THREE PATIENTS received identical doses of codeine for postprocedural pain 2 hours ago. Dora Ames has good pain relief and is now smiling and joking with her husband, but Tony Silva is still complaining of pain, grimmacing, and moaning. Patricia Stevens isn’t complaining about anything, but she seems groggy.

Why have these three patients responded so differently to the same dose of the same drug? Each patient’s genetic makeup plays a part. In this article, I’ll introduce you to pharmaco-genetics, the study of how genetic variations influence a patient’s response to drugs. A working understanding of pharmacogenetics will help you individualize your interventions so each patient gets the maximum benefit from his medications with minimal adverse reactions.

To find out why these three patients responded so differently to codeine, let’s look into drug-metabolizing enzymes.

How enzyme variability affects response
Enzymes in the cytochrome P-450 (CYP 450) system help metabolize from 25% to 30% of currently available drugs. Approximately 40 CYP 450 genes have been identified. A genetic variation in any of these genes can affect how a person metabolizes certain drugs.

• Extensive metabolizers, who make up 75% to 80% of the population, have normal enzyme activity. People like Dora Ames, who achieve good pain control from a standard codeine dose, are in this group.

• Poor metabolizers are people who carry two decreased activity or loss-of-function alleles; they account for 10% to 15% of the population. People like Tony Silva who don’t achieve good pain control from a standard codeine dose, are in this group. For them, increasing the drug dose won’t improve pain relief. Instead, when one of these patients reports that he isn’t getting good pain relief despite standard doses of codeine, he should receive directly active opioid analgesics such as morphine or another drug derived from morphine.

• Ultrarapid metabolizers carry genes that are duplicated one or more times. People in this category (from 1% to 10% of the population) convert codeine to morphine too quickly. Like Patricia Stevens, they’re susceptible to adverse reactions, such as oversedation, from a standard codeine dose. Recent research suggests that ultrarapid metabolizers should receive low doses of the CYP 2D6 inhibitor quinidine.

A new way of typing
Some labs can now perform genotyping, a pharmacogenetic test, to identify extensive metabolizers, poor me-
tabolizers, and ultrarapid metabolizers. (See New genetic blood test approved.) This testing can improve efficacy, prevent adverse drug reactions, and help to determine the optimum dosage for the patient.

Although not practical for widespread use, genotyping is already being used when certain drugs are prescribed, such as tricyclic antidepressants and cancer chemotherapy. Antineoplastic drugs such as mercaptopurine, for example, can cause severe hematologic toxicity and death in 1 out of every 300 patients. Genotyping and functional assays of thiopurine S-methyltransferase (TPMT) in red blood cells can identify patients who can’t metabolize the drug.

About 10% of people have an inherited gene mutation that results in TPMT deficiency. These patients can now be safely treated with doses that are one-tenth to one-fifteenth of the usual dose, avoiding toxicity.

**Your role**
As a nurse caring for someone receiving drug therapy, you can take pharmacogenetics into consideration by:

* assessing the patient’s personal and family history for indications of pharmacogenetic risk; for example, an unexpected adverse drug reaction in the past
* arranging genetic testing to determine her genotype if indicated
* teaching her why genetic testing is being done after a diagnosis has been reached but before therapy begins
* telling her why she may be receiving a different drug than most people with her condition receive
* helping her understand the benefits and limitations of a drug regimen tailored to her genotype
* assessing and documenting her response to therapy.

Applying the principles of pharmacogenetics will help you anticipate and avoid adverse reactions and optimize your patient’s drug therapy.

**SELECTED REFERENCES**


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