With the recent expansion of genetic science, its evolving translation to clinical medicine, and the growing number of available resources for genomics in primary care, the primary care provider must increasingly integrate genetics and genomics into daily practice. Because primary care medicine combines the treatment of acute illness with disease prevention and anticipatory guidance, the primary care provider is in an ideal position to evaluate and treat patients for genetic disease. The notion that genetic knowledge is only rarely needed will have to be replaced with a comprehensive approach that integrates “genetic thinking” into every patient encounter. Genomic competencies will need to be added to the primary care provider’s repertoire; such competencies include prevention, assessment, evaluation, and diagnosis of genetic conditions; the ordering and interpreting of genetic tests; communication with families; appropriate referrals; and the management or comanagement of care. The process of deciding when to order genetic tests, what tests to order, and how to interpret the results is complex, and the tests and their results have specific risks and benefits, especially for pediatric patients. The longitudinal nature of primary pediatric care provides the opportunity to obtain and continually update the family history, which is the most powerful initial genetic “test.” The ongoing provider–family relationship, coupled with the astounding number of advances in genetic and genomic testing, also necessitates a constant re-evaluation of past diagnosis or nondiagnosis. Pediatrics 2013;132:S231–S237
The recent expansion of genetic and genomic science and its evolving translation into clinical medicine mandate that primary care pediatricians be prepared to integrate genetics and genomics into their daily practice.1

MH, a 13-year-old girl, comes into her pediatrician’s office on Saturday morn- ing as a new patient, with a history of “fainting” while playing soccer earlier in the morning. She had no warning and “just went down.” She has abrasions on her forehead and knees but otherwise feels well.

For decades, knowledge of genetics has played a large role in the health care of a few patients and a small role in the health care of many. Genomic advances over the past several decades, however, have broadly increased our understanding of the genetic contributions to health and disease, and not just for rare conditions.2 Therefore, the notion that genetic knowledge is only rarely needed will have to be replaced with a comprehensive approach that integrates “genetic thinking” into every patient encounter. In addition, public awareness of the explosion of genetic and genomic knowledge coupled with the increased availability of DNA-based testing has led patients and families to demand genetic information and advice from their primary care physicians.

Primary care medicine combines the treatment of acute illness with disease prevention and anticipatory guidance. This combination places the primary care pediatrician in an ideal position to evaluate and treat patients for genetic disease and to provide advice about genomic information. The longitudinal nature of primary pediatric care also provides the opportunity to obtain and continually update the family health history, our most powerful initial genetic “test,” and to incorporate new genomic applications as they become clinically appropriate. The primary care pediatrician’s roles in genomic medicine will include prevention, evaluation, and diagnosis; communication with families; ordering and interpreting genetic tests; making appropriate referrals; and managing or comanaging care. Important components of this information exchange with families will include understanding the familial, psychosocial, and ethical issues raised by genetic testing.

**HISTORY OF GENETICS IN PRIMARY CARE**

Primary care physicians have integrated genetics into practice for decades. Since Sir Archibald Garrod’s description of alkaptonuria in 1908, physicians have understood the genetic transmission of many rare diseases.3 Since the advent of testing for phenylketonuria in the 1960s, newborn screening has been a part of primary care for mothers and newborns.4 The rapid increase in the number of congenital conditions that are included in state-mandated newborn screening programs and the robust public health support for these programs has provided a model for early diagnosis and treatment of genetic diseases.5 As a result of newborn screening guidance, health care providers have ordered genetic testing on virtually every newborn in their care during the last 5 decades and have been expected to provide both short- and long-term follow-up for those patients. With the establishment in 1956 that the human chromosome complement is 46 chromosomes° and the discovery in 1959 that trisomy of chromosome 21 is the cause of Down syndrome,7 the use of cytogenetics for diagnosis became part of the practice of primary care.

The rise of molecular genetics in the 1970s and 1980s led to the successful sequencing of the human genome in 2001 as a result of the Human Genome Project.8 This milestone led to an exponential growth in genetic knowledge, with the result that primary care providers now deal with a continuously expanding array of genetic tests. The advent of whole-genome sequencing in the clinical setting adds urgency to the need for providers to effectively and responsibly integrate genetics into their daily practice.9

**EVALUATION AND DIAGNOSIS**

Individually, single-gene disorders are often rare, but collectively they constitute a significant proportion of both pediatric and adult-onset disorders. A systematic review of 5747 consecutive admissions to a children’s hospital in 1996 found that 71% of admitted children had disorders with a genetic determinant. The 34% of admissions with clearly genetic underlying disorders accounted for 50% of the total hospital charges.10 The public health burden of genetically related disorders becomes even more substantial when we include complex conditions with a genetic component to their etiology, such as cancer, obesity, and heart disease.

The wide variety of genetic conditions that may be encountered in primary care challenges the clinician and requires both a systematic alertness for identifying genetic clues when evaluating a clinical condition or when assessing the family history and a methodologic approach when considering genetic etiologies in the differential diagnosis.

A focused family history reveals MH’s mother had a number of fainting episodes as a teenager, but none in the past 20 years. MH has a sister, age 11 years, who is well, and had a brother who died of sudden infant death syndrome at age 8 months. Her maternal grandmother died at age 56 years due to “heart disease.”

Every patient warrants a family history, but a multigenerational family history is usually not necessary. A directed, “just-in-time” family history will often meet the needs of the primary care practitioner at a specific clinical
encounter. Nevertheless, the multigenerational family history is sometimes an important tool. It should be taken on an as-needed basis and can help inform a diagnosis and identify other at-risk family members who might benefit from genetic counseling or testing. It can also be used to identify individuals at risk for conditions that might be prevented or mitigated by lifestyle changes, increased monitoring, or genetic testing. The primary care pediatrician is in an ideal position to obtain a progressive and dynamic family health history throughout the life stages of a child and his or her family.

A family health history, whether targeted or multigenerational, can be captured in many formats. The 5-generational pedigree that illustrates the biological relationships within the family calls attention to patterns that suggest a genetic etiology. Regardless of the format, the family health history should document diagnoses in the family, ages of onset of affected family members, and the relationships of family members. Some red flags that provide clues to a genetic condition include multiple family members affected with the same condition, earlier-than-expected age of onset, presentation in the less-frequently-affected gender, ethnic background associated with certain conditions, multifocal or bilateral occurrence in paired organs, and intellectual impairment with or without major or minor malformations. When a specific genetic condition is suspected, a more targeted family health history is helpful to look for red flags associated with that condition, because many genetic conditions have variable presenting features.

Ideally, the family health history would be captured in an electronic medical record, would be updated regularly to capture new information, and would include clinical decision support to aid the clinician in identifying patients for whom additional genetic evaluation and testing are warranted. Unfortunately, however, many electronic medical records do not handle family history information well, and support tools for clinical decision-making are not available. This situation will need to be addressed if the full potential of genomic medicine is to be realized in clinical care. The inclusion of a family health history objective in the stage 2 meaningful use criteria for the development of electronic health records should help stimulate the development of such tools.

Many genetic disorders can be diagnosed solely from the presenting features, the family health history, or both. The role of the primary care pediatrician in establishing a genetic diagnosis will depend on his or her training and familiarity with the presenting features and variable expression of genetic conditions. Some pediatricians will prefer to initiate an evaluation and then refer to a geneticist, and others will refer directly to a geneticist when a genetic etiology is suspected. In either scenario, the importance of a diagnosis cannot be overstated; a diagnosis can inform treatment, aid reproductive decision-making, identify other family members at risk, and alleviate the psychosocial burden of the diagnostic odyssey on families.

GENETIC TESTING AND COMMUNICATION OF RISK

The original laboratory report on the cousin’s genetic testing (performed in 2002) revealed the following result: “No LQTS mutations detected.” Although some diagnoses can be made clinically, many require confirmation with the use of genetic testing. Even when the diagnosis is certain, genetic testing can identify the specific mutation responsible, and at-risk family members can therefore be tested or reproductive decisions can be made. The challenge for the clinician is developing a strategy for incorporating genetic testing into patient care. Primary care physicians should anticipate an influx of genetic information and will need to become adept at interpreting this type of predictive information, while recognizing the unique ethical, legal, and social implications of genetic testing in children, such as the testing of children for adult-onset disorders.

The process of deciding which patient (or family member) to test, when to test, what test to use, how to interpret the results on the basis of clinical scenario and family health history, and when to refer for medical genetics consultation can be complex. Efficiently managing this triage process requires physicians to think genetically while using their skills in diagnosis and management (up to their comfort level) and providing patients with a cost-effective route to the most appropriate genetics professional at the most appropriate time or times in the patient’s care. A primary care physician who can answer the set of questions in Table 1 is thinking genetically.

When developing a testing strategy, primary care physicians should consider the various uses of genetic
testing: (1) making a diagnosis in symptomatic and asymptomatic patients; (2) assessing risk; (3) informing prognosis and medical management; (4) guiding reproductive decision-making; and (4) screening populations. In addition, primary care physicians must consider the degree to which a child will participate in the informed consent process. The age of the child, the reason for testing, the ability of the child to understand and participate in the decision-making process, and parental wishes must be considered.

Identifying the correct test and the appropriate laboratory for testing can be challenging, although Web-based resources such as the Genetic Testing Registry have facilitated those tasks somewhat. In addition, the Centers for Disease Control and Prevention’s Office of Public Health Genomics has divided genetic tests and applications into 3 tiers according to levels of evidence and recommendations from various review groups.18

MH’s pediatrician consulted with a medical geneticist at a nearby tertiary care medical center who recommended retesting because of a number of new mutations that had been reported in the past 8 years. LQTS panel results: “Mutation in SNTA1 [LQT 12].” This mutation is an uncommon cause of LQTS first reported in 2008.19

Pharmacogenetic tests represent a special category of predictive genetic tests that will likely play an increasingly important role in clinical practice. These are tests for gene variants, usually in genes that encode drug-metabolizing enzymes, which predict an individual’s response to a drug or class of drugs. Because such tests will allow personalized drug prescribing, they offer a potential means to reduce adverse reactions and increase the efficacy of drug treatment. A few of these tests are currently being used, and a number of them are undergoing prospective evaluation to ensure that they provide a health outcome benefit.20

Management and Coordination of Care

Once patients and families have a genetic diagnosis, their ongoing care typically falls to the primary care physician. This care should be provided within the medical home model of care developed by the American Academy of Pediatrics.21 The medical home model was adopted by the major primary care organizations in 2007 in the form of the Patient-Centered Medical Home standards. The medical home is a model for providing care that meets preventive, primary, and tertiary needs and is accessible, continuous, comprehensive, family-centered, coordinated, compassionate, and culturally effective.

Because LQTS is an autosomal dominant disease that typically presents with syncope but can manifest as sudden cardiac death, this family was referred to both a pediatric cardiologist and medical geneticist for extended clinical and molecular genetic testing. The results for extended SNTA1 mutation testing were all positive for MH, her mother, her cousin, and her uncle.

For children and youth with special health care needs, an essential component of the medical home model is the care coordination that links children and their families with appropriate services and resources.22 Patients with genetic diagnoses often have a number of medical providers involved in their care. It is also common for care to be coordinated across all elements of the health care system (eg, subspecialists, hospitals, home health agencies, public health agencies) and the patient’s community (eg, family and public and private community-based services). This complexity highlights the importance of effective communication between the primary care physician, subspecialty physicians, and the family.

A key element of the medical home model of care is a comprehensive assessment of needs and strengths, developed in conjunction with the family. The information from this assessment and the resulting care plan support effective collaboration within the medical system and among community partners. The assessment should include a thorough review of medical and nonmedical needs. In addition to the general care plan (or action care plan), the medical team should develop an emergency care plan for children and youth with special health care needs. This plan must be portable and immediately available to personnel working in hospital emergency departments, offices and clinics, community settings (eg, school, child care facilities, athletic venues), and even in the family home. This plan often has a substantial genetic component or requires significant input from the genetics subspecialist.
THE ETHICAL, LEGAL, AND SOCIAL ISSUES OF GENOMICS IN PRIMARY CARE PRACTICE

In the clinical application of genomic information, numerous complex ethical, legal, and social issues can arise in the clinical application of genomic information. These include issues such as confidentiality, genetic discrimination, direct-to-consumer genetic testing, predictive genetic testing in children, duty to contact, access, health disparities, cultural awareness, and race and genetics. In this section, we address several of these issues that are particularly relevant to the primary care practitioner.

The fear that health insurance providers and employers might use genetic information against a person is commonly cited as a reason not to obtain a genetic test. The Genetic Information Nondiscrimination Act (GINA), which was passed in May 2008 and went into effect in November 2009, was created to address this barrier to the use of genomic information (Table 2). Under GINA, group and individual health insurers cannot use a person’s genetic information (which includes family health history, carrier testing, prenatal genetic testing, susceptibility and predictive testing, and tumor testing for somatic mutations) to set eligibility requirements or establish premium or contribution amounts and cannot request or require a person undergo a genetic test. Likewise, an employer cannot use a person’s genetic information in decisions about hiring, firing, job assignments, or promotions and cannot request, require, or purchase genetic information about an employee or family member. The protections afforded under GINA are limited, however. GINA does not provide protection when a condition has already been diagnosed or manifested, and it does not apply to life, disability, or long-term care insurance.23 The primary care provider can help families navigate these issues by providing accurate information about the legal protections afforded by GINA.

The psychosocial impact of predictive genetic testing in children has long been debated by ethicists, geneticists, psychologists, and primary care pediatricians. Most professional guidelines admonish against testing children, but attitudes and practices vary.24 Support tends to be strongest when there is a clear medical benefit, such as in the case of testing for familial adenomatous polyposis; however, there is no agreement about the age at which testing should occur.25 In 2010, a systematic review of the literature examining the effects of carrier and predictive testing found little evidence of a significant negative or positive impact.26 However, the authors cautioned that the methodologic approaches and the size of the studies might have been inadequate to detect nuanced and important effects on children’s emotions, self-perception, and social well-being, and the authors called for a more robust research agenda going forward. Special attention should be paid to the impact of direct-to-consumer genetic testing of children, ranging from carrier tests, to tests for predicting adult-onset diseases, to tests that purport to predict a child’s sports performance.

As in other areas of health care, disparities in access to genetics-based diagnosis and treatment already exist. New technologies can either exacerbate or mitigate such disparities, depending on how the technologies are disseminated and implemented. Patient educational materials should be written at the appropriate literacy and numeracy levels for the US population in culturally sensitive language and should be available in other languages for individuals not proficient in English. Access to genetics services and relevant resources should be increased for individuals living in underresourced communities.

GENETIC RESOURCES FOR PRIMARY CARE

As the field of genomics moves into primary care, primary care pediatricians increasingly will need access to resources and information to help them incorporate new findings into their practices. Identifying local genetics experts and clinics is a good place to start. In addition, the number of online resources available to assist primary care providers is also growing; Table 3 lists a selection of such resources.

KEY POINTS

The potential roles of primary care pediatricians in genetic medicine are numerous and critical to the health and well-being of children. Primary care pediatricians are in an ideal position to:

- evaluate and treat patients with genetic diseases;
- identify individuals who may benefit from genetics services, including those with a genetic disorder and those at increased risk for having or transmitting a genetic disorder;
- recognize historical and physical features of common genetic conditions;
- monitor the health of individuals with a genetic disorder; in collaboration with an appropriate subspecialist;
- provide basic genetic information to patients and families to improve
understanding and encourage informed decision-making;

- provide a medical home for individuals with complex genetics services needs;

- recognize the special psychosocial issues for families in which 1 or more members are affected by a genetic disorder or susceptibility;

- assist patients in accessing the full range of genetics services from which they might benefit;

- refer patients with additional genetics services needs; and

- facilitate the use of genetics services.

MH and her extended family are doing well. All positively identified LQTS members are taking β-blockers, and 1 member has an implantable cardioverter-defibrillator.

REFERENCES


### TABLE 3 Genomic Resources

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<td>Health Professionals and Genetic Testing: What You Need to Know</td>
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<td>Information for consumers and patients</td>
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<td>National Coalition for Health Professional Education in Genetics</td>
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Primary Care and Genetics and Genomics
Joan Scott and Tracy Trotter
Pediatrics 2013;132;S231
DOI: 10.1542/peds.2013-1032H

The online version of this article, along with updated information and services, is located on the World Wide Web at:
/content/132/Supplement_3/S231.full.html