While research from as far back as the 1960s indicates that genetic variations are directly responsible for different medication responses, only recently have the reduced costs of testing made the benefits of pharmacogenomics (PGx) available to many patients. Incorporating PGx insights into the consideration of medication options results in more safe, efficacious, and cost-effective drug therapies that improve patient care by reducing the need for “trial-and-error” periods.

The understanding of and support for PGx is expanding. The National Institutes of Health (NIH) maintains a list of clinical trials involving PGx¹ and works to maximize the benefits of pharmacogenomics research for individuals and society². The U.S. Food and Drug Administration (FDA) also maintains a list of around 200 biomarkers for genetic variations that are included in different sections of drug labels³.

It is important to view this information in the proper context to best serve the patient. While the list of clinical trials and pharmacogenetic tests is continually expanding, many medications are not yet associated with clinically useful guidance. The science is evolving and will require clinical resources that are already set up to monitor and interpret rapid advancements.

In both 2014⁴ and 2016⁵, the Journal of the Medical Library Association (JMLA) identified Lexicomp® as the strongest online resource for point-of-care clinical use of PGx information.
Case in Point: The Effect of Gene Variability on Pain Management

With both 11 percent of the adult U.S. population reporting some form of chronic pain and continuing concerns about opioid-related death, controlling misuse of the opioids prescribed to mitigate that pain is a major challenge for patient care teams. An increasingly viable method of ensuring that opioids are not overprescribed or abused is to consider how the patient’s genetic variations may affect opioid response.

A noteworthy example of applying PGx insights when prescribing pain medication is the association of the CYP2D6 genotype and the metabolism of opioids. Gene variations can affect the metabolism of some pain medications, such as codeine, resulting in lower or higher drug concentrations. This variability leads to patients being categorized as poor, intermediate, normal, or ultra-rapid metabolizers. Approximately 5-10 percent of patients have been found to have a deletion of the CYP2D6 gene (no activity), and between 1-2 percent and more than 20 percent of patients have multiple copies, or increased activity.

Although testing for CYP2D6 genotypes as a means of choosing a dose for any of these compounds is not yet considered standard practice, Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines provide CYP2D6 genotype-based recommendations for codeine use, along with additional recommendations for tramadol, oxycodone and hydrocodone, based on the available clinical evidence. Limited data is also available that guides the use of non-opioids, including tricyclic antidepressants.

When identifying patients who may potentially benefit from genomic screening before prescribing pain treatments, clinicians may want to consider the following factors:

- History: Has the patient tried and failed many therapies in the past?
- Polypharmacy: Multiple medications combined can create drug-drug and drug-gene interactions.
- Age: 50-75 percent of the elderly population experiences chronic pain; analysis of Medicare prescription plans reveals that only one-third of those covered by the plans had access to treatments other than opioids due to the low cost of opioids.
- Condition: Cancer patients and those suffering from post-surgical pain have been shown to struggle with longer-term management of pain.

By consulting the “CYP2D6 - Codeine Monograph” in Lexicomp, both physicians and pharmacists can be made aware of special considerations they should keep in mind when faced with this drug-gene pairing, including recommendations on when to perform genetic testing, alternate therapies to consider, and in-depth discussion of the gene on metabolization of codeine.
Case in Point: The Effect of Racial Heritage on Drug Disposition

The impact of race/ethnicity on drug disposition is understood to varying degrees by clinicians when making treatment decisions. Ongoing research is increasing the availability of information for clinicians to consider; in a 2015 review, researchers stated that approximately 20 percent of the new drugs approved in the past several years have known racial/ethnic differences in disposition.

One of the most well-known examples of race-specific pharmacogenetic responses involves G6PD deficiency, which is more common in individuals of African or Mediterranean heritage. The G6PD deficiency has been associated with a high risk for hemolysis with potentially significant consequences when these individuals are exposed to any of dozens of specific medications, including many antimalarial medications, phenazopyridine, nitrofurantoin, and other medications.

Two other less common relationships that are reflected in approved drug labeling include:

• Risk for severe hypersensitivity reactions due to carbamazepine in patients of Asian heritage, associated with presence of HLA-B*15:02.
• Risk for death due to excessive conversion of codeine into morphine, which is thought to vary by ethnicity, but is associated with the presence of multiple functional copies of the gene encoding CYP2D6.

Summary

As more medication responses are matched to genetic variations, it is important to use a clinical resource that recognizes the value of an evolving science that may permit more rapid identification of safer and more effective drug therapies. Lexicomp can serve as a first resource to find information and references on many genes and their interactions with common drugs, including those discussed above. The Pharmacogenomics field in applicable Lexicomp monographs also discusses management of treatment and ongoing research to monitor.

Lexicomp drug information and UpToDate clinical recommendations are developed by a global network of in-house and external clinical and pharmacy experts. With these resources aligned for care, your teams can enhance communication, reduce inconsistent practices, and connect clinical and pharmacy decisions to increase effectiveness.

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