Testing for inherited disorders includes a broad spectrum of diseases and is rapidly expanding into complex yet common diseases that are now recognized as having a genetic component. Genetic tests are routinely performed to confirm a suspected diagnosis, to predict the possibility of future disease or illness, to detect the presence of a carrier state in individuals who may be unaffected but whose children may be at risk, and to predict improved therapeutic responses. As we begin to experience the benefits of a completed Human Genome with the identification of more and more genes, genetic testing is becoming an increasingly common medical practice. While genetic testing can provide a definitive diagnosis for many inherited diseases, the complexities of applying these same principles to multifactorial diseases is a new frontier for the clinical laboratory. Given the rapid advances in new technologies, as well as a better understanding of genotype-phenotype correlations, it is inevitable that such testing will become a routine part of healthcare for all.

Genetic tests and labs offering them
Diagnostic laboratories now offer hundreds of genetic tests and databases — such as those found at Lab Tests Online (AACC), GeneTests Online, and the Association for Molecular Pathology — that can help identify specific tests and the laboratories that are offering them. For example, a current carrier-screening test for cystic fibrosis (CF) looks for 23 different mutations in the CFTR gene while other genetic tests may only look for a single mutation or polymorphism as in the case of the Factor V Leiden test associated with thrombophilia or the JAK2 assay associated polycythemia vera. Still other genetic tests may examine chromosomes to determine if the number is correct and if evidence exists of any chromosomal rearrangement or other abnormality. This kind of test can detect Down syndrome (an extra chromosome 21).

Most recently, cystic fibrosis carrier screening has been in the spotlight of the clinical laboratory community. Cystic fibrosis is an extremely heterogeneous disease and one of the most common autosomal recessive diseases known to occur in the European Caucasian population. In 1997, a National Institutes of Health consensus conference convened to address the need for a national screening program for CF. Outcomes range from early death from pulmonary complications to mild atypical disease in the second and third decades, and, rarely, a normal lifespan. The goal of screening for CF carrier status is to identify couples at risk for having a child with CF, allowing them to consider a range of reproductive options. For example, knowledge of carrier status may affect decisions concerning conception, use of donor gametes, pre-implantation genetic diagnosis, or prenatal genetic testing.

Testing for genetic diseases in families
Genetic testing for cystic fibrosis carrier status may be considered medically necessary for adults with a positive family history of CF, reproductive partners of individuals with CF, couples planning a pregnancy, and couples seeking prenatal testing. The American College of Medical Genetics (ACMG) in conjunction with the American College of Obstetricians and Gynecologists (ACOG) now recommend that all pregnant couples and those planning pregnancy be offered screening with a minimum panel of 23 CFTR mutations.

The majority of genetic testing for inherited diseases is conducted for families with a pronounced history of the disease. Prenatal genetic tests may be conducted through pre-implantation genetic diagnosis (where the diagnosis is made of an individual embryo before implantation), chorionic villus sampling or CVS, or amniocentesis.

Testing for inherited predisposition to common diseases such as cancer and heart disease is emerging. Genetic research is making great progress in identifying individuals at above average risk for
cardiovascular disease or CVD, such as deep vein thrombosis, hyperlipidemia, or atherosclerosis. Finding the genetic mutations or variations that lead to coronary heart disease and heart attack can lead to the design of new drugs intended to prevent or treat heart disease. As of now, coronary heart disease remains the No. 1 killer in the developed world. This avenue of genetic testing coupled to novel therapeutics could help to save countless lives.

**PGx and medical management of patients**

Related to this application of genetic testing is pharmacogenomics (PGx). PGx introduces the field of pharmacology to the human genome. PGx involves the assessment of genetic polymorphisms not typically associated with disease but, rather, benign variants that may be responsible for increased or decreased enzymatic activity of those enzymes involved in the metabolism of therapeutic drugs. While this concept is not new, the PGx field is now emerging as one of the potentially fastest growing applications in genetic testing.

Each individual has a unique genetic makeup and a specific family and personal history. In the medical management of a patient, each patient also has individual symptoms and reactions, both to disease and disease treatments. Scientists have spent the last few years identifying variations in genes and correlating those variations with the way patients metabolize different drugs. As a result, for many drugs it is becoming possible to better predict how an individual patient is going to respond to the drug or dosage of a particular drug. With this knowledge, physicians can adjust the dosage or even select alternative therapy. This, ultimately, will lead to a decrease in the risk for developing adverse drug reactions. These promising developments in genetic testing to predict a patient’s response to therapeutics are leading the way to what is being termed personalized medicine.

**The future of healthcare**

While current genetic testing may be applicable to about 2% of the general population, the frontiers of genetic testing in development promise future applicability to more than 60% of the population. Within the next five to seven years, there will be wider availability of genetic tests with more clinically useful indications.

Clinical laboratories will be in the forefront of the field of personalized medicine. DNA testing services will be a valuable tool in risk assessment of predisposition to disease as well as its treatment. As molecular diagnostics and new drug therapies grow together, more prognostic, diagnostic, and therapy monitoring tests will be required, particularly as new genetic variants are discovered.

Genetic testing is going to influence the future of medicine, drug research, and the development of new treatment options as it maps human molecular interactions that cause disease. Developments underway include individual patient genotypes (personal genetic profiles), prescription and drug dosage protocols based on genotype, and discovery of gene-variants associated with drug-receptors (making possible specific selection drug type).