

Brave New World?

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The focus for the front cover of *CJHP* in 2002 has been the Human Genome Project and advances in science, medicine, and technology related to this project.

In the cover stories for *CJHP* this year, we have reviewed various aspects of the Human Genome Project. From a pharmacist's perspective, this brave new world is captured in the word "pharmacogenomics",^{1,2} the study of how an individual's genetic inheritance affects the body's response to drugs.³ Environment, diet, age, lifestyle, and state of health can all influence a person's response to a drug, but understanding his or her genetic makeup is thought to be key to creating personalized drugs with greater efficacy and safety.^{3,4}

The hope of pharmacogenomic research is that the 20th century's "one drug fits all" approach will evolve into an individualized approach to therapy whereby drugs are matched to a patient's unique genetic profile for optimal effectiveness.⁴ The assumption underlying this approach is that drug therapy specific for genetically defined subpopulations can be more efficacious and less toxic than in a broad population.⁵ However, in such a world the health care practitioner must know the phenotypic or genotypic profile of each patient. Is this requirement reasonable? First, would this not entail each of us giving up vast quantities of personal information? Second, to some extent, we already have at least some information of this type. For example, we are aware of inter-individual and inter-ethnic variation in cytochrome isozyme activity (CYP3A4⁶ and CYP2D6,⁷ among others⁸), P-glycoprotein (Pgp associated with multidrug resistance [MDR1]) activity,⁹ and responses to various drugs.¹⁰ Yet do we use this information to prospectively design dosage regimens for patients? No! Instead, we first use the drug or drugs that we feel would be best for the disease or condition being treated, usually starting with a standard dosage, possibly adjusted for weight, and if the response is not what we expect, we adjust the regimen (by increasing or



Image of the Earth taken by the Apollo 17 crew as they travelled toward the Moon on December 7, 1972. The extent of the photograph ranges from the Mediterranean Sea area to Antarctica. This was the first time the Apollo trajectory made it possible to photograph the south polar ice cap, visible at the bottom of the image. Photograph courtesy of the National Aeronautics and Space Administration (<http://grin.hq.nasa.gov/subject-space.html>)

decreasing dose) or we switch the patient to another drug. Similarly, how many readers are aware of the genetic variant of cytochrome that results in hypersensitivity to warfarin?¹¹ Such patients are often discovered during initial dose titration of warfarin, whereupon a much lower dose is eventually prescribed, and no further investigations are undertaken. Only rarely, outside the spheres of research and microbiology (specifically susceptibility profiles for bacteria or the human immunodeficiency virus), do patients prospectively undergo tests to determine phenotype, which is then used in selecting medications.

From these few examples it is clear that we are not using currently available drugs in a way that takes full advantage of the patient information that could be accessed, so why should we expect to magically do so once we have the results of pharmacogenomic research? Today, the primary reason for not completing phenotypic tests is cost, in terms of both resources and time. What evidence is there that in the future we will

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have the money and the time to obtain a phenotypic or genotypic profile for every patient to determine genetic susceptibilities and prescribe the drug that best fits the profile?

Here is another perspective from which to examine the issue: How badly are we doing with currently available drugs, in terms of managing disease and limiting adverse effects? If our current record isn't so good, maybe it's because we are not using the available drugs properly. Maybe we don't need a whole new generation of drugs that will also be used improperly.

The situation presented in *Gattaca*, a 1997 Sony film in which employment and mate selection in a futuristic society were based largely on nonconfidential genetic information, may simply represent a more advanced version of the scientifically engineered society described in Aldous Huxley's *Brave New World*.¹² However, I don't believe that this new world will be upon us any time soon. In the next 20 years, we pharmacists should devote our efforts to making sure the drugs we have are used properly.

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