The collection of family history has always been a tool for genetic evaluation, but it remains an essential tool even in the age of genomic medicine. Patients may have a risk for a disease based on family history regardless of the results of genetic and genomic tests. How this information is collected is less important than that relevant information is collected in the first place. There are many tools for collecting medical and family history information both by hand and electronically. Genetic and genomic testing should always be interpreted in the context of the personal and family history.

Historically, both pretest and posttest genetic counseling has been standard of care for genetic testing. This model should be adapted for primary care providers (PCPs) willing to learn critical information about the test and key concepts that patients need to make an informed testing decision. It is helpful for PCPs to discuss a few initial patients with a genetic counselor to prepare for the key concepts of pretest and posttest counseling. This article provides guidance about the recommended level of involvement of PCPs based on the test indication, test complexity, disorder management, and the potential for psychosocial sequela.

Pharmacogenomics (PGx) is a powerful tool that can predict increased risks of adverse effects and sub-therapeutic response to medications. This article establishes the core principles necessary for a primary care provider to meaningfully and prudently use PGx testing. Key topics include in which patients PGx testing should be considered, how PGx tests are ordered, how the results are translated into clinical recommendations, and what further advancements are likely in the near future. This will provide clinicians with a foundational knowledge of PGx that can allow incorporation of this tool into their practice or support further personal investigation.
Genetic Causes of Liver Disease: When to Suspect a Genetic Etiology, Initial Lab Testing, and the Basics of Management

Emily A. Schonfeld and Robert S. Brown Jr

Genetic causes of liver disease lead to a wide range of presentations. This article describes hereditary hemochromatosis, Gilbert syndrome, alpha-1 antitrypsin deficiency, Wilson disease, PFIC, BRIC, and LAL-D. The most common cause of hereditary hemochromatosis is a C282Y mutation in the HFE gene. Gilbert syndrome is a benign cause of indirect hyperbilirubinemia. Alpha-1 antitrypsin deficiency causes both lung and liver disease. Wilson disease can cause neurologic disease and liver disease. Progressive familial intrahepatic cholestasis and benign recurrent intrahepatic cholestasis are rare causes of cholestasis. LAL-D is a rare disease that can appear similar to NAFLD in adults.

Genetics and Precision Medicine: Heritable Thoracic Aortic Disease

Erin Demo, Christina Rigelsky, Andrea L. Rideout, Madeline Graf, Mitchel Pariani, Ellen Regalado, and Gretchen MacCarrick

Heritable thoracic aortic disease (HTAD) can have life-threatening consequences if not diagnosed early. Affected individuals and at-risk family members benefit from both cardiology and genetic evaluations, including genetic testing. Important information can be obtained through family history, medical history, and genetic testing to help guide management and assess risk. A genetic diagnosis can guide cardiovascular management (type and frequency of vascular imaging, timing of surgical intervention), risk assessment for arterial aneurysm/dissection, evaluation of nonvascular features, and familial testing.

Symptomatic Joint Hypermobility: The Hypermobile Type of Ehlers-Danlos Syndrome and the Hypermobility Spectrum Disorders

Brad T. Tinkle and Howard P. Levy

Joint hypermobility may be syndromic or nonsyndromic, asymptomatic or symptomatic. However, asymptomatic joint hypermobility can cause repetitive use injury, alter biomechanics, or become symptomatic later in life. Symptomatic joint hypermobility can result from soft tissue injury or muscular strain caused by muscular imbalance. Treatment is straightforward once joint hypermobility is recognized. Generalized joint hypermobility can be assessed using a standardized in-office examination. Generalized joint hypermobility may also be a feature of a heritable connective tissue disorder with other systemic findings. Therefore, assessing joint hypermobility in the context of musculoskeletal complaints may lead to recognizing systemic manifestations and allow treatment accordingly.

The Diagnosis and Management of Neurofibromatosis Type 1

K. Ina Ly and Jaishri O. Blakeley

Neurofibromatosis type 1 (NF1), NF2, and schwannomatosis are related, but distinct, tumor suppressor syndromes characterized by a predilection for tumors in the central and peripheral nervous systems. NF1 is one of the
most common autosomal dominant conditions of the nervous system. NF1 has a high degree of variability in clinical presentation, which may include multiple neoplasms as well as cutaneous, vascular, bony, and cognitive features. Some of these manifestations overlap with other genetic conditions. Accurate diagnosis of NF1 is important for individualizing clinical care and genetic counseling. This article summarizes the clinical features, diagnostic work-up, and management of NF1.

**Approach to Assessment of Parkinson Disease with Emphasis on Genetic Testing**

Katelyn Payne, Brooke Walls, and Joanne Wojcieszek

This article presents a nongeneticist’s guide to understanding the genetics of Parkinson disease (PD), including clinical diagnostic criteria, differential diagnoses, symptom management, when to suspect a hereditary factor, a summary of autosomal dominant and recessive PD genes, and proposed algorithm for genetic testing. There is increasing availability of genetic testing for PD but there are few recommendations on how these tests should be used in clinical practice. This article guides clinicians on the overall management of patients with PD, with emphasis on determining which patients should have genetic testing and how to interpret the results.

**Population Whole Exome Screening: Primary Care Provider Attitudes About Preparedness, Information Avoidance, and Nudging**

Patrick R. Heck and Michelle N. Meyer

Compared to clinicians previously surveyed, primary care providers employed in a health system known for clinical genomics were more likely to have ordered or referred a patient for genetic testing, but had only modestly more genetics training and reported similarly low levels of comfort answering patient questions about genetic risk. Most supported population genomic screening, reported willingness to get screened themselves, and judged a hypothetical patient’s decision to be screened favorably relative to a similar patient’s decision to decline screening. Stakeholder perceptions of the ethical appropriateness of nudging at-risk patients to discuss testing with counselors were mixed.