Medicine Personalized with a Genomic Twist

As a primary care provider, I am a bit skeptical of those who suggest that the concept of "personalized medicine" is new. Every day we sit down with our patients, listen to their concerns, make diagnoses, and attempt to tailor treatment to our patient's physical and psychosocial needs. In short, we personalize medicine. But do we really do this as well as we might? Though we rationalize our medication choices to ourselves and our patients, in the end, much of how we prescribe medicine relies on trial and error. This is inefficient and, all too often, dangerous.

The new vision of "personalized medicine" as touted today by academia, industry, and others could probably be better thought of as "genomically personalized medicine". In many ways, this vision truly represents a revolution in healthcare. A central axiom of the movement is the concept of 'The right drug at the right dose for the right person at the right time'. To illustrate the axiom, consider the following simple example. Assume you have a patient with a certain diagnosis that can be effectively treated with both drug X and drug Y. However, drug X and Y are toxic if not metabolized effectively. In 2007, as you have no idea how the patient might respond, you might choose drug X because it happens to be generic. Now consider the value of knowing *a priori* (through genetic testing) that your patient can't metabolize drug X but can metabolize drug Y. Given the toxicity of the un-metabolized drug X, this knowledge would dictate your choice of drug Y, thereby avoiding harm and expense. Powerful stuff.

Advances in pharmacogenomics – the science of studying how genetics and genetic variation influence drug therapy - are rapidly narrowing the gap between vision and reality. Already, specialty medicine is using FDA-approved tests like the UGT1A1 gene assay (which measures ability to metabolize the chemotherapeutic irinotecan) to make more rational drug choices.

Primary care won't be far behind. This is perhaps best illustrated by current clinical trials which are examining whether pre-emptive genetic testing for the ability to metabolize warfarin improves outcomes in patients requiring oral anticoagulation. As many readers know too well, warfarin has frustrated health care providers for many years, largely because of its narrow therapeutic index, high toxicity (devastating bleeding events), and wide variability in patient response to a given dose. Over the last several years, it has been shown that knowledge of variations in two genes (*CYP2C9* and *VKORC*) can allow accurate prediction of warfarin metabolism, and that this prediction can effectively guide selection of the starting dose. As well, genetic testing technology has advanced so that point of care analysis of an individual's genes affecting metabolism is feasible. Many have speculated that such testing may not only greatly reduce the burden of suffering associated with the use of warfarin, but also create a health care cost savings. Given the potential cost of introducing this technology into mainstream healthcare, others have been less sanguine. Ongoing trials examine whether incorporating genetic test results into warfarin management protocols enhances outcomes

(less time out of INR range, fewer adverse events) when compared to standard of care and, to some degree, the cost impact. Results from these trials will likely be out before the year's end. Similar clinical trials are underway that look at whether genetic testing that predicts selective serotonin re-uptake inhibitor metabolism improves clinical outcome.

In reality, using genetic information to predict how patients will metabolize currently available drugs is only a single facet of personalized medicine. In a somewhat longer time frame (perhaps in the next 10 years) primary care providers will likely be able to use at least a few drugs that target the molecular consequences of a patient's disease-causing gene variants. Fantasy? No, this is already true for the choice of herceptin in breast cancer therapy. An increasingly sophisticated form of "personalized medicine" is here to stay.