Indications for genetic referral: a guide for healthcare providers

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Key Words: *genetic screening, genetic evaluation, prenatal testing, preconceptional testing, genetic referral*

Disclaimer: *This guideline is designed primarily as an educational resource for medical geneticists and other healthcare providers to help them provide quality medical genetic services. Adherence to this guideline does not necessarily assure a successful medical outcome. This guideline should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. In determining the propriety of any specific procedure or test, the geneticist should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. It may be prudent, however, to document in the patient's record the rationale for any significant deviation from this guideline.*

Geneticists and genetic counselors are often asked what may be appropriate reasons for referral to a genetics service. The Professional Practice and Guidelines Committee of the American College of Medical Genetics has generated lists of the more common reasons for referral and provide them for use by genetics professionals and other healthcare providers for guidance. The lists are divided into pediatric, prenatal, and adult indications.

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Approved by the Board of Directors July 16, 2006. Go to www.geneticsinmedicine.org for a printable copy of this document.

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DOI: 10.1097/GIM.0b013e318064e70c

As genetic health professionals, we are frequently asked under what clinical circumstances a genetic consultation is warranted. Although there is a vast array of indications for referral, here are a number of common indications for a genetic office visit. These lists have been divided into pediatric, preconceptional/prenatal, and adult categories for simplicity's sake; findings are paired with consultation objectives. These lists are clearly not intended to be exhaustive or comprehensive, but will hopefully serve as a guide for primary care providers who may have questions about specific clinical circumstances. As the field of genetics expands and genetic technologies uncover new genes and genetic associations on a weekly basis, these lists will quickly become outdated. However, for now, these may help to provide a framework for patient centered specialty referrals (Tables 1–3).

Table 1

Genetic consultation may be helpful under the following circumstances for preconceptional or prenatal patients

Prenatal or preconceptional patient who is or will be:	
Finding	Reason to consider consultation
Age 35 years or older at the time of delivery (for a singleton pregnancy)	Discuss testing options for identifying an age-related chromosome anomaly
Age 33 years or older at the time of delivery (for a twin pregnancy)	Discuss testing options for identifying an age-related chromosome anomaly
A close blood relative of her partner (consanguineous union)	Review pedigree and assess degree of relatedness; discuss potential additional fetal risks and testing options before and/or after delivery
Prenatal or preconceptional patient who has:	
Finding	Reason to consider consultation
An abnormal first or second trimester maternal serum ± nuchal translucency screening test	Discuss risks to pregnancy and testing options
Exposure to a teratogen or potentially teratogenic agent during gestation such as radiation, high-risk infections (cytomegalovirus, toxoplasmosis, rubella), drugs, medications, alcohol, etc.	Discuss risks to pregnancy and testing options and rule out significant fetal ± maternal risks
A fetal anomaly or multiple anomalies identified on ultrasound and/or through echocardiography	Discuss risks to pregnancy and testing options
A personal or family history of pregnancy complications known to be associated with genetic factors such as acute fatty liver of pregnancy	Rule out significant fetal risks ± maternal risks, including a metabolic disorder
Either member of the couple with:	
Finding	Reason to consider consultation
A positive carrier screening test for a genetic condition such as cystic fibrosis, thalassemia, sickle cell anemia, Tay-Sachs, etc.	Discuss additional testing strategies and inheritance
A personal history of stillbirths, previous child with hydrops, recurrent pregnancy losses (more than two), or a child with sudden infant death syndrome (SIDS)	Rule out a chromosomal, metabolic, or syndromic diagnosis that may be associated with an unexplained neonatal death or SIDS
A progressive neurologic condition known to be genetically determined such as a peripheral neuropathy, unexplained myopathy, progressive ataxia, early onset dementia, or a familial movement disorder	Discuss a potential diagnosis, the differential diagnosis, inheritance, and testing options
A statin-induced myopathy	Discuss a potential mitochondrial disorder, inheritance and testing options
Either member of the couple with a family or personal history of:	
Finding	Reason to consider consultation
A birth defect such as a cleft lip ± palate, spina bifida, or a congenital heart defect	Discuss recurrence risks and testing options; discuss folate supplementation, if appropriate, for subsequent pregnancies
A chromosomal abnormality such as a translocation, marker chromosome, or chromosomal mosaicism	Discuss risks to the fetus and testing options
Significant hearing or vision loss thought to be genetically determined	Discuss risks to the fetus and testing options
Mental retardation or autism	Discuss risks to the fetus and testing options

Table 2
Genetic consultation may be helpful under the following circumstances for adult patients

Personal history of:	
Finding	**Reason to consider consultation**
Abnormal sexual maturation or delayed puberty	Rule out an intersex condition, chromosomal abnormality or syndromic diagnosis (e.g., androgen insensitivity, Klinefelter syndrome)
Recurrent pregnancy losses (RPLs) (more than 2)	Rule out a chromosomal rearrangement such as a balanced translocation or inversion; causes 5%–7% of RPLs
Tall or short stature for genetic background	Rule out a skeletal dysplasia, chromosomal or syndromic diagnosis (e.g., dyschondrosteosis, Klinefelter syndrome, Marfan syndrome)
One or more birth defects	Rule out a chromosomal or syndromic diagnosis (e.g., 22q deletion, Noonan syndrome); provide genetic counseling and discussion of preconception folate supplementation, if appropriate
Six or more café-au-lait macules >1.5 cm in diameter	Rule out neurofibromatosis type 1
Statin-induced myopathy	Rule out a mitochondrial disorder
Personal or family history of:	
Finding	**Reason to consider consultation**
A cancer or cancers known to be associated with specific genes or mutations such as breast, ovarian, and colorectal in the context of a compelling family history; young age at onset, bilateral lesions, and familial clustering of related tumors	Rule out an identifiable mutation in a gene such as BRCA1, FAP, etc.; rule out a cancer syndrome (e.g., MEN2 or von Hippel-Lindau); discuss surveillance, treatment, testing options (if presymptomatic), and inheritance
Cardiovascular problems known to be associated with genetic factors such as cardiomyopathy, long QT, hyperlipidemia, etc.	Rule out a mutation in a causative or contributory gene; discuss surveillance, treatment, testing options, and inheritance
Suspected genetic disorder affecting connective tissue	Rule out a syndromic diagnosis (e.g., Ehlers-Danlos, Marfan syndrome, familial joint hypermobility); discuss surveillance, treatment, testing options, and inheritance
Hematologic condition associated with excessive bleeding or excessive clotting (as evidenced by recurrent deep vein thromboses or pulmonary emboli)	Confirm or rule out genetic condition (e.g., one of the hemophilias, von Willebrand, one of the genetic thrombophilias); discuss treatment, testing options, and inheritance
Progressive neurologic condition known to be genetically determined such as a peripheral neuropathy, unexplained myopathy, progressive ataxia, early-onset dementia, and a familial movement disorder	Confirm or rule out suspected diagnosis, discuss surveillance, treatment, testing options, and inheritance
Visual loss known to be associated with genetic factors such as retinitis pigmentosa, early-onset macular degeneration, and cataracts	Rule out a syndromic diagnosis (e.g., Stickler syndrome); discuss testing options, if applicable, and inheritance
Early-onset hearing loss	Rule out a syndromic or nonsyndromic genetic form of hearing loss; discuss surveillance, testing options, and inheritance
Recognized genetic disorder including a chromosomal or single gene disorder	Confirm the diagnosis; discuss prognosis, medical management, and inheritance
Mental illness such as schizophrenia, depression, bipolar disorder, etc.	Discuss diagnosis, inheritance, recurrence risks, and identify syndromes (e.g., 22q deletion), when possible
Family history of:	
Finding	**Reason to consider consultation**
A close relative with a sudden, unexplained death, particularly at a young age	Rule out a genetic condition associated with this history, e.g., long QT, Marfan syndrome, and other cardiac conditions

Table 3
Genetic consultation may be helpful under the following circumstances for pediatric patients

A neonate with:	
Finding	Reason to consider consultation
An abnormal newborn screening test	Rule out an inborn error of metabolism or other treatable condition; provide genetic counseling about recurrence risks
Congenital hypotonia or hypertonia	Rule out a chromosomal, metabolic, or syndromic diagnosis (e.g., Prader-Willi syndrome, congenital myotonic dystrophy, hyperekplexia).
Unexplained intrauterine growth retardation	Rule out a chromosomal or syndromic diagnosis (e.g., Russell-Silver syndrome, trisomy 18)
A neonate, infant, or child with:	
Finding	Reason to consider consultation
A single major, or multiple major and/or minor anomalies	Rule out a chromosomal or syndromic diagnosis; provide genetic counseling for recurrence and possible preventive measures (e.g., folate supplementation in subsequent pregnancies)
Dysmorphic features that are not familial, especially if accompanied by developmental delay or mental retardation	Rule out a chromosomal or syndromic diagnosis (numerous conditions)
Failure to thrive	Rule out a chromosomal, metabolic, or syndromic diagnosis, or genetic condition (e.g., IGF1R mutations)
A known metabolic disorder or symptoms of a metabolic disorder such as intractable seizures, hepatosplenomegaly, acidosis, cyclic vomiting, persistent hypoglycemia, developmental regression, and unusual body odor	Diagnose an inborn error of metabolism; discuss treatment and management; provide genetic counseling
Abnormal brain MRI findings such as leukodystrophy, periventricular calcifications, unidentified bright objects, or a malformation	Rule out a chromosomal or syndromic diagnosis (e.g., neurofibromatosis, tuberous sclerosis); provide genetic counseling (e.g., some brain malformations such as Dandy-Walker malformation may be genetic)
An unusual growth pattern such as overgrowth, short stature, or hemihypertrophy	Rule out a chromosomal, syndromic, or metabolic diagnosis (e.g., Sotos syndrome, Beckwith-Wiedemann syndrome, Turner syndrome)
Evidence of a connective tissue disorder such as extreme joint laxity, poor wound healing, or a marfanoid habitus	Rule out a connective tissue disorder, such as Ehlers-Danlos syndrome, Marfan syndrome
Congenital eye defects or blindness associated with problems such as microophthalmia, cataracts, megalocornea, retinitis pigmentosa, or cone-rod dystrophy	Rule out a syndromic diagnosis; provide genetic counseling for potentially hereditary ocular conditions
Significant hearing loss or deafness not secondary to recurrent otitis media	Rule out a syndromic form of hearing loss (e.g., Waardenburg syndrome) or identify a genetic form of nonsyndromic hearing loss
Cardiomyopathy not secondary to a viral infection	Rule out a mitochondrial disorder or other syndromic or metabolic diagnosis (e.g., carnitine deficiencies, Noonan syndrome, several forms of muscular dystrophy); provide genetic counseling for potentially hereditary forms of cardiomyopathy
Six or more café-au-lait macules >0.5 cm in diameter	Rule out neurofibromatosis type 1
Unusual skin findings such as multiple types of lesions, multiple lipomas, numerous hypo- or hyperpigmented lesions, and albinism	Rule out a chromosomal or syndromic diagnosis (e.g., chromosomal mosaicism, tuberous sclerosis, Cowden syndrome)
Born to a parent with a known chromosomal abnormality or rearrangement (balanced or unbalanced), especially if there are dysmorphic features and/or cognitive impairment	Rule out a chromosomal abnormality
Bilateral or multifocal malignancies such as retinoblastoma or Wilms tumor	Rule out a cancer syndrome or other chromosomal or syndromic diagnosis (e.g., aniridia-Wilms tumor caused by 11p13 deletion); provide genetic counseling for recurrence
Problems with clotting including disorders such as hemophilia and thrombophilia	Rule out an inherited clotting disorder as well as some syndromes (e.g., Noonan syndrome)
A recognized or suspected genetic syndrome including a chromosomal or single gene disorder	Confirm the diagnosis and discuss the prognosis, medical management, inheritance, and recurrence risks
A significant family history of medical or psychiatric conditions that puts the patient at risk of developing the same or similar disorder	Discuss diagnosis, inheritance, and possible testing options

(*continued*)

Table 3.
Continued

A child with:	
Finding	Reason to consider consultation
Unexplained mental retardation or global developmental disorder	Rule out a chromosomal, syndromic or metabolic diagnosis (e.g., fragile X, sex chromosome anomaly, some forms of mucopolysaccharidoses)
Autism or pervasive developmental disorder	Rule out a chromosomal or syndromic diagnosis (e.g., fragile X, Angelman syndrome, Rett syndrome)
Unusual behaviors, especially when associated with minor malformations and developmental delay or mental retardation	Rule out a chromosomal or syndromic diagnosis (e.g., Smith-Magenis syndrome, Lesch-Nyhan syndrome)
An immunodeficiency or significant immune problem	Rule out a syndromic diagnosis (e.g., 22q deletion) or genetic form of immunodeficiency (e.g., severe combined immunodeficiency syndrome)
Progressive muscle weakness that might be associated with a genetic disorder such as a form of muscular dystrophy, spinal muscular atrophy, or myotonic dystrophy	Confirm suspected diagnosis and provide genetic counseling
Other neurologic condition that might be associated with a genetic predisposition such as a peripheral neuropathy, unexplained myopathy, progressive ataxia, or any progressive neurologic disorder without a clear, nongenetic cause	Rule out a genetic diagnosis (e.g., spinocerebellar ataxia, Huntington disease), provide genetic counseling