# Cytochrome p450, Part 1
## What Nurses Really Need to Know

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**KEYWORDS**

• Adverse drug reactions • Adverse drug events • Pharmacogenetics
• Cytochrome p450 • Medication variation • Pharmacokinetics • Pharmacodynamics

**KEY POINTS**

- The purpose of this first article in a series of three is to describe the cytochrome p450 (CYP), to familiarize nurse practitioners with the nomenclature, and to explain the basis for variations in drug metabolism at it relates to the CYP family of enzymes.
- Because more pharmaceutical companies are including this information on their products, it is imperative that a thorough understanding of the meaning and function of the enzymes be included when prescribing medications.
- It is important to consider patients' classifications with regard to their ability to metabolize drugs based on variants in the enzyme system and the genetic basis for the distinctions.
- Gender and race considerations are demonstrable factors in the effect of medications and the levels of efficacy and toxicity or no effect.
- Through understanding the information that is available, and using the information in clinical practice, nurse practitioners will be more effective prescribers, have fewer adverse events, and have overall faster and better patient outcomes.

An abundance of literature and recent studies describes the impact of the CYP enzyme system and its impact on patient pharmacokinetics and pharmacodynamics as more pharmaceutical companies are including CYP information on their products. This important information has not translated, however, in practice, resulting in undermedicating patients, overmedicating patients, and treating patients with medications that simply do not work for those patients. In the absence of this information, or more accurately, not using or understanding the information that is available, clinicians prescribe medications in a trial-and-error approach, hoping for the desired outcome. Nurses administering medications must be vigilant for common side effects and for evaluating the efficacy of the medication, which can vary tremendously. In current clinical practice, when the desired results are not achieved by a specific medication, a different medication is prescribed, and then another and another until a desired outcome is reached. Each time this occurs, the patient becomes an experiment in

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finding the right medication for the situation. In the meantime, although patients are not experiencing therapeutic effects of medications, they may experience drug events that are harmful and in some cases even lethal. This is largely due to the genetic variations and drug interactions mediated by the CYP enzyme family.

Although well understood and enlightened by scientific research, the clinical application of the CYP enzyme family in nursing and in medicine remains embryonic. This is the first article in a series of 3 articles that hopes to provide nurses with an overview of the CYP family of enzymes, to describe their impact on drug metabolism, and to provide nurses at the bedside and nurses that prescribe with the tools needed to incorporate existing information about the enzymes into their practices to safely achieve effective patient outcomes.

## INTERINDIVIDUAL VARIATION IN DRUG RESPONSE

Interindividual variation in drug response poses a serious problem in the management of patients who are receiving medications to treat or prevent any disease or illness. Bioavailability of drug concentrations can vary more than 600-fold between two individuals with the same weight and using the same drug dosage.[1] Genetic variants can make a difference between two people even when treated with the same medications and same dose. Additionally, due to individual variations in response to drug therapy, this variability can result in toxicity and adverse drug reactions (ADRs). There are many factors that may account for differences in drug response, such as lifestyle choices or cultural practices, that inherently have the potential for alteration and change and, thus, are to some extent modifiable. Factors, such as gender, genetic makeup, and race, cannot be easily altered, if at all, and warrant consideration when determining which medication and dosage will provide appropriate treatment. Persons who are administering or prescribing medications can make the best decisions with regard to the most effective medication regimen when they understand fundamental aspects of interindividual variations at the cellular level that account for the disparities in drug responses. It is important for patient-centered care for nurses to have fundamental knowledge about the human CYP system, its impact on variant medications, current considerations in the management of specific clinical outcomes, and the ability to incorporate this information into nursing practice.

## ADVERSE DRUG REACTIONS

Nurses who administer medications have known for years that substantial interindividual variability occurs in clinical responses to drug treatments of acute and chronic diseases. The proportion of patients who respond to medications as intended is, on average, only approximately 50%, with a range of 25% to 60%.[2,3] This not only contributes to the incidence of ADRs but also poses a delay in reaching an appropriate therapeutic level of another drug and in achieving beneficial outcomes for patients. A landmark meta-analysis suggested that ADRs ranked between the fourth and sixth leading causes of death in the United States in 1994, having an impact on more than an estimated 2 million patients.[4–6] A more recent study identifies ADRs as the seventh leading cause of death[7]; there is evidence to support that fatal ADRs occur in approximately 0.32% of hospitalized patients.[6] Approximately 2 days of prolonged hospitalization are attributed to ADRs in the United States, and 100,000 deaths annually are estimated due to ADRs.[8,9]

Although ADRs have not been studied in the pediatric population to the same extent as in adults, the significance of the problem is a major concern. ADRs have been reported as the cause of 4.3% of pediatric hospital admissions in children under 2 years