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Pharmacogenomics for the primary care provider: Why should we care?

SINCE THE HUMAN GENOME was sequenced in 2000, the American public has continued to hold hope that our growing understanding of genetics will revolutionize the practice of medicine.

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One way genetics promises to improve the quality and value of health care is in personalized medicine, by helping us tailor treatment to a person's individual genetic makeup. One such approach is called *pharmacogenomics*.

Pharmacogenomics uses knowledge of a person's genetics to understand how a particular drug will work, or not work, in his or her body. For instance, some people might carry genes that make them more sensitive than average to a drug, and therefore they would require a lower dose. Others might have genes that make them resistant to the drug, meaning the drug is ineffective unless they receive a higher dose.

Adverse drug reactions are a leading cause of death in hospitalized patients in the United States and are responsible for billions of dollars in health care costs.^{1,2} Our current practice of prescribing for adult patients is largely trial-and-error, with the same dose given to all patients, in many cases with little regard even to sex, height, or weight.

Pharmacogenomics promises to change this way of prescribing to a customized approach that uses genetic information to predict an individual's response to medications. It is one piece of an overall initiative to personalize patient care based on the patient's individual characteristics and preferences.

OVERCOMING BARRIERS TO USING PHARMACOGENOMICS IN PRACTICE

If personalized medicine has promised to improve the quality and value of health care for our patients, why have we been so slow to adopt this information in clinical practice?

The usual barriers to clinical adoption certainly exist. We need further studies to determine whether genetic-based prescribing is truly valid, and for which patient populations. We need to determine whether this approach is cost-effective and better than the current standard of care. We need to work on payment options.

However, one of the largest barriers for busy primary care physicians is the lack of time to keep up with new information. Many practicing physicians were taught little about formal genetics in medical school. The body of scientific literature on pharmacogenomics is fragmented, and it crosses disease states and specialties, making it difficult to unite. Given the breadth of diseases treated and drugs prescribed by primary care physicians, it is unrealistic for most to keep track of the vast body of literature of pharmacogenomic testing and to decipher how to apply this to clinical practice.

In this issue of the *Journal*, Kitzmiller et al³ provide one solution to this problem, giving an overview of pharmacogenomic applications that might be pertinent to practicing physicians. However, as we try to make pharmacogenomics accessible to busy physicians, we need other solutions to integrate pharmacogenomic information efficiently into the clinical work flow. One approach might be to build pharmacogenomics into the electronic medical record. We can also store the integrated information

Personalized medicine promises to improve the quality and cost of care, but how do we adopt it?

in research databases and provide clinical recommendations on Internet sites such as www.pharmgkb.org, and we can develop applications to run on cell phones and iPads.

■ **QUESTIONS REMAIN**

Kitzmilller et al discuss an important step in this process, highlighting several key questions:

Should we seek genetics-based information to personalize drug selection? Based on the information presented in the literature and in the Kitzmilller paper, there may be circumstances when it is appropriate to consider doing so. While the evidence is not yet compelling to order these tests on a regular basis in clinical practice, this information might be helpful in some situations, such as for patients who have had adverse effects from minimal doses of antidepressants.

For now, clinicians should not abandon their current practice of personalizing patient care on the basis of personal, cultural, and economic preferences. Rather, they should consider pharmacogenomic information an additional piece of information when selecting drug therapy. We should also encourage health care systems and interested providers to be early adopters and to study how their outcomes compare with the standard of care.

Once we have this information, what is our obligation to use it? An increasing number of patients already have genetic information in their health record, either ordered by or provided to their physicians. However, there is little in the scientific literature to guide us in this arena.

Yet most of us would agree that if we have information (genetic or otherwise) that can help to select a drug type or dose or reduce adverse events or costs, we should consider this information in our decision-making. Several circumstances are documented in this paper and in the literature in which prior knowledge

about drug metabolism can help in selecting a dose of medication. One example would be the 50% recommended reduction in tricyclic antidepressant dose if the patient is a CYP2D6 poor metabolizer.⁴

■ **MOVING FORWARD AS A TEAM**

In summary, Kitzmilller et al bring to light the promise and the uncertainties that currently exist in the field of pharmacogenomics. While it is unclear if we should incorporate pharmacogenomic tests into standard medical practice at this time, it is clear that this information is becoming more readily available, whether or not we have requested it. Some would argue that, once we have the information, we have an obligation to use it, just as we use other information in our clinical decision-making. This means we need to develop tools and resources to help practitioners evaluate pharmacogenomic data and incorporate it into clinical care in an efficient manner.

The authors also highlight the need for more education about drug metabolism in general, and they cite several instances in which knowledge of drug interactions and metabolism can clearly influence decision-making. An example is paroxetine (Paxil) inhibition of tamoxifen (Nolvadex).⁵

Lastly, regardless of our personal feelings about the clinical usefulness of genetic testing in large populations, we need to work together to determine clinical utility and validity and to develop efficient ways to put into practice findings that could affect patient care. As we move forward, we need to work as a team, utilizing our clinical partners—pharmacists, pharmacologists, metabolism and health information technology experts, and medical geneticists. Working as a team, pooling our resources and tools, we move closer to providing world-class personalized health care. ■

If we have information that can help, we should use it in our decision-making

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