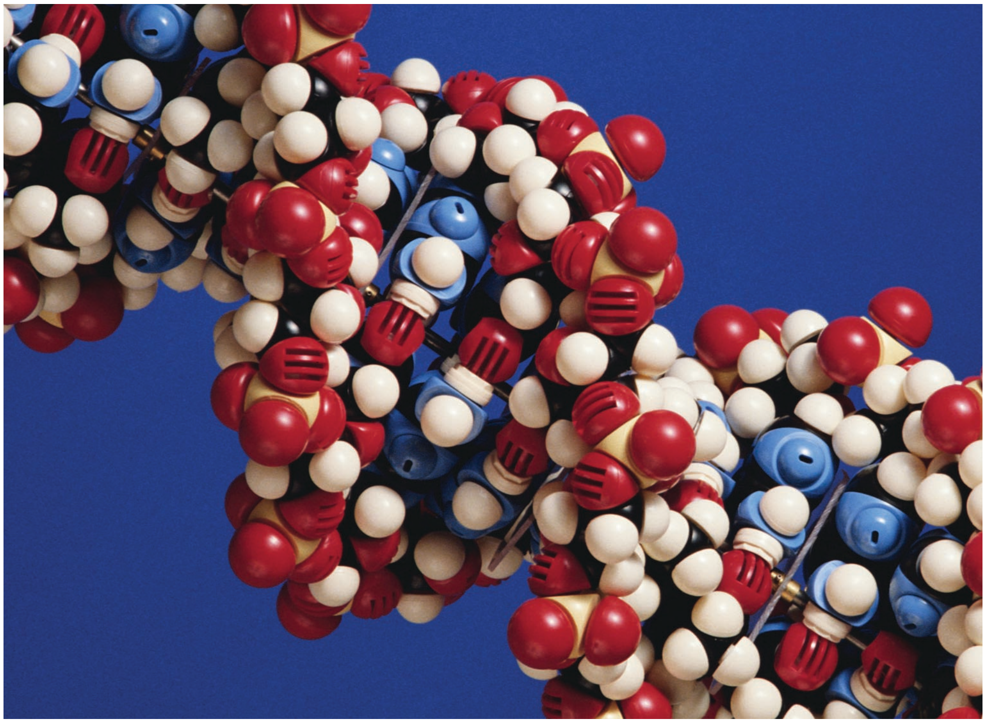
The Importance of Individualizing Prescribing among Genetically and Culturally Diverse Groups

BY VALENTINE J. BURROUGHS, M.D.



Addressing individual patient needs can provide better overall utilization of health care resources and improve health outcomes. Because patients differ in how their bodies process drugs due to many factors—age, gender, genetic variations, etc.—patients may experience different levels of effectiveness from drug therapies and variations in side effects associated with a particular drug. Thus individualized prescribing is key to making sure that each patient receives the right drug, in the right dose, and at the right time.

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The report of the Institute of Medicine, "Unequal Treatment: Confronting Racial and Ethnic Disparities in Healthcare," illustrates that disparities do exist and are prevalent both in the treatment of illness and in the delivery of health care services to minorities in the United States. Furthermore, these disparities are not confined to any one aspect of the health care setting and can even be found in the delivery of pharmaceutical services.

Research in the last 35 years has uncovered significant differences among population groups in their rates of drug metabolism, in clinical responses to drugs, and in drug side effects due to genetic variations, suggesting that those treating these patients need to take special care when prescribing pharmaceuticals. This issue is complicated by the difficulty in determining which patients will be affected by genetic variations and in what ways.

The grouping of humans into specific categories is a very crude predictor of response to therapy. However, until genetically-based diagnostic and prescribing practices can be incorporated into everyday medicine, these groupings—no matter how imprecise—can indicate an increased or decreased likelihood of atypical drug responses.

But treating individuals appropriately involves more than awareness of genetic variations. Apart from the physiological complexities associated with prescribing for different populations, practitioners face the added challenge of delivering effective pharmaceutical care to people within a psychosocial context appropriate to their culture and level of health literacy. The great diversity in our patient population demands a framework within which the practitioner can approach all patients, regardless of their background, as egalitarian partners in care.

The factors determining response to medications are complex and interdependent. Environmental factors such as climate as well as lifestyle choices such as smoking or alcohol consumption may have a profound effect on the way the body handles drugs. Cultural or psychosocial factors may affect a patient's adherence to a drug regimen, thus influencing the effectiveness of the drug. However, most of the variability in drug effects among individuals is determined principally by genetic factors. The study of genetically determined variations in drug response is called pharmacogenetics.

Pharmacogenetics

Pharmacogenetics research in the past few decades has uncovered significant differences among population groups in the metabolism, clinical effectiveness, and side-effect profiles of many drugs important in treating age-related diseases. Most studies have concentrated on cardiovascular medicines, including beta-blockers, diuretics, calcium channel blockers, and ACE inhibitors, and on drugs used to treat mental illness, such as antidepressants and antipsychotics. Analgesics such as acetaminophen and codeine, as well as antihistamines and alcohol, also show varying physiological effects among different populations.

> PHARMACOGENETICS COULD BE VERY BENEFICIAL IN PREDICTING DRUG INTERACTIONS AND ADVERSE REACTIONS.

Due to genetic variations, there can be significant differences in how proteins are encoded—and thus how drugs are metabolized—among population groups. Variations occur in all human genes, some of which alter the functioning of proteins. Encoded proteins that may show variation include the enzymes controlling the rate of drug metabolism and the proteins involved in drug response or disease progression.

Genetic variations alter the structure of drug-metabolizing enzymes by making them either less effective or more effective. Thus, people who carry these variations are either slow metabolizers or fast metabolizers of the drugs handled by that enzyme. A drug may become more highly concentrated in the bloodstream of poor metabolizers, which can result in stronger or longer drug action and side effects. Conversely, the drug is less concentrated in the bloodstream of fast metabolizers, resulting in weaker or briefer drug action or side effects.

Tests are now being developed to assess the levels of enzymes in the body that metabolize drugs used for cancer chemotherapy. Individual variations in the levels of these enzymes determine both the efficacy and toxicity of the drugs. Patients who are deficient in these enzymes may suffer severe, potentially fatal toxicity when exposed to standard doses of these medications, whereas chemotherapy may be less effective for patients with an excess of the enzymes. Other genetic tests are being evaluated for applications in treatments for Crohn's disease, rheumatoid arthritis, and kidney transplantation.

Pharmacogenetics research is also targeting a liver enzyme responsible for the metabolism of nearly 25 percent of all drugs, including many cardiovascular agents, antidepressants, antipsychotics, and morphine derivatives. By testing for the level of this enzyme, physicians can determine the correct dosage for their patients. For example, patients with a deficiency in this enzyme metabolize the antidepressant nortriptyline slowly and can tolerate only one-tenth the normal dosage. But patients who have inherited an ultra-rapid metabolism may require as much as five times the normal dose to receive a therapeutic effect. Variations in the gene controlling this liver enzyme differ in frequency among groups. Five to ten percent of African Americans and Caucasians and one to two percent of Asians have inherited the gene deficiency and are poor metabolizers. Interestingly, some African populations are rapid metabolizers.

Researchers hope to use pharmacogenetics testing to predict the effectiveness of non-pharmaceutical interventions as well by helping to understand the underlying pathophysiology. For instance, patients with high blood pressure are often advised to follow a low-salt diet, even though this intervention is effective in only a small percentage of patients because not all high blood pressure is salt sensitive. A test is now being developed to determine whether a patient carries a variant of a gene that controls salt retention.

Pharmacogenetics could also be very beneficial in predicting drug interactions and adverse reactions. This knowledge would be especially useful for treating elders and the chronically ill, who are at particular risk for drug interactions due to interventions involving multiple medications, as well as age-related changes in body functions. Pharmacogenetics testing will be valuable in assessing those diseases for which treatment response is difficult to evaluate, such as asthma, Alzheimer's, and depression.

Since different medications in the same drug class are often processed by different metabolic pathways, drugs of a given class may differ in their susceptibility to genetic differences in metabolism. In light of these differences, drug therapy for specific populations and patients should be individualized to achieve the most effective health outcomes. Physicians should resist pressures to apply drug therapy that does not take into account the ethnic origin of their patients. Physicians also should be alert to atypical drug responses or unexpected side effects—especially with cardiovascular or psychiatric drugs. Dosage adjustments may be required.

However, targeting the right medication in the right dose to the right patient is only half the battle. Health care providers must also be sensitive to cultural factors that may influence a patient's willingness or ability to comply with prescribed treatments.

Cultural Factors

Patients' beliefs regarding the properties and effects of medications are of central importance in determining compliance. For instance, some patients from non-Western backgrounds are unfamiliar with the practice of taking long-term medication for chronic illness and with the notion of accepting unpleasant side effects as the price for effective treatment. These reasons may account for why some patients stop taking their medication.[1] Variations in attitudes toward medicines tend to be driven by national characteristics, culture, and philosophy.[2] Immigrants from countries with different medical cultures may therefore have different expectations regarding the type of drug prescribed, tolerance of side effects, dosage form preference, or other aspects of drug therapy. This clash between patient and provider expectations may result in noncompliance with medications.

In comparison to other societies, American medicine tends to be very aggressive, leading to a greater focus on the effectiveness of treatment and a greater tolerance of side effects.[3] Downward dosage adjustment by Asian patients is common and results from the perception that Western medicines are too strong and that even relatively benign side effects are intolerable.

In Japan, in general, a medicine's safety profile is stressed more than its effectiveness.[4] This "pharmaceutical conservatism" mirrors the Japanese focus on slow and careful building of personal relationships and consensus-based business decisions.[5] This emphasis on safety and a systematic approach may explain, in part, the general use of lower dosages compared with dosages used in the West, and the lower incidence of side effects reported by Japanese compared with American and European patients.[6,7] In addition, patients in Japan frequently are treated with multiple medications because Asian patients often believe that multiple drugs are more effective than monotherapy since multiple herbal ingredients are usually prescribed by traditional Asian doctors.[8]

European medicine reflects a middle position between the poles of American and Japanese medical cultures. European practices differ in terms of the patterns and types of drugs prescribed, the preference for different dosage forms (the French favor suppositories, Latin Americans expect injections), and diagnoses in some countries that are not used in others (see Payer[9] for a detailed discussion).

THE CLASH BETWEEN PATIENT AND PROVIDER EXPECTATIONS MAY RESULT IN NONCOMPLIANCE WITH MEDICATIONS.

There is also a general expectation among many cultures that medicines will provide quick relief from symptoms and thus do not need to be taken long-term. In some developing countries, medications are customarily prescribed for only a day or two.[10] These beliefs may reflect their experiences with indigenous herbal preparations, which generally cause fewer side effects, and with analgesics and antibiotics, which work rapidly.[11] Hispanics and Asians often expect rapid results and are cautious about the side effects of Western medicines.[12,13] These beliefs may interfere with the acceptance of drugs with a delayed onset of action (e.g., antidepressants).

Lastly, poor health literacy may negatively impact patients' ability to take medications properly. Health literacy refers to the set of skills needed to read, understand, and act on basic health care information. More than 90 million adults in the U.S. have low health literacy skills, with limited ability to read and understand the instructions contained on prescriptions or medicine bottles, appointment slips, informed consent documents, insurance forms, and health educational materials.[14] Individuals for whom English is a second language or those who are socioeconomically disadvantaged may have limited literacy skills; and there is a relationship between low literacy and self-management skills, including taking medications properly.[15,16]

As a result of advances in pharmacogenetics research, more consideration is now being given to the need for individualized drug therapy. The availability of a broad range of medicines enables physicians to treat patients with precision and provides options when the first agent used is ineffective or not tolerated, or proper compliance is not achievable. Often, one drug cannot simply be substituted for another of the same class because its clinical effects may vary among population groups due to differences in drug metabolism. In order for health care practitioners to engage in appropriate prescribing, a wide range of options must therefore remain available.

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THE LANGUAGE OF MEDICINE

Due to the highly technical nature of the language of medicine, patients may not understand seemingly common medical terms. Compounding the problem is the skill of patients in concealing their poor health literacy. They usually will not acknowledge their deficiency due to feelings of shame, even though it interferes with their health.*

In a study of health vocabulary, only 13 percent of participants understood the meaning of the word "terminal," only 18 percent understood "malignant," and only 35 percent understood "orally."+

In a study of Medicare patients, striking deficiencies were found in their understanding of critical areas of health care:++

- 48 percent did not understand written instructions to "take medicine every six hours."
- 68 percent could not interpret a blood sugar level.
- 27 percent did not understand "take medicine on an empty stomach."
- 27 percent could not identify their next appointment.
- 100 percent could not understand a statement of Medicaid rights written at a 10th grade reading level.

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***Valentine J. Burroughs, M.D.**, is chair, Health Policy Committee for the National Medical Association Board of Trustees. Dr. Burroughs is a practicing, board-certified endocrinologist and internist. He is associate medical director and chairman of medicine at North General Hospital in Manhattan and medical director of Health Care New York IPA. Dr. Burroughs has special expertise in managing health care delivery and wellness programs for minority communities in managed care and public health environments.*