Exploring the human genome, and relearning genetics by necessity

The field of medical genetics continues to advance far beyond what many of us were exposed to in medical school and postgraduate training. Clinical genetics has evolved in tandem with advances in molecular biology, which now can realistically be called molecular medicine. We increasingly rely on molecular-based diagnostic tests instead of biochemical assays. Learning the basics and limitations of these tests is sufficient reason for us to update our knowledge of molecular medicine, but there are many more reasons for us to retool our thinking.

The ability to scan the entire human genome and to recognize variations in specific nucleotides within recognized genes is more than a technologic feat. It is now possible to assess the risk of some genetic diseases before they are phenotypically expressed. We are increasingly able to predict whether specific drugs will be effective or pose higher risks of adverse effects in individual patients, a field called pharmacogenomics. How much pharmacogenomics can and should be incorporated into our practice as part of personalized medicine remains to be determined.

Genome-wide association studies can answer certain research questions, but also raise additional ones. In some ways, these studies are like molecular epidemiology—they can demonstrate a statistical association between a risk factor and a clinical event such as a heart attack, but just as in traditional epidemiologic studies, association does not always equate with causation.

As discussed by Drs. Manace and Babyatsky in this issue of the Journal (page 182), additional techniques can be used to try to sort out the issue of association vs causation—in this case, whether C-reactive protein (CRP) is merely associated with cardiovascular events or is a cause of them. Using the tools of traditional clinical research, it would be ideal to demonstrate that the use of a highly specific inhibitor of the risk factor (CRP) prevents the disease. CRP levels can be lowered with statins, but these drugs also reduce levels of low-density lipoprotein cholesterol, which will lower the risk of cardiac events. Thus, statins do not have the specificity to prove that CRP causes myocardial infarction.

This paper is one of the first in the Journal to discuss advances in genomics that may affect our practice. Beginning in May, the Journal will begin a new series on personalized medicine to highlight the role that genetics and molecular medicine can play in our clinical practice and in our understanding of pathophysiology.