The American College of Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

COMMITTEE OPINION

Number 643 • October 2015
(Reaffirmed 2019)

Committee on Genetics

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Identification and Referral of Maternal Genetic Conditions in Pregnancy

ABSTRACT: Advances in the understanding of genetic conditions, reproductive technologies, and improved medical and surgical care have enabled an increasing number of women with genetic conditions to achieve a normal pregnancy outcome. However, management of certain genetic conditions during pregnancy is complex and may require a multidisciplinary approach from preconception through the postpartum period. Patients with certain genetic conditions, or those at risk of having a particular genetic condition, should have a preconception evaluation with their obstetrician–gynecologists, genetics specialists, maternal–fetal medicine specialists, or other appropriate subspecialists to optimize their care. Given the rarity and complexity of some genetic conditions in pregnancy and their evolving management strategies, a coordinated, multidisciplinary approach to care may provide the best opportunity to improve maternal and fetal outcomes.

Recommendations

- Management of many genetic conditions during pregnancy is complex and may require a multidisciplinary approach from preconception through the postpartum period.
- Patients with genetic conditions, or those at risk of having a particular genetic condition, should have a preconception evaluation with their obstetrician–gynecologists, genetics specialists, maternal–fetal medicine specialists, or other appropriate subspecialists to optimize their care.
- Patients with established causative mutations for a genetic condition, and who desire prenatal genetic testing, should be offered preimplantation genetic testing with in vitro fertilization by a reproductive endocrinologist or prenatal diagnostic testing once pregnancy is established.
- Once pregnant, the patient with a genetic condition should have her initial prenatal examination early in the first trimester. This will allow for coordination of prenatal screening or testing and evaluation of pregnancy risks.

Introduction

Advances in the understanding of genetic conditions, reproductive technologies, and improved medical and surgical care have enabled an increasing number of women with genetic conditions to achieve a normal pregnancy outcome. The care of women with genetic conditions can pose many challenges and often requires a multidisciplinary approach from the time pregnancy is contemplated or planned through the postpartum period. The medical team may involve obstetricians, maternal–fetal medicine specialists, genetics specialists, anesthesiologists, and other medical and surgical specialists depending on the specific genetic condition. Crucial components of care for these patients include counseling regarding genetic condition-associated risks during pregnancy, optimizing maternal medical management, performing risk assessment for offspring, and offering prenatal testing as indicated. Individuals with genetic conditions should be referred for consultation to a practitioner with detailed knowledge of these conditions, ideally in the preconception period for optimal counseling and evaluation.

Table 1. Overview of Select Maternal Genetic Conditions in Pregnancy ⇦

Genetic Condition	Mode of Inheritance	Key Features
Pulmonary		
Cystic fibrosis	Autosomal recessive	Sinopulmonary disease, obstructive lung disease, recurrent infections, gastrointestinal and nutritional deficiencies, obstructive azoospermia, salt loss syndromes, diabetes, and pancreatic insufficiency
Cardiac		
Marfan syndrome	Autosomal dominant	Aortic root enlargement with risk of dissection; mitral valve prolapse; ectopia lentis; myopia; skeletal manifestations, including joint laxity and pectus abnormalities; dural ectasia; and lung bullae
Neurocutaneous		
Neurofibromatosis Type 1	Autosomal dominant	Café au lait spots, inguinal and axillary freckling, neurofibromas, Lisch nodules, learning disabilities, scoliosis, and optic nerve and central nervous system gliomas
Tuberous sclerosis	Autosomal dominant	Skin abnormalities—hypomelanotic macules, facial angiofibromas, shagreen patches, fibrous facial plaques, and ungual fibromas Brain findings—cortical tubers, subependymal nodules, and seizures Kidney issues—angiomyolipomas, cysts, and renal cell carcinomas Heart and lung issues—rhabdomyomas, arrhythmias, and lymphangioleiomyomatosis
Renal		
Autosomal dominant polycystic kidney disease	Autosomal dominant	Renal cysts; liver and other organ cysts; vascular malformation, including intracranial aneurysms; abdominal wall hernias; hypertension; renal insufficiency; aortic root dilation with risk of dissection; and mitral valve prolapse
Metabolic		
Classic phenylketonuria (PKU)	Autosomal recessive	Children born to women with PKU on unrestricted diets at risk of intellectual disability, microcephaly, and congenital heart defects Universal newborn screening for PKU in the United States Before conception, patients should consume a low-protein diet and use a phenylalanine-free medical formula to achieve plasma phenylalanine concentrations of 120–360 micromole/L (2–6 mg/dL)
Noonan syndrome	Autosomal dominant	Short stature; characteristic facial features; congenital heart defects, including pulmonic stenosis; lymphatic dysplasias; intellectual disability of varied degree; pectus deformity; varied coagulation defects; and renal abnormalities
Myotonic dystrophy Type 1	Autosomal dominant–trinucleotide repeat disorder with expansion during gametogenesis (anticipation)	Three types: 1. Mild (cataract and mild myotonia) 2. Classical (muscle weakness, myotonia, cataracts, and cardiac conduction abnormalities) 3. Congenital (severe hypotonia, respiratory failure, intellectual disability, and early death)

Preconception Considerations

Patients with genetic conditions may benefit from a preconception evaluation with their obstetrician–gynecologists, genetics specialists, maternal–fetal medicine specialists, or appropriate subspecialists to optimize their care. Precise identification of maternal genetic conditions in the preconception period is important for many reasons: to optimize maternal health before pregnancy; to review maternal health risks and neonatal morbidities associated with pregnancy; to counsel the patient and partner regarding mode of inheritance, partner carrier screening, assessment of genetic condition risk in the offspring, and the availability of prenatal diagnosis or preimplantation genetic diagnosis; and to create a plan of care that addresses potential maternal, fetal, and neonatal risks. The need for a multidisciplinary approach to care or in-depth preconception counseling will vary and the level of care should be commensurate with the complexity of the patient's condition.

A thorough evaluation of maternal health is necessary for assessing maternal risks during pregnancy. At times, medical or surgical management of some conditions may be recommended before or during pregnancy. Furthermore, for some genetic conditions associated with significant maternal morbidity and mortality, consideration should be given to avoiding pregnancy altogether and providing appropriate family planning and contraception counseling. Each patient should be informed about the use of prenatal vitamins and folic acid supplementation before conception, the optimization of medication regimens or supplements to avoid or minimize exposure to teratogens (when medically feasible), as well as any dietary guidelines specific to the patient's genetic condition. Patients with complex medical conditions may require treatment with medications that have potential teratogenic effects. Patients should be counseled that medications should not be discontinued until a thorough discussion with the appropriate members of the multidisciplinary team to review the risks, benefits, and therapeutic alternatives. In some circumstances, the changes in treatment need to be made before conception to minimize reproductive risks. Patients with established causative mutations for a genetic condition, and who desire prenatal genetic testing, should be offered preimplantation genetic testing with in vitro fertilization by a reproductive endocrinologist or prenatal diagnostic testing once pregnancy is established.

Pregnancy and Postpartum Considerations

Once pregnant, the patient with a genetic condition should have her initial prenatal examination early in the first trimester. This will allow for coordination of prenatal screening or testing and evaluation of pregnancy risks. Regular prenatal care, including referral to specialists, when appropriate, is important for optimization of maternal and fetal outcomes. It also is important to recognize that in addition to the issues surrounding the maternal genetic condition, the patient remains at risk of population-based occurrence of aneuploidy, other congenital anomalies, and maternal complications of pregnancy. Intrapartum and peripartum care depend on the underlying biology of each genetic condition and associated organ system abnormalities. Some of these potential complications may require specialized monitoring, assisted delivery, or both. Finally, modified postpartum and neonatal care, including on-going postpartum evaluations, may be indicated for certain genetic conditions.

Summary

Given the rarity and complexity of some genetic conditions in pregnancy and their evolving management strategies, a coordinated, multidisciplinary approach to care may provide the best opportunity to improve maternal and fetal outcomes. A number of resources are available for obstetric providers seeking more information about the care of patients with specific genetic conditions (see Table 1).

For More Information

These resources are for information only and are not meant to be comprehensive. Referral to these resources does not imply the American College of Obstetricians and Gynecologists' endorsement of the organization, the organization's web site, or the content of the resource. The resources may change without notice.

ACOG has identified additional resources on topics related to this document that may be helpful for ob-gyns, other health care providers, and patients. You may view these resources at www.acog.org/MoreInfo/MaternalGeneticConditions.

ISSN 1074-861X

Identification and referral of maternal genetic conditions in pregnancy. Committee Opinion No. 643. American College of Obstetricians and Gynecologists. Obstet Gynecol 2015;126:e49–51.