Gee Whiz, What's a GWAS?

Have you looked at your local newspaper today? Odds are that there is a news tidbit related to a genetic discovery buried within its pages. Moreover, whereas the genetics-related news article of five years ago likely reported on a discovery about a clinical fascinoma, today's article probably describes a discovery about a bread and butter disorder of primary care. Since many of us lack the time to read even the newspaper, a few examples of discoveries about the genetics of common disease that recently made news seem in order.

Diabetes. In the last few months seven new common genetic variants - inherited changes in DNA sequence at specific points in the genome - contributing to type 2 diabetes risk have been discovered. The total is now 10! At least one model suggests that individuals inheriting the highest risk variants are four times more likely to develop type 2 diabetes than those inheriting the lowest risk variants. *Prostate cancer*. In the last year, at least seven new genetic variants contributing to prostate cancer risk in the general population have been described. Inheritance of a subset of these variants very likely explains much of the disproportionate burden of prostate cancer among young African-American men. *Macular degeneratio*n. In the last two years, five common genetic variants contributing to the risk of macular degeneration have been described. Individuals inheriting the high-risk version of all five genetic markers appear to have a 250-fold increased risk of developing AMD in comparison to those that inherited the lowest risk variants.

A few of you cynical types out there might be thinking that the genetics research community has at long last recognized the importance of common disease. In truth, science has only recently developed tools that allow the successful study of complex disorders - those in which multiple genes and environment strongly interact. The information windfall has roots in the convergence of several factors, including the exponentially decreasing cost of sequencing DNA and the completion of a tool for studying the human genome called the HapMap. Making a long and fascinating story short, it is now feasible to look at statistical associations between disease status and large numbers of genetic variants across the genome in large numbers of people. Amazingly, what five years ago would literally have taken billions of dollars, several large labs, and years to complete can now be done by one lab group in a matter of months for less than a million dollars. This approach to learning about the genetics of common, complex disorders is known as a genome-wide association study (GWAS). Properly applied, the GWAS approach has incredible power to detect common genetic variants that contribute to small or large increases in disease risk in any one individual. The scientific yield is already enormous and the end is not in sight – in fact the examples cited above are the beginning drops of what should be a flood of such reports in the next few years.

But, how and how quickly will the data translate to clinical applications? Already at least one company has developed and is planning to market a genetic test for predicting the risk of developing diabetes. Numerous companies are targeting newly identified genes

for rational drug design. Studies are underway to examine how testing patients with panels of genetic risk markers for multiple common diseases may improve patient care as well as how patients themselves will react to this type of testing. Can you order testing for your patients based on the results of knowledge learned from GWAS-type studies today? Actually, yes. Should you? That remains to be seen. What is starkly apparent is that patient care will be strongly influenced by this tide of information, and primary care will have a front row seat.