

Could the chronic overproduction of the cysteinyl leukotrienes lead to dysregulation of the receptor to protect the airways by shifting to a ligand (LTE₄) that under normal circumstances is several logs less potent? Why would a further burst of cysteinyl leukotrienes after aspirin challenge desensitize a dysregulated receptor and sustain the state with long-term therapy? Could one class of prostanoid receptor regulate the cysteinyl leukotriene pathway and another increase the expression of cysteinyl leukotriene receptors?

The study by Sousa et al. provides insight into the abnormalities of the cysteinyl leukotriene pathway in patients with aspirin-sensitive asthma. At present, their findings cannot yet be linked to the two other critical observations in aspirin-sensitive asthma: the overproduction of cysteinyl leukotrienes and regulation by prostaglandin E₂ of that overproduction. Perhaps when that link is forged we will understand this complex disorder.

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GETTING READY FOR GENE-BASED MEDICINE

DESPITE much journalistic hyperbole, the publication last year of nearly complete sequences of the human genome^{1,2} did not mean that the practice of medicine would be abruptly and radically transformed. Medicine has not been a gene-free art form in living memory — a knowledge of genetics has had an increasingly important role in medicine for over a century. Nor will it soon, if ever, become an impersonal, information-based science enabling every person to know from birth the ailments he or she will have and the perfect way to treat them.

Still, changes in medical practice are already occurring at an accelerating pace under the influence of the elucidation of genomes. Medical genetics, once a tool for diagnosing a handful of relatively rare diseases inherited in a simple mendelian fashion, has expanded into new territories: the prediction of a healthy person's risks of even common diseases such as cancer and cardiovascular disease; the analysis of patterns of gene expression as an adjunct to conventional diagnostic methods, such as histopathology; and the evaluation of multigenic diseases and responses to environmental agents and drugs. Knowledge about the genomes of microbes is expanding the opportunities for diagnosing, preventing, and treating infectious diseases, and it is likely that such knowledge will soon contribute to defending our nation against bioterrorism. But the full potential of a DNA-based transformation of medicine will be realized only gradually, over the course of decades, as we try to understand the content of genomes and, most important, the physiological consequences of variations in their sequence.

The pace of this transformation will be limited not only by the pace of discovery, but also by the need to educate practicing physicians, their coworkers, and their patients about the uses and shortcomings of genetic information. Unfortunately, most medical schools did not anticipate the changes that molecular genetics would bring to modern medicine. As a result, the ranks of medical geneticists are sparse, and many physicians struggle with the new biology. Furthermore, the nation's battalion of genetic counselors has never grown to the size that would be needed in order to compensate for these deficiencies. As a result,

doctors, nurses, and the public will have to do some work on their own to learn about the genes and genomes that will progressively change medical practice.

With this issue, the *Journal* initiates a series of review articles — a number are scheduled to be published during the coming months — that should help health care professionals to help themselves. The first installment, by Guttmacher and Collins,³ describes some fundamental principles of modern genetics and genomics, illustrates the ways in which variations in single genes can influence medical decisions, and provides a helpful glossary of terms that will soon be incorporated into the daily language of medicine. In future issues, there will be articles about assessing the risk of disease with DNA tests, used either in selected persons or in large populations; about using genetic information to help control some common conditions, including metabolic and neurologic diseases; and about the disturbingly difficult ethical and legal issues raised by a gene-based approach to medicine. By the final installment, readers will understand how far-reaching the effects of genetics are likely to be and how far we have already come.

These changes in medicine are particularly gratifying to those of us who have devoted most of our professional lives to deciphering gene-based mechanisms of disease in the hope of improving health. But one message that emerges from the need for this new series of articles is the imperative to do a better job of anticipating and planning for all the consequences of such profound changes. If we are to provide the pub-

lic with the full benefits of medical science, we must now begin to ask some troubling questions: How can we better train the next generations of physicians to practice genetic medicine? How can increasingly complex genetic knowledge be made readily accessible to all practitioners when they need it? How much will the expanded use of gene-based methods further escalate the cost of health care, and who will pay for it? How can we ensure that these products of our science, largely financed by federal dollars, will reach all the citizens of our country? If the series begun in this issue of the *Journal* refocuses attention on these vexing social issues, it will serve a function just as important as the mission of teaching doctors, nurses, and patients the state of the science.

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Editor's note: This editorial and the Genomic Medicine Series it describes will be available without charge at <http://www.nejm.org>.

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