Genetic Services in the KP Southern California Region: Delivering the Promises of Tomorrow Today

Abstract

The impact of advances in molecular biology over the past 25 years—especially the completion of the Human Genome Project—touches every branch of medicine and will continue to have profound influence on medical practice. Advances in genetic technology are changing the traditional patient/doctor paradigm. For some medical conditions, current genetic technology and predictive testing enable us to offer medical management before a patient is diagnosed with a disorder. However, advances in genetic technology impose on all clinicians the added requirement of identifying patients who may benefit from having access to this technology. Kaiser Permanente (KP) provides a unique, integrated approach to this challenge by serving as a model for delivery of genetic services. This article outlines the history and current status of genetic services provided in the KP Southern California Region and summarizes current and future developments in medical genetics technology.

Dawn of a New Era

The integral role of genetics in everyday medical practice is the result of more than five decades of revolutionary clinical and molecular research. The impact of advances in molecular biology over the past 25 years—especially the completion of the Human Genome Project—touches every branch of medicine and will continue to profoundly influence medical practice. Application of genomics to the study of responses to pharmaceuticals is opening new opportunities in drug development and in pharmacogenetic tools for lowering risks of drug therapy and for increasing its benefits. While genetic technology continues to evolve, however, clinicians face the daunting task of integrating emerging technologies into daily medical practice to improve the health and welfare of patients. As medical genetics gained unparalleled prominence in the 1990s, Kaiser Permanente (KP) has enhanced its unique system of integrated health care services by becoming a national leader in delivering cutting-edge genetic services to KP members. This article outlines the history and current status of genetic services available in the KP Southern California Region (KPSC) and summarizes current and future developments in medical genetics technology.

From Humble Beginnings to State-of-the-Art Practice

Clinical geneticist Nancy Shinno, MD—who is now KPSC Chief of Regional Genetic Services—started her KP career in 1978 as one of only four KPSC clinical geneticists. In those early years, KP geneticists divided their time between medical genetics practice and pediatrics. Moreover, the practice of genetics primarily consisted of evaluating children with dysmorphic features and developmental delay and counseling women about the risks of advanced maternal age. Other than cytogenetic analysis performed to determine chromosome abnormality, few options existed for prenatal diagnosis of genetic disorders.

Now Dr Shinno leads the KPSC Regional Genetics Department, which includes 8 full-time medical geneticists, 22 genetic counselors, a regional genetic screening program, and a regional metabolic genetics program. The KPSC Genetics Department provides genetic ser-

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services to KP members at every KPSC medical center. The “menu” of available genetic tests has expanded exponentially, and the practice of genetics has grown beyond the realm of prenatal and pediatric genetics to include cancer genetics and neurogenetics, among other areas (see Tables 1 and 2). KPSC geneticists and genetic counselors also participate in programs where genetic disorders are managed by other specialists, such as those practicing in the craniofacial service, the sickle-cell disease center, and clinics that evaluate patients for neuromuscular or neurodegenerative disorders.

The impact of genetic technology on diagnosis and management of genetic disorders over time is clearly illustrated by treatment of Fabry disease, an X-linked recessive storage disorder first described in 1898. The disorder causes painful, disabling crises in boys as young as ten years of age; progressive damage to the kidneys, heart, and central nervous system, among other organs; and generally results in renal failure that can lead to early death in men in their thirties and forties. Fabry disease is caused by mutation in the alpha galactosidase A (GAL) gene.

This genetic mutation causes deficient activity of the alpha galactosidase enzyme. This deficiency results in progressive accumulation of glycosphingolipids, especially in vascular endothelium, leading to ischemia and infarction of small vessels and resultant renal, cardiac, and cerebrovascular dysfunctions.

In 1978, when Dr Shinno counseled a young woman whose brother and a maternal uncle had Fabry disease, doctors could offer such women little other than the information that they had a 50% chance of being a carrier of the condition. At that time, Fabry disease could be diagnosed in the woman’s brother by using enzyme analysis of leukocytes to identify alpha galactosidase deficiency, but this diagnostic test could not reliably diagnose the carrier state. Prenatal diagnosis using enzyme analysis could be used to detect an affected male fetus, but no treatment (other than kidney transplantation) was available for any affected sons the woman might bear.

By the early 1990s, scientists had mapped the gene for Fabry disease, and DNA analysis was available to inform women whether or not they were carriers of the disease. If results of DNA analysis were negative, the woman had no need to worry about bearing sons destined to have the disorder; if results of the test were positive, the woman could have prenatal diagnosis using sequence analysis, which could detect nearly 100% of mutations in the GAL gene.

By 2003, medical geneticists could inform a carrier patient that enzyme replacement therapy (a drug spinoff from identifying the gene) was available for her affected sons to help prevent renal failure, cardiac and cerebrovascular sequelae, and pain.

At KP, careful evaluation and selection of patients has helped to maximize the benefits provided by agalsidase beta (Fabrazyme, Genzyme Therapeutics, Cambridge, MA) a new recombinant enzyme treatment for Fabry disease. Treatment of at least one patient via compassionate protocol began nearly two years before marketing of Fabrazyme. Fabrazyme infusion therapy became available in KPSC in 2003, soon after the drug was approved by the US Food and Drug Administration (FDA). Infusion treatment is currently administered at the Metabolic Genetics Service at the KP Los Angeles Medical Center—KPSC’s state-of-the-art center for diagnosis and management of metabolic disorders—under the direction of Rebecca Mardach-Verdon, MD. Infusion therapy is available also at the KP Bakersfield and San Diego Medical Centers. Now, more than two years after FDA approval of the drug, several patients are being treated with this enzyme replacement therapy, and reports have described reduction or elimination of neuropathic pain, retardation of cardiac involvement, and improved ability to resume work and social activity.

A KP multidisciplinary Fabry Disease Advisory Panel including experts from the genetics, cardiology, neurology, nephrology, ophthalmology, and gastroenterology departments meets regularly to discuss and create management guidelines and to review nonclassic cases of Fabry disease. Treatment of this disease illustrates the potential for treatments derived from expanded knowledge about the genetic basis for disease and developed through new technology for pharmaceutical development. Indeed, the story of Fabry disease illustrates how advances in genetic technology have transformed management of this condition from simply offering in-
formulation (ie, about risk of disease recurrence) to accurate diagnosis and carrier testing and, finally, to use of enzyme replacement to treat and prevent complications.

Genetic Testing, Screening, and Counseling

Genetic testing analyzes human DNA, RNA, genes, chromosomes, or a combination of these structures to detect heritable or acquired genotypes, mutations, phenotypes, or karyotypes that can cause a specific disease or condition. Genetic testing also analyzes human proteins and certain metabolites, which are predominantly used to detect heritable or acquired genotypes, mutations, or phenotypes. Many different types of genetic tests are currently available (see Table 3).

Most genetic testing in KPSC is conducted at our state-of-the-art Regional Genetic Testing Laboratory. During the past year, the laboratory conducted more than 12,000 cytogenetic tests, 14,000 molecular tests, and more than 20,000 biochemical tests. In addition, each year the laboratory conducts revenue-generating tests, including approximately 56,000 maternal serum alpha-fetoprotein (AFP) tests reimbursed by the California Expanded AFP Screening Program. The biochemical genetics section of the laboratory also provides services (eg, analysis of amino acids, organic acids, tandem mass spectrometry) to other KP Regions, including Northern California and Hawaii. Since 1991, the number of cancer cytogenetic tests performed at the KPSC Regional Genetic Testing Laboratory has increased by more than 500%, the number of fluorescent in situ hybridization (FISH) procedures has increased by nearly 2000%, and the number of cytogenetic studies of prenatal specimens has remained fairly consistent. Moreover, during the past five years, the Regional Genetic Testing Laboratory has seen a dramatic decrease in the number of molecular tests sent to outside laboratories while the number of inhouse DNA tests has increased even more dramatically (Figures 1 and 2).

Genetic tests are often more complex than other types of medical tests. Testing for genetic susceptibility to disease (eg, examination of breast cancer susceptibility genes BRCA1 and BRCA2) is inherently complex because of its probabilistic and familial nature. Tests of this type identify empirical risks on the basis of genetic linkage studies of populations, not studies of risk in individual persons. This type of population testing has social and ethical consequences that extend beyond medical management and reveals information that affects not only the patient but also the patient’s blood relatives. For this reason, genetic counseling is always an integral part of genetic testing. At KPSC, an outstanding team of 22 genetic counselors works alongside SCPMG medical geneticists to provide pedigree collection and risk assessment; education about genetic diseases and genetic testing options; discussion of options for disease manage-

<table>
<thead>
<tr>
<th>Table 3. Types of genetic tests</th>
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<tr>
<td><strong>Diagnostic Tests:</strong> Used to confirm or exclude suspected genetic conditions (eg, Duchenne muscular dystrophy) in symptomatic persons of any age.</td>
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<td><strong>Predictive Tests:</strong> Offered to asymptomatic persons concerned about possible susceptibility to a genetic disorder. Two types:</td>
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<tr>
<td>Presymptomatic, where eventual development of symptoms is certain, eg, Huntington disease.</td>
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<tr>
<td>Predispositional, where eventual development of symptoms is likely but not certain, eg, inherited susceptibility to breast and ovarian cancer.</td>
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<tr>
<td><strong>Carrier Tests:</strong> Used to identify healthy persons who have a genetic mutation coding for an autosomal or X-linked recessive disorder which puts their children at risk for having the disorder. Carrier tests may be conducted in persons with a family history of the condition or in ethnic groups known to have a higher carrier rate for the condition (eg, cystic fibrosis).</td>
</tr>
<tr>
<td><strong>Prenatal Tests:</strong> Used to diagnose genetic conditions in the fetus. Offered to pregnant women who, because of any conditions (maternal age, personal or family history, ethnicity, suggestive results of either multiple-marker screening or fetal ultrasound), are at increased risk for having a child with a genetic condition or congenital defect.</td>
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<tr>
<td><strong>Newborn Screening Tests:</strong> Used in newborns to determine whether they are at increased risk for specific genetic conditions that usually need immediate treatment.</td>
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<td><strong>Pharmacogenetic Tests:</strong> Used to determine how a person’s genetic makeup may affect that person’s reactions to specific drugs. These tests may help clinicians to prescribe drugs that are most effective and cause the least side effects.</td>
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<tr>
<td><strong>Preimplantation Genetic Diagnosis (PGD):</strong> Used to test embryos for genetic disorders before transfer of the embryo to the uterus. PGD has limited application and is considered on a case-by-case basis.</td>
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<th>Table 4. Most common cancer susceptibility syndromes</th>
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<tr>
<td>Syndrome</td>
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<tr>
<td>HBOC</td>
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<tr>
<td>Li-Fraumeni</td>
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<tr>
<td>FAP</td>
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<tr>
<td>HNPCC</td>
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<td>Cowden</td>
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ment, treatment, and surveillance; psychosocial support; and case management.

The KPSC Genetic Screening Program administers the California Expanded AFP Screening Program as well as the Regional Cystic Fibrosis (CF) Program and the Newborn Screening Program. In California, all pregnant women are offered prenatal “multiple marker screening” through the California Expanded AFP Program. The current panel reports a detection rate of 70% for Down syndrome and detection rates ranging from 85% to 97% for neural tube defects (depending on the type of neural tube defect). “Quad” screening, which adds another analyte to the assay, is under development and is expected to substantially improve prenatal detection rates for Down syndrome over the current “triple screen.” Prenatal CF carrier screening is offered to women on the basis of their ethnicity or on request. KP members who receive positive test results are immediately referred for genetic counseling to help them understand their risks, evaluate their options for additional testing, and make informed medical and personal decisions about having additional genetic tests.

KPSC also participates in the California Newborn Screening Program, which has for many years been screening newborns for phenylketonuria (PKU), sickle-cell anemia, congenital hypothyroidism, and galactosemia. Since its inception, the program has screened virtually all babies born to KPSC members. The program was expanded in 2005 to screen for 40 additional disorders through use of tandem mass spectrometry. Among the disorders detected by this method are medium-chain-acyl CoA dehydrogenase (MCAD) deficiency and glutaric acidemia type I (GA1).

Cancer Genetics

For decades, physicians have been able to identify families that have clearly hereditary patterns of cancer; however, physicians had little to offer these families other than recommending vigilance toward all family members without knowing who was (or was not) at risk. That situation changed in the past decade, thanks to the discovery and mapping of several genes associated with susceptibility to cancer. Commercial testing for familial adenomatous polyposis (FAP, the most thoroughly characterized hereditary form of colorectal cancer) was first made available in 1995 and was closely followed by testing for BRCA1 and BRCA2 (breast cancer susceptibility genes 1 and 2)—testing which first became available in 1996—and testing for hereditary nonpolyposis colorectal cancer (HNPCC). Opportunities for commercial and research testing for other cancer syndromes continue to evolve (see Table 4). KP has always
been a leader in the area of cancer genetics and was one of the first healthcare organizations in the nation to address the issues related to BRCA1/BRCA2 testing. In 1997, the National KP Guidelines for BRCA Counseling and Testing were among the first such guidelines developed in the United States. Geneticists and genetic counselors from KPSC were key contributors to development of that guideline, and today these professionals continue to provide comprehensive risk assessment, genetic testing and interpretation, and management information to patients who are at risk for hereditary cancer susceptibility, as well as to their families.

Diagnosis and management of FAP are excellent examples of how genetic technology has substantially changed the way that hereditary cancer susceptibility is diagnosed and treated today. FAP is an autosomal dominant condition which affects approximately 1 in 5000 persons and is characterized by development of numerous (often more than 1000) colon adenomas; virtually all affected patients are at risk for colorectal cancer by age 40 years. Before 1995, diagnosis of FAP was based on family history of either polyposis, early colon cancer, or both, and sometimes based on presence of extracolonic characteristics (eg, congenital hyperpigmentation of retinal epithelium). Because of the early manifestations of the disorder, all children of affected parents were scheduled for annual endoscopic examination beginning around ten years of age. Before 1995, diagnosis of FAP was based on family history of either polyposis, early colon cancer, or both, and sometimes based on presence of extracolonic characteristics (eg, congenital hyperpigmentation of retinal epithelium). Because of the early manifestations of the disorder, all children of affected parents were scheduled for annual endoscopic examination beginning around ten years of age.

Because each child had a 50% chance of being affected, half of the children receiving endoscopy had the procedure unnecessarily. After genetic testing became available and the family mutation could be identified, children at risk could be tested; and only those carrying the family mutation would need to be screened for colon cancer. This genetic testing technology thus spares unaffected children from being tested and allows families and the healthcare systems to focus their resources where they are most needed.

Thanks to recent developments in molecular diagnostics, the rate of detecting the mutations in FAP families has increased from about 80% (in the 1990s) to 90% today.

### Table 5. Enzyme Replacement Therapy commercially available or pending FDA review

<table>
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<tr>
<th>Enzyme</th>
<th>Disorder</th>
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<tbody>
<tr>
<td>imiglucerase (Cerezyme)*</td>
<td>Type 1 Gaucher disease</td>
</tr>
<tr>
<td>laronidase (Aldurazyme)*</td>
<td>Mucopolysaccharidosis I (MPS I)</td>
</tr>
<tr>
<td>agalsidase beta (Fabrazyme)*</td>
<td>Fabry disease</td>
</tr>
<tr>
<td>galsulfase (Naglazyme)*</td>
<td>MPS VI (Maroteaux-Lamy syndrome)</td>
</tr>
<tr>
<td>alpha-glucosidase</td>
<td>Pompe disease</td>
</tr>
<tr>
<td>iduronate-2-sulfatase</td>
<td>MPS II (Hunter syndrome)</td>
</tr>
</tbody>
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*Commercially available in the United States as of late 2005.

### Table 6. Minimum requirements for obtaining family medical history

- Obtain family history information on at least three generations.
- Ask about all individuals in both sides of the patient’s family and record pregnancy history, including losses/stillbirths/neonatal deaths, age at diagnosis of significant disease, current age (or age at—and cause of—death).
- Ask about history of mental retardation or developmental delay, birth defects, known genetic disorders.
- Record ethnicity and race.
- Record consanguinity.

### Pharmacotherapy for Heritable Disorders

Recombinant versions of enzymes have been developed for treating several heritable disorders of lysosomal storage. Enzyme replacement therapy is available for patients with Gaucher disease, Fabry disease, and some forms of mucopolysaccharidosis (MPS). Other forms of enzyme replacement therapy may soon be approved for treating Pompe disease and another type of MPS (see Table 5).

Throughout California, semianual collaborative videoconferences have been held by KP geneticists and other specialists (eg, cardiologists, neurologists, nephrologists, ophthalmologists, and gastroenterologists) who treat these patients.
Videoconference participants review the newer enzyme replacement products as well as issues surrounding therapy. This interactive approach provides an optimum perspective on complex diseases, enables sharing of information, and helps clinicians who are making treatment decisions regarding enzyme replacement therapy.

The Promise of Personalized Medicine

News articles have heralded the approach of personalized medicine, a vision of the future wherein type and dose of medication will be chosen on the basis of each patient’s own genetic profile as determined by pharmacogenetic pretesting. This envisioned future will probably occur in small steps, because testing is not yet widely available for most genetic variants and because outcome data must first be collected to guide prescription adjustments based on pretesting. This futuristic model of personalized medicine must also account for multiple factors that can affect gene expression.

Pharmacogenetic information has already been added to the FDA-approved labeling of some medications. Many others will follow, adding new facets to treatment decisions in individual cases. In addition, pharmacogenomic analysis conducted during the drug development process will result in more accurately targeted drugs with more limited toxicity. This achievement may bring new therapies to the consumer market, because improved efficacy and lessened toxicity could justify FDA approval of drugs which could not have been approved for less-well-defined target populations.

During the past five decades, research has led to considerable increase in knowledge concerning the metabolizing enzymes affected by polymorphisms of single genes. Examples of these enzymes include:

- N-acetyltransferase (NAT2), related to alterations in pharmacokinetics of isoniazid, hydralazine, procainamide, and sulfonamides
- Cytochrome-P450 isoenzymes, such as CYP2D6, CYP2C19, and CYP2C9, which affect metabolism of many drugs
- UDP-glucuronosyl transferases (UDP-GT), which has an isoform (UGT1A1) that converts the active metabolite of irinotecan to an inactive glucuronide

Patients with one of these polymorphisms may be at increased risk for adverse reactions or for inefficacy of the substrate drugs when these drugs are used at usual doses.

With new pharmacogenetic applications and expanded information about associations between drug therapy and genetic variations, the challenge presented to KP includes the need for careful, evidence-based evaluation regarding use of pharmacogenetic testing in drug therapy. This evaluation will require the coordinated efforts of physicians, clinical laboratory staff, and pharmacy staff. In most instances, we will find value in development of evidence-based guidelines, educational tools, and internal KP review by the Biotechnology and Emerging Pharmaceutical Technology Assessment Committee (BEPTAC), physician committees, and the Pharmacy and Therapeutics Committee.

Genetic Testing and Drug Therapy

At least two types of genetic testing will be used in pharmacogenetic applications that affect choice of drug therapy.

One such type of testing measures genetic variation in a disease, such as mutations in tumor tissue. One of the best-known examples of gene testing related to drug therapy is testing of tumor tissue in metastatic breast cancer patients as a determinant of whether trastuzumab (Herceptin, Genentech, South San Francisco, CA) might be effective.

Overexpression of the HER2 protein has been found in some human primary tumors and has been identified in 25% to 30% of patients with breast cancer. Available methods of testing include an immunohistochemical (IHC) assay to test for overexpression of HER2 protein and a FISH test using a DNA probe to determine HER2 gene amplification. Testing has become both a standard feature of treatment plans and requisite for use of trastuzumab in a specified subset of patients diagnosed with metastatic breast cancer. The other type of genetic testing is testing for genetic variations in an individual person. An example of such variation is the gene variant for UGT1A1 enzyme, which converts the active metabolite of irinotecan (Camptosar; Pharmacia, Peapak, NJ), indicated for metastatic colorectal carcinoma) to an inactive metabolite. This polymorphism (UGT1A1*28) leads to decrease in UGT1A1 enzyme activity, which in turn leads to increased irinotecan toxicity (eg, severe neutropenia). About 10% of North Americans are homozygous for the polymorphism and are at increased risk for this toxicity. Another 40% of the North American population are heterozygotes and may also have some increased risk for toxicity. The FDA has recently added this information to the irinotecan product label. Oncologists, pharmacists, laboratory personnel, and geneticists are interacting to determine how to use this pharmacogenetic information most effectively.
The Family Medical History: A Timeless Tool

Although genetic technology continues to evolve at an unprecedented pace, the family medical history remains a valuable clinical tool in delivery of genetic services to our patients. Indeed, one forecast has stated that “Personal and family [medical] history will continue to be the key indicator for clinical use of genetic tests.” Collection and interpretation of information on family medical history is essential for several purposes: to identify persons at risk for genetic conditions, to determine genetic testing options, to interpret results of genetic tests, and to choose appropriate options for clinical care management. The FAP example presented above is a perfect illustration of how knowing a patient’s family medical history affects diagnosis and management of a genetic condition.

Physicians in all specialties will face increasing demands to explore family medical history, explain genetic testing options, and separate genetic hype from reality for their patients—roles for which physicians currently receive little or no training. Recently, several professional organizations have focused on increasing genetic competency among primary care practitioners. The National Coalition for Health Professional Education in Genetics (NCHPEG) has defined core competencies in genetics for all health professionals and has developed education tools to promote integration of genetics into healthcare practice.

The American Academy of Family Physicians chose genomics as their Annual Clinical Focus (ACF) for 2005 and invited Francis Collins, MD, Director of the Human Genome Project, to kick off the program; and the CDC declared Thanksgiving 2004 as “Family History Day” to launch its Family History Initiative.

The family medical history should include information on at least three generations from both sides of the family (see Table 6). Physicians must recognize that family history is dynamic. As relatives age, they may be diagnosed with new disorders that were not part of the original history collected for the patient. For data on family medical history to be accurate, it must be updated regularly. Collecting and updating information on family medical history should not be the sole responsibility of primary care practitioners, however. Because some KP members rarely see a primary care practitioner, all clinicians should seize the opportunity to collect and update information about their patient’s family medical history.

KP HealthConnect will provide an opportunity for collecting and tracking some data on family medical history. Moreover, a KP interregional committee of genetics specialists is currently exploring options for developing expanded databases of family medical history and pedigree.

We hope that these initiatives will allow family history interpretation software to become widely available to assist primary care practitioners in identifying patients at risk for genetic conditions and to improve clinical care of these patients. Until those tools are universally available, clinicians should familiarize themselves with some of the more common “clues” that suggest the need for a referral to the genetics service (Table 7).

Present and Future Evaluation of Genetic Technology at KPSC

The KPSC Regional Genetics Department works closely with many other departments and processes to ensure that the following occur:

- Decisions regarding introduction of new genetics technology are evidence-based
- All aspects of service quality and cost are considered during the planning and implementation process
- An ongoing management structure for existing technologies is provided. Groups who interact with the KPSC Regional

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**Table 7. Genetic “red flags” in the family medical history**

<table>
<thead>
<tr>
<th>Description</th>
<th>Example</th>
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<tbody>
<tr>
<td>Children with birth defects, developmental delay, unexplained short stature, clinically significant hearing loss, unusual dermatologic conditions, ambiguous genitalia, or tumors with possible hereditary component (eg, retinoblastoma, Wilms’ tumor)</td>
<td></td>
</tr>
<tr>
<td>Family history of mental retardation, birth defects, or known genetic disorders (eg, muscular dystrophy, hemophilia, neurofibromatosis)</td>
<td></td>
</tr>
<tr>
<td>Family history of multiple pregnancy losses, stillbirths, or unexplained neonatal death</td>
<td></td>
</tr>
<tr>
<td>Consanguinity</td>
<td></td>
</tr>
<tr>
<td>Evidence of autosomal dominant (vertical) transmission</td>
<td></td>
</tr>
<tr>
<td>Evidence of autosomal recessive (horizontal) transmission</td>
<td></td>
</tr>
<tr>
<td>Three or more relatives (on same side of family) with same disorder (eg, colon cancer)</td>
<td></td>
</tr>
<tr>
<td>Early age at diagnosis of common cancer (eg, breast or colon cancer at age &lt;50 years)</td>
<td></td>
</tr>
<tr>
<td>Multiple primary cancers in same individual</td>
<td></td>
</tr>
<tr>
<td>Constellation of tumors consistent with specific cancer syndrome (eg, breast and ovary, or colon and endometrium, in the same side of the family)</td>
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Genetics Department include National KP and KPSC Medical Technology Assessment and Deployment Committees, the Biotechnology and Emerging Pharmaceutical Technology Assessment Committee, the Regional Laboratory, and the Research and Evaluation Department.

Advances in genetic technology are changing the traditional patient-doctor paradigm. Because of current genetic technology and predictive testing, medical management is now available for some conditions before they are diagnosed in a patient, and diagnosis is possible for many conditions for which no effective treatment currently exists. In both situations, genetic counseling of patients is imperative for helping them and their families to understand this complex information. In the future, evolving genetic technology will allow physicians to manage their cases on the basis of each patient's individual genetic makeup, the disorders to which these patients are predisposed, and how these patients respond to treatment.

The impressive power of genetic technology brings with it an equally impressive three-part responsibility: equitable access, clinically responsible care, and timely use of genetic technology for patients who may benefit from it. Collecting, documenting, and acting on information about each patient's family medical history are key factors in this equation. The physicians and counselors at the KPSC Regional Genetics Department are already delivering on the promises of genetic technology and will continue to combine powerful, state-of-the-art medicine with a personal touch and with the same excellence that exemplifies genetic services in each KP region.

References

Glossary
- Genetics is the study of single genes and their effects.
- Genetic Medicine includes the diagnosis and treatment of conditions caused by mutations in a single gene (eg, Huntington disease) or chromosomal abnormality (eg, Down syndrome). Genetic counseling, genetic testing, and genetic-disease management are services that have been associated with genetic medicine practice.
- Clinical geneticists are Board-certified or Board-eligible physicians who have completed a fellowship approved by the American Board of Medical Genetics. The American Board of Medical Genetics, recognized by the American Board of Medical Specialties in 1991, certifies physicians in clinical genetics along with physicians and PhDs in clinical biochemical genetics, clinical cytogenetics, and clinical molecular genetics. In the past, clinical geneticists were interested primarily in dysmorphology and evaluation of children with birth defects, mental retardation, or both. Although this interest continues to be a part of their practice, clinical geneticists now engage in a wide range of clinical endeavors involving patients of all ages.
- Genetic Counselors are medical professionals trained in all areas of medical genetics who have completed a master's degree program accredited by the American Board of Genetic Counseling and who are Board-certified or Board-eligible. In addition to collecting and interpreting information of a patient's family history, genetic counselors educate and counsel patients about genetic disorders, inheritance patterns, genetic testing options, interpretation of test results, and the medical and social implications of genetic disorders. Genetic counselors work under the supervision of, and in collaboration with, clinical geneticists. Genetic counselors provide preconception and prenatal genetic counseling to determine family history of birth defects or inherited conditions, possible teratogenic exposure, consanguinity, suspected personal or family history of cancer susceptibility, and other conditions.
- Genomics is the study of the whole genome—how individual genes interact with each other and how they may interact with the environment to spur development of disease. When genomics is fully developed as a field, genetics will be a subset of genomics, and genetic medicine will be part of the prevention, diagnosis, and treatment of all disease, not just genetic disorders.
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Wonder was the motive that led people to philosophy.
Philosophy is to the cure of the soul what medicine is to the cure of the body.
Wonder is a kind of desire in knowing.
It is the cause of delight because it carries with it the hope of discovery.
—Thomas Aquinas, circa 1225-1274, Italian Catholic philosopher and theologian