** study the amount or activity level of proteins; abnormalities in either can indicate changes to the DNA that result in a genetic disorder.

**Prenatal and newborn testing**

Prenatal testing looks for alterations in chromosomes or DNA of a fetus. Recent scientific advances may allow for serum testing; however, at this time, the most common approach is capturing fetal cells through amniocentesis. These cells are tested for chromosomal abnormalities or metabolic disorders. One such abnormality is Trisomy 21, or Down syndrome, characterized by three copies of chromosome 21.

Newborn screening tests are performed when an infant is between 24 and 72 hours old. Depending on state requirements, these tests screen for 30 to 50 genetic alterations that can cause conditions such as phenylketonuria, cystic fibrosis, and sickle cell disease.

**Carrier and presymptomatic testing**

Carrier testing may reveal a specific gene alteration that can affect a patient's or offspring's health. For example, tests for the BrCA1 or BrCA2 mutation may detect an increased risk of developing breast or ovarian cancer. Carrier testing can determine if a patient has the same genetic alteration as a family member.

A patient may undergo presymptomatic testing to determine if he or she has a specific gene alteration that may indicate a high likelihood of becoming symptomatic for a particular condition. As in carrier testing, patients who get tested usually know about a specific condition that runs in their family; for example, Huntington disease, an adult-onset, degenerative condition that begins around age 40 to 60.

Presymptomatic testing is reserved for conditions with a high likelihood of occurring. In other words, the genetic variation has a high likelihood of producing an as-
Understanding the basic vocabulary of gene science is important. For instance, the words *genetic* and *genomic* are often used interchangeably but have different meanings. Use the glossary below as a guide.

**Gene** — a specific sequence of DNA on a single chromosome that encodes a particular product, such as an enzyme

**Genetics** — the study of heredity with a focus on the functioning and composition of individual genes

**Genetic testing** — examination of specific bits of DNA that have a known function, usually in a protein-coding gene

**Genome** — the entire set of genetic information across all 23 chromosome pairs in a human being

**Genomics** — the study of all genes and their interrelationships to identify their combined influence on growth and development

**Pharmacogenetics** — the study of a single gene’s role in a patient’s response to a drug

**Pharmacogenomics** — the study of how genes affect a patient’s response to drugs. It combines pharmacology and genomics toward the goal of developing effective, safe medications and doses specifically tailored to a patient’s genetic makeup; it encompasses the patient’s response to drugs, the entire genome, and gene–gene interactions. In this article, we use *pharmacogenomics* when discussing patient response to individual drugs.

The premise underlying pharmacogenomics is that knowledge of specific *genomic factors* affecting drug responses can be used to achieve greater precision in drug therapy.

With the development of trastuzumab (Herceptin), a humanized monoclonal antibody that targets the HER2 protein and improves prognosis and survival odds. It’s now standard practice to test for the HER2 biomarker when evaluating and managing breast cancer and before administering humanized monoclonal antibody therapy.

The examples that follow show in greater detail how pharmacogenomics helps to individualize and improve drug therapy.

**6-mercaptopurine**

In patients with acute lymphoblastic leukemia, metabolism of this drug is associated with an enzyme called thiopurine S-methyltransferase (TPMT). In some pediatric patients, reduced or absent TPMT enzyme will have implications for pharmacogenomics.

- Changes in TPMT activity may lead to increased levels of cytotoxic metabolites and increased risk for severe bone marrow suppression.
- Testing TPMT activity is recom-
mended and, if necessary, dosage is adjusted according to guidelines from the Clinical Pharmacogenetics Implementation Consortium.

Abacavir
In patients with human immunodeficiency virus, adverse effects of this antiviral drug may include a fatal multisystem hypersensitivity reaction characterized by fever, rash, and GI and respiratory symptoms.
• This reaction is associated with the human leukocyte antigen B HLA-B*57:01 variant.

• Genetic testing for HLA-B*57:01 is available.
• All patients about to start abacavir or abacavir-containing medications should be screened for the HLA-B*57:01 allele.
• Avoid using abacavir alone or in combination with other drugs in
Understanding the role of genetic mutations

DNA is constantly subject to mutations—accidental alterations in its code. Some mutations can cause missing or malformed proteins, which in turn can lead to disease.

Alterations may occur during cell division, when DNA gets duplicated. If cells don’t divide correctly, the daughter cell has different genetic material than the parent cell. When this happens, the new genetic code of the daughter cell goes through cell division, transcription, and translation with the mutation intact.

Mutations can be inherited or acquired, as when DNA is damaged by environmental factors like ultraviolet radiation, chemicals, or viruses. Many mutations have no effect at all; these are called silent mutations. Some mutations are beneficial; over time, they create genetic diversity, which keeps populations healthy. However, as nurses, our greatest concern is mutations that lead to illness.

Human genome under the microscope

Our genetic code, which determines things such as height, eye color, physique, and drug response, can be analyzed by sequencing the entire genome. The international Human Genome Project, started in 1990 and completed in 2003, was dedicated to this purpose. Scientists mapped out the genetic sequence of people with similar features and compared their findings to the sequences of people with different features. This enabled them to discover which specific variants in the genetic sequence—termed single nucleotide polymorphisms (SNPs)—are associated with the characteristic under study. While some SNPs are benign and code for characteristics like eye color, others appear in people with conditions such as diabetes, heart disease, and mental health conditions.

In this way, certain conditions can be mapped back to specific genes and genetic mutations. Some disorders can be traced back to the mutation of a single gene—cystic fibrosis, sickle cell anemia, Tay-Sachs disease, and phenylketonuria, to name a few. However, scientists discovered that multiple genes play a role in most conditions; these conditions are termed complex or multifactorial.

Today, modern technology continues to sequence DNA, looking for alterations in the genomes of persons with and without disease to better understand health and illness and exploring ways to use this information to treat and possibly prevent conditions.

Carbamazepine

In people of Asian descent who take this anticonvulsant, a genetic variation is strongly associated with Stevens-Johnson syndrome or toxic epidermal necrolysis.

- This reaction is associated with the human leukocyte antigen B HLA-B*15:02 variant.
- Genetic testing for HLA-B*15:02 is available.
- All patients about to start taking carbamazepine should be screened for the HLA-B*15:021 variant.
- Avoid using carbamazepine in HLA-B*15:02-positive patients to reduce risk of Stevens-Johnson syndrome or toxic epidermal necrolysis.

Psychiatric drugs

Certain psychiatric drugs are metabolized by the liver enzyme cytochrome P450, specifically CYP2D6. These include tricyclic antidepressants, multiple antipsychotics, and some selective serotonin reuptake inhibitors. Depending on genetic variation, the CYP2D6 enzyme can act as:

- an ultrarapid metabolizer—requires the administration of more drug to maintain a steady state
- an intermediate or extensive metabolizer—requires administration of a standard dose to maintain a steady state
- a poor metabolizer—requires the administration of a reduced standard dose to maintain a steady state or the use of an alternate agent if needed.

Tests are available and recommended but not required before initiating treatment.

Warfarin

Clinicians can improve drug efficacy and reduce adverse effects based on tests of the liver metabolism enzyme (CYP2C9 genotype) and the vitamin K epoxide reductase enzyme (VKORC1 genotype):

- **CYP2C9 genotype.** This genotype expresses the hepatic enzyme responsible for metabolizing S-warfarin, a form of the warfarin molecule. Genetic variations CYP2C9*2 and CYP2C9*3, which are common in the general population, result in decreased clearance and increased blood levels of S-warfarin. Patients with these genetic variations will receive a reduced warfarin dosage.
- **VKORC1 genotype.** This genotype codes for VKOR, which inhibits warfarin. Variations within this gene affect the patient’s response to warfarin; the major variation is the 1639G>A genotype, which reduces expression of VKOR. Patients with these genetic variations will receive a reduced warfarin dosage.

**Clopidogrel**

In patients taking this antiplatelet agent (CYP2C19), variants alter the conversion of the prodrug to an active metabolite.

- **CYP2C19 *1/*1 genotype.** This is the most prevalent genotype (referred to as the wild type); patients with this genotype receive standard dosing.
- **CYP2C19 *2/*8 genotype.** This genotype expresses the mutant or loss of function enzyme, leading to reduced conversion of the prodrug to active metabolite, or no conversion. In this case, an alternative antiplatelet drug will be ordered.
Ethical and legal considerations
Overarching ethical principles relevant to genomics are privacy, autonomy, and justice:

- **Privacy** is the principle that guides decisions related to access to and distribution of genetic information. For example, if a patient undergoes a genetic test, who will be able to access the results other than his or her medical provider? Does the lab own them? Does the patient? In what instances can they be shared with others without the patient’s consent?

- **Autonomy** addresses a patient’s right to accept or refuse a course of action. In genetics, the principle of autonomy underlies a patient’s right to consent to or to refuse a genetic test as well as the right to receive nondirective, comprehensive counseling. This principle also underlies the patient’s right to withdraw his or her consent for testing or research or to change his or her mind about a genetic test.

- **Justice**, also known as equity, is the principle that guides provision of equal and fair treatment for all. An example of justice in genetic testing is widespread access to the newborn screening process. Across the United States, all newborns are screened for a panel of genetic, metabolic, and endocrine conditions before leaving the hospital. However, full equity in the distribution of health care may not be possible. Not everyone has access to the same level of care; nor is everyone able to afford care. Genetic testing tends to be expensive and may not be covered by insurance, which means benefits from advances in the field may not reach everyone in the population.

The National Human Genome Research Institute (NHGRI), a branch of the National Institutes of Health, is committed to addressing these and other ethical issues. The NHGRI website is dedicated to providing information and education to the public about legal and ethical issues important to the genetics community.

Ethics in pharmacogenomics
As researchers develop genetically targeted medications, the risk increases that individuals will be labeled based on information from their genetic code. Insurers, and even some clinicians, tend to oversimplify the relationship between genes and behavior, leading to a narrow view of the patient.

You have an ethical obligation to remain impartial once you become aware of a patient’s genetic makeup.

For example, an alcoholic patient may take a drug designed to help him or her overcome addiction. Healthcare providers may focus on possible genetic factors causing the behavior rather than working with the patient in a holistic manner. Or an obese patient may be labeled as having the “obesity gene.” Healthcare providers and family members may ignore or excuse environmental, social, and psychological aspects of their condition. Patients who are labeled by others based on genetic information may feel dehumanized.

As a nurse, remember that most conditions linked to genetics are not the result of genetics alone. Most conditions (examples include hypertension, obesity, depression, and diabetes) result from a combination of a genetic predisposition and the environment. Holistic care is still needed to promote health for patients.

Keep in mind the Code of Ethics for Nurses put forth by the ANA. In particular, Provision 1 says, “the nurse practices with compassion and respect for the inherent dignity, worth, and unique attributes of every person.” This provision further instructs you to work with all persons under your care without “any bias or prejudice.” Similar to how the law prohibits insurers from discriminating based on genetic information, you have an ethical obligation to remain impartial once you become aware of a patient’s genetic makeup.

Privacy concerns
Before participating in research, patients are usually given an opportunity to ask questions and then required to sign a consent form stating the purpose of the genetic sample. However, the privacy of a patient’s genetic code may still be at risk.

Suppose, for example, researchers find a patient has a unique SNP not relevant to the current study. Several years later, an opportunity arises to use the same sample in another, groundbreaking research study. Researchers may need to address questions such as:

- Can the sample be used for the second test?
- Is another consent form necessary?
- If a treatment is found for a condition caused by this unique SNP, should researchers be required to notify the patient who gave the sample?

These questions may need to be addressed in the consent form when a patient participates in research. The NHGRI website offers sample consent forms that can be modified for your specific project.

If you work in a research setting, become familiar with the language of consent forms you use. Talk to each patient who participates in a research study to get a sense of whether he or she understands the research project and what consent
A wealth of resources

The following resources can help you learn more about genomics.

Clinical Pharmacogenetics Implementation Consortium
- www.pharmgkb.org/page/cpic
Here you’ll find peer-reviewed guidelines for translating genetic laboratory test results into actionable prescribing decisions for specific drugs.

DNA from the Beginning
- www.dnaftb.org/#molecules
Look here for educational information about genetics. The website is sponsored by Cold Spring Harbor Laboratory, a private, not-for-profit research and education institution at the forefront of molecular biology and genetics.

DNA Learning Center
- https://www.dnalc.org
Here you’ll find educational videos, and hands-on and webinar learning opportunities, also from the Cold Spring Harbor Laboratory. If you click on the resources link, you’ll find three-dimensional visualizations of cellular and molecular processes, including DNA transcription and translation.

Genetic Discrimination
- www.genome.gov/10002077/genetic-discrimination/
This link takes you to the section of the National Human Genome Research Institute (NHGRI) website that addresses genetic discrimination.

Genetics Home Reference
- ghr.nlm.nih.gov/primer
This site includes basic genetics education as well as information about specific genetic conditions. Genetics Home Reference is a service of the National Library of Medicine, which is part of the National Institutes of Health (NIH).

Genetic Nondiscrimination Act
- www.eeoc.gov/laws/statutes/gina.cfm

NHGRI
- www.genome.gov/
This site contains information about research projects, grants for research, and results from genomic research. It also provides basic education and addresses legal, ethical, and social issues.

Pharmacogenomics Knowledgebase
- www.pharmgkb.org/
Here you’ll find a comprehensive resource for clinicians and researchers with information about the effects of genetic variations on drug responses.

restricts employers from using or requesting genetic information for employment-related decisions. These two protections are meant to encourage patients to seek presymptomatic or carrier testing, as recommended by their clinicians, without fear that it may affect employment decisions or insurance coverage. This enables high-risk individuals to better plan for their own care. For example, if a patient knows she is at a higher risk for breast cancer than the general population, she and her clinician may choose for her to have more frequent mammograms or preventive surgery.

As science advances and medications continue to target an individual’s genetic makeup, patients will need reassurance that their genetic information will remain private, will be used properly for research, and will not become the basis for discrimination. These issues will likely be addressed through additional legislation at the national level. (See A wealth of resources.)

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Selected references
Please mark the correct answer online.

1. Which of the following chemical base pairing for DNA is correct?
   a. Thymine and cytosine
   b. Adenine and guanine
   c. Guanine and thymine
   d. Thymine and adenine

2. The study of how genes affect a patient’s response to drugs is called:
   a. pharmacogenomics.
   b. pharmacogenetics.
   c. genome.
   d. genomics.

3. Which statement about the role of translation in protein synthesis is correct?
   a. The ribosome and messenger RNA (mRNA) reads translation DNA.
   b. The double helix of DNA divides into two equal strands.
   c. Newly transcribed mRNA leaves the nucleus and moves to the cytoplasm.
   d. RNA interprets the genetic code on the DNA, using the same base pairs.

4. The combination of a base, sugar, and phosphate is called a:
   a. gene.
   b. protein.
   c. nucleotide.
   d. mutation.

5. Which statement about genetic mutations is correct?
   a. Variants in the genetic sequence are called single nucleotide polymorphisms (SNPs).
   b. Multiple genetic mutations rarely play a role in clinical disorders.
   c. SNPs are benign changes in the genome.
   d. Multiple genetic mutations play a role in cystic fibrosis and sickle cell anemia.

6. Newborn screening tests are performed when an infant is between:
   a. 12 and 24 hours old.
   b. 24 and 72 hours old.
   c. 72 and 84 hours old.
   d. 84 and 96 hours old.

7. Which statement about carrier and presymptomatic testing is correct?
   a. Presymptomatic testing is reserved for conditions with a high likelihood of occurring.
   b. Presymptomatic testing is reserved for conditions with a low likelihood of occurring.
   c. Carrier testing can determine if a patient has the same genetic alteration as a nonfamily member.
   d. Carrier testing for the BrCA1 or BrCA2 mutation reveals that a person has a decreased risk of breast cancer.

8. Your patient who had a stent placed in his left anterior descending artery is prescribed clopidogrel. Testing reveals he has the CYP2C19 *1/*1 genotype, so you anticipate that he will receive:
   a. an alternative drug.
   b. lower dosing.
   c. standard dosing.
   d. higher dosing.

9. Your patient, who is being started on warfarin, has the 1639G>A genotype. Based on this information, you would expect her to receive:
   a. an alternative drug.
   b. lower dosing.
   c. standard dosing.
   d. higher dosing.

10. Your patient with epilepsy is prescribed carbamazepine. Which of the following should you keep in mind?
    a. In people of African-American descent who are taking this drug, a genetic variation is strongly associated with Stevens-Johnson syndrome or toxic epidermal necrolysis.
    b. In people of Asian descent who are taking this drug, a genetic variation is strongly associated with Stevens-Johnson syndrome or toxic epidermal necrolysis.
    c. All patients about to start taking carbamazepine should be screened for HLA-B*57:01 variant.
    d. All patients about to start taking carbamazepine should be screened for the HLA-CYP2D6 enzyme.

11. Which of the following statements about the ethics of pharmacogenomics is correct?
    a. It has no impact on the risk that individuals will be labeled based on information from their genetic code.
    b. It decreases the risk that individuals will be labeled based on information from their genetic code.
    c. The Code of Ethics for Nurses does not include a statement relevant to how nurses should respond when they know a person’s genetic makeup.
    d. The Code of Ethics for Nurses says nurses have an ethical obligation to remain impartial once a person’s genetic makeup is known.

12. The benefits of genetic testing may not reach everyone, which relates to which ethical principle?
    a. Justice
    b. Autonomy
    c. Privacy
    d. Independence

Post-test passing score is 80%. Expiration: 3/1/20