PROGRAM CNE003 • RELEASE DATE: DECEMBER 20, 2010 • EXPIRATION DATE: DECEMBER 20, 2011
ESTIMATED TIME TO COMPLETE: 1.0 HOUR

Genetic Counseling: Family History Risk Assessment

Sarah Keilman, MS, CGC; Eric Czuprenski, BS; Rosanne Keep, MS, CGC
Ms Keilman is a Certified Genetic Counselor and Mr Czuprenski is a Molecular Biologist, Genesis Genetics Institute, Detroit, MI; Ms Keep is a Certified Genetic Counselor, Abington Reproductive Medicine, PA

STATEMENT OF NEED
The family history is the most important tool for diagnosis and risk assessment in medical genetics. Taking a detailed family history for people planning to have a child is a useful tool for identifying individuals who may carry a risk for a genetic disorder, and it can improve the medical care of these patients.

The detailed family history allows clinicians and other healthcare professionals to identify patients who may benefit from predictive genetic testing. Many women and men do not find out that they are at high risk for having a child who may be affected with a genetic disease until the woman is already pregnant or after delivery.

Finding a potential genetic disease in the family history during pregnancy can add a significant level of anxiety to the pregnancy that could have been avoided with preconception genetic counseling. Such an assessment is often not conducted in the primary care setting.

TARGET AUDIENCE
Nurses whose primary interest is women's health and infertility.

LEARNING OBJECTIVES
After completing this activity, the reader should be able to:
- Describe patient-associated risk factors that may contribute to the potential of a genetic disease
- Discuss the key genetic factors that increase the risk for a genetic disease in the context of family planning
- Review the patterns of inheritance in human genetics that can affect specific diseases, such as cystic fibrosis, hemophilia, and neural tube defect
- Describe the role of family history in the risk for Huntington disease and breast or ovarian cancer

CONTINUING NURSING EDUCATION ACCREDITATION AND CONTACT HOURS STATEMENT
Science Care is approved by the California Board of Registered Nursing, Provider number 15559, for 1.0 contact hour.

METHOD OF PARTICIPATION
1. Read the article in its entirety
2. Go to www.obgyn-infertility-nurse.com
3. Select "Continuing Education"
4. Click on this article's title from the list shown
5. Select "Click here to complete the posttest and obtain a CE certificate online"
6. Complete and submit the CE posttest and CE activity evaluation
7. Print your Certificate of Credit

This activity is provided free of charge to participants.

Recent advances in the understanding of the human genome have led to increased knowledge and awareness of genetics and inherited diseases. These developments have enhanced the interest in using family history as a model for targeting individuals who are at greater risk for familial (ie, genetic) diseases.

The Significance of the Genetic Link

Taking a detailed family history is a useful tool for identifying individuals who may need further consultation, and it can improve the medical care of these patients.[1] Such detailed family history also allows clinicians and other healthcare professionals to identify patients who may benefit from predictive genetic testing. Rich and colleagues indicate that the family history is the most important tool for diagnosis and risk assessment in medical genetics, and that a family history promises to serve as a critical element in primary care medicine.[2]

When an individual is planning to start a family, there are benefits to knowing her/his family history before conception. Many women and men do not find out that they are at high risk for having a child who may be affected with a genetic disease until the woman is already pregnant or after delivery.

Finding a potential genetic disease in the family history during pregnancy can add a significant level of anxiety to the pregnancy that could have been avoided with preconception genetic counseling. A detailed review of the family history before pregnancy enables us to educate patients about potential risks and additional reproductive options that may be available.

Table 1 Patterns of Inheritance in Human Genetics

Inheritance pattern	Definition	Disease example
Autosomal dominant	1 affected gene copy is all that is needed to cause disease	Retinoblastoma
Autosomal recessive	2 affected gene copies are necessary to cause disease 1 affected gene copy results in a carrier of the condition	Cystic fibrosis
X-linked dominant	A dominant genetic mutation is carried on the X chromosome	Rett syndrome
X-linked recessive	1 affected gene copy on the X chromosome will affect males, but females will be carriers	Hemophilia
Multifactorial	Caused by environmental factors as well as mutations in multiple genes	Neural tube defects

Key Factors

A number of important factors must be considered when taking a detailed family history in the context of family planning. These include:

1. *A patient's pregnancy history:* Multiple miscarriages can indicate a chromosomal abnormality, whereas certain prenatal ultrasound findings can indicate other inherited conditions[3]

2. *The degree of relatedness:* If a patient has a sister affected with an inherited disease, there is a higher risk to the patient than if the affected individual was a first cousin[3]

3. *Full or half sibling status:* Half siblings share only 25% of their DNA, whereas full siblings share 50% of their DNA[3]

4. *Modes of inheritance:* **Table 1** outlines the common inheritance patterns and provides examples for these

5. *Consanguinity:* If a woman and her partner are first cousins, there is an increase in risk for adverse outcomes in pregnancy compared with a couple that

FACULTY DISCLOSURES
As a provider accredited by the California Board of Registered Nursing, Science Care must ensure balance, independence, objectivity, and scientific rigor in all its activities. All course directors, faculty, planners, and any other individual in a position to control the content of this educational activity are required to disclose to the audience any relevant financial relationships with any commercial interest. Science Care must determine if the faculty's relationships may influence the educational content with regard to exposition or conclusion and resolve any conflicts of interest prior to the commencement of the educational activity. Disclosures are as follows:
- Eric Czuprenski, BS, has nothing to disclose.
- Rosanne Keep, MS, CGC, has nothing to disclose.
- Sarah Keilman, MS, CGC, has nothing to disclose.
- Harvey J. Stern, MD, PhD, has nothing to disclose.
- Dalia Buffery, MA, ABD, has nothing to disclose.
- The staff members of Science Care have nothing to disclose.

DISCLAIMER
The opinions and recommendations expressed by faculty, authors, and other experts whose input is included in this program are their own and do not necessarily represent the viewpoint of Science Care or Novellus Healthcare Communications, LLC.

is not blood related; the widely accepted risk in the general population of malformations in a pregnancy is between 3% and 4%; the risk to second cousins and beyond is statistically similar to the risk of an unrelated couple (**Table 2**).[4,5]

Examples of Challenging Diagnoses

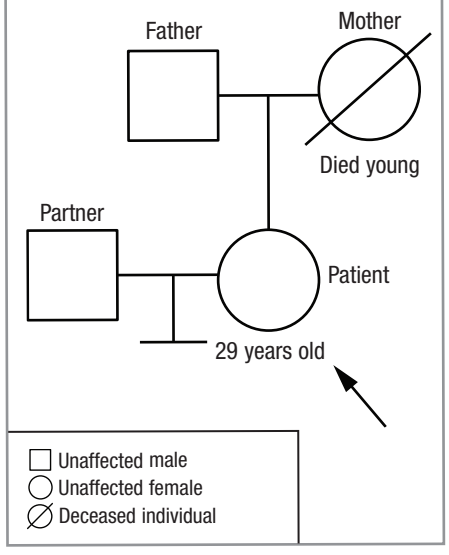
In addition to accurately interpreting family history and risk for inherited conditions, genetic counselors also discuss the benefits and limitations of relevant genetic testing options and help patients to understand and adapt to the implications of inherited diseases. Genetic counselors specialize in many areas of medicine, including oncology, pediatrics, and obstetrics.

Case 1A

A 29-year-old woman is contemplating starting a family. Taking a detailed family history is essential in her risk assessment. When asked about her parents' health, she states that her father is in good health, but that her mother died very young in a car accident.

By gathering data only from the patient's first-degree relatives, the patient would appear to have no significant health risks (**Figure 1**). As we go further into the family history, however, more information is discovered that suggests potential genetic risks, as can be seen in Case 1B below.

Figure 1 No Significant Family History



Case 1B

A 29-year-old woman is contemplating starting a family. Taking a detailed family history is essential in her risk assessment. When asked about her parents' health, she states that her father is in good health, but her mother died very young in a car accident. When asked about her mother's parents, she states that her mother's father is affected with Huntington disease, as are 2 of her maternal uncles. Her mother might have had the Huntington disease mutation, but because she died young, she did not live long enough to display symptoms.[3] **Figure 2** demonstrates the role of family history in Huntington disease.

It is clear from Case 1B that by obtaining a thorough family history, health risks to the patient become apparent. If information on each grandparent was not requested, this woman might never have realized that she was at risk for Huntington disease. It would be important to refer this woman to a genetic counselor, so that she could be properly counseled on her potential risk for Huntington disease and the options for testing. As she gets older, her risk for developing symptoms increases, and a proper diagnosis could be instrumental to her treatment.

Table 2 Risk of Malformations in Couples of Varying Degrees of Relatedness

Degree of relation	First cousins	Not related
Risk, %	Up to 6.8	3-4

Source: Bennett RL, Motulsky AG, Bittles A, et al. Genetic counseling and screening of consanguineous couples and their offspring: recommendations of the National Society of Genetic Counselors. *J Genet Couns*. 2002;11:97-119.

This patient also has a number of reproductive options. She may choose to have her children soon. She may choose to be tested for the condition before having a family, or she may even choose to use preimplantation genetic diagnosis to reduce the risk of transferring this disease to her children.

> If information on each grandparent was not requested, this woman might never have realized that she was at risk for Huntington disease.

If a detailed family history had not been taken, the patient might not have realized that she was at risk for a progressive disease. With more information obtained about a family, more of an accurate assessment can be made for a patient's risk of inherited conditions.

Such a detailed family history is often not obtained in primary care and obstetric settings. Any healthcare provider can obtain a patient's family history; however, accurately interpreting that history can be challenging. When a family history is significant for an inherited or suspected condition, it is appropriate to refer the patient to a genetic counselor, who has specialized training in interpreting family and medical histories to assess the risk for disease.

Case 2

A 32-year-old woman presents to her gynecologist for her annual checkup. She reports that since her last appointment, her mother has been diagnosed with breast cancer at age 52 years. Because of the possibility of inherited breast cancer, her gynecologist asks about any other cancer diagnoses in other family members. The patient reports that her maternal aunt had ovarian cancer at age 52 years, and her maternal grandmother had breast cancer at age 70 years. Given this family history, the patient's physician refers her to a genetic counselor to discuss the possibility that this history is indicative of hereditary breast and ovarian cancer syndrome, as shown in **Figure 3**.

Before their scheduled appointment, the genetic counselor was able to obtain medical records from the patient's mother, maternal aunt, and maternal grandmother. A detailed review of this information makes it apparent that the maternal aunt did not have ovarian cancer. Instead, she had cervical cancer.

In addition, because this patient has not had a blood relative diagnosed with breast cancer before the age of 50 and has no family history of ovarian

Continued on page 20

Figure 2 Family History of Huntington Disease

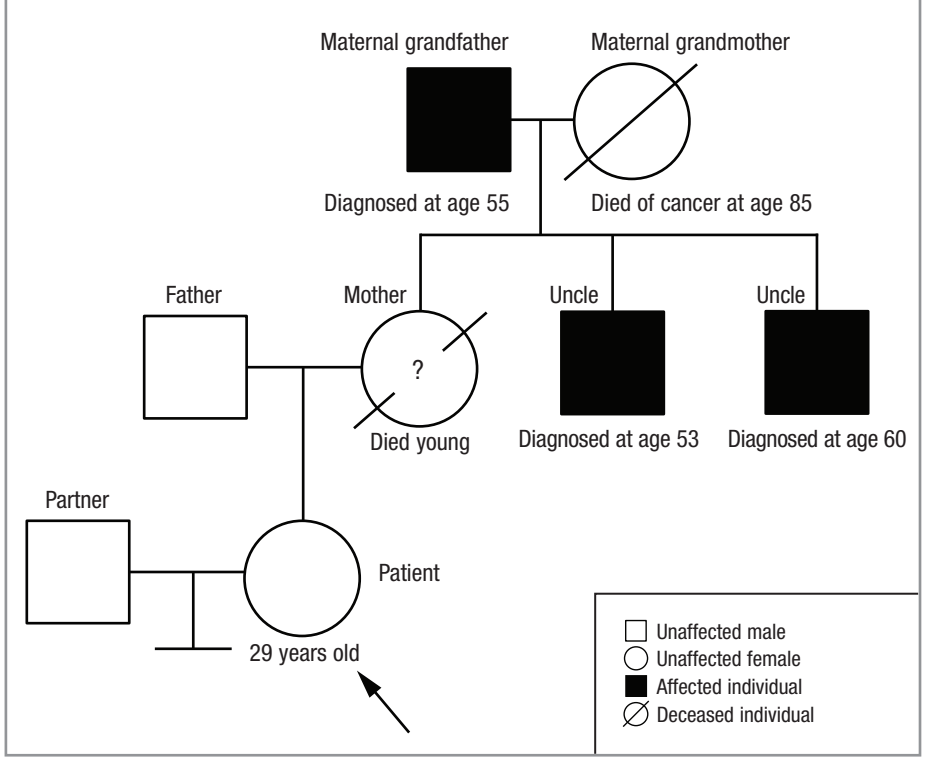
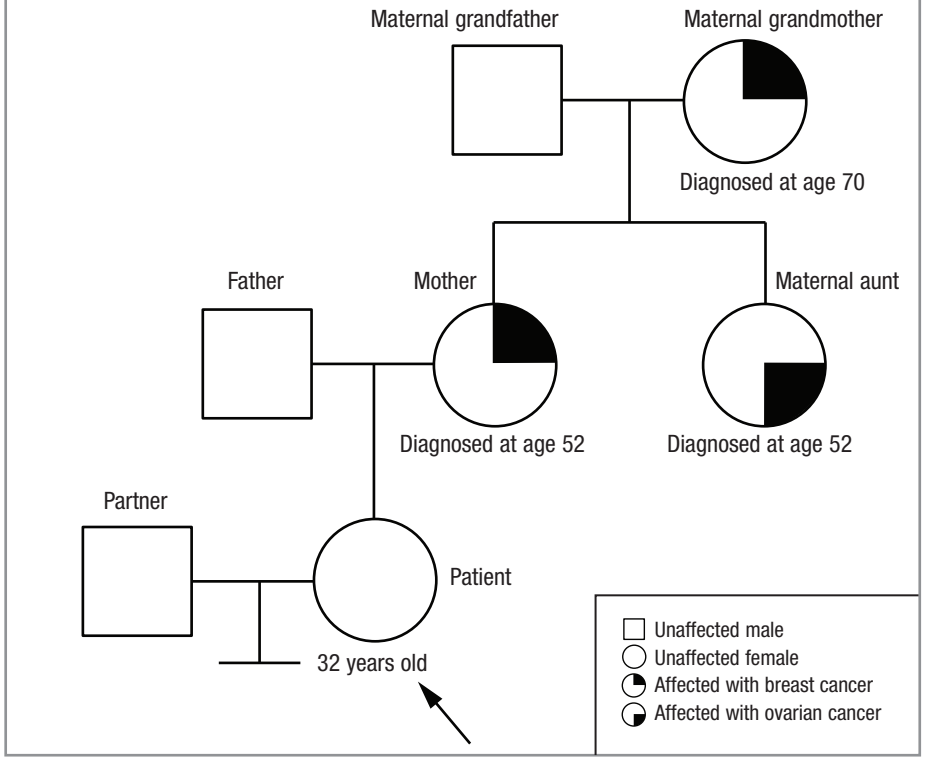
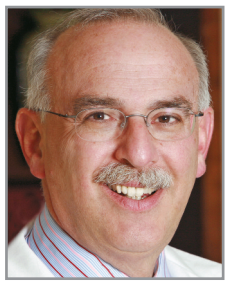


Figure 3 Family History of Breast and Ovarian Cancer



COMMENTARY



Understanding Reproductive Genetics

Harvey J. Stern, MD, PhD
Director, Reproductive Genetics
Genetics & IVF Institute, Fairfax, VA

Reproductive genetics has become an intrinsic part of helping couples who are undergoing assisted reproductive technologies (ART). As in general obstetrics, couples attempting to achieve pregnancy through in vitro fertilization (IVF) or other ART procedures need to be made aware of their potential genetic risks.

An individual's genetic liability is composed of disease-related genetic traits accumulated from their ethnic background and unique family history. Population statistics estimate that the average healthy person carries 5 to 8 gene alterations associated with recessive genetic disorders.[1] Even when the carrier is healthy, family planning and reproduction can be risky. If the reproductive partner happens to carry a gene alteration for one of the genetic conditions, the pregnancy would be at risk for a child with that disease.

Prenatal genetic counseling is a process by which couples are advised of potential genetic liabilities; the probability of a fetus developing a disease; and ways the disease may be prevented, avoided, or ameliorated in the offspring.

The 2 procedures used to obtain a more accurate assessment of genetic liability are a detailed assessment of the family history and appropriate prenatal genetic testing. During a genetic counseling session, patients are asked questions about their personal and medical history, as well as questions about the medical history of siblings, parents, cousins, and grandparents, to obtain complete information on 3 generations.

After assessment of this core family group, obtaining information on additional family members may provide a deeper understanding of familial patterns.

Anything suggesting potential genetic disorders or other noted risks is then discussed in detail. Couples are educated about their risks for recurrence of a disorder and early warning signs, and are counseled about the emotional, social, and familial implications of the identified risks. With a basic understanding of the various options, couples can then have control over how or if they pursue further information. Many times, couples elect specific genetic testing to gather more information.

> Population statistics estimate that the average healthy person carries 5 to 8 gene alterations associated with recessive genetic disorders.

The American College of Obstetricians and Gynecologists has issued standard recommendations for ethnic and general population genetic screening in couples of reproductive age.[2] Testing is available for more than 2000 genetic disorders, including common diseases, such as sickle-cell anemia, cystic fibrosis, and spinal muscular atrophy, or more complex conditions, such as mental retardation or congenital heart disease.

The family history (ie, pedigree) is the mainstay of reproductive genetic risk assessment. The cases discussed in the main article demonstrate that failure to take an accurate 3-generation pedigree can lead to missing important information regarding the couple's true risk for genetic disease in their offspring.

Many IVF centers and even some OB/GYN practices now employ genetic counselors who are experts in obtaining and interpreting genetic risk information. Tools to help collect family history are widely available; the Centers for Disease Control and Prevention has compiled a list that includes resources from the US Surgeon General, the Genetic Alliance, and the American Medical Association.[3] If genetic risk factors are identified, or if the patient has concerns regarding potential risks for the offspring, referral to a geneticist or genetic counselor is appropriate. ■

References

1. Milunsky A, Milunsky JM. Genetic counseling: preconception, prenatal and perinatal. In: Milunsky A, Milunsky JM, eds. *Genetic Disorders and the Fetus: Diagnosis, Prevention and Treatment*. Wiley-Blackwell: Oxford, UK; 2010.
2. Committee on Ethics, American College of Obstetricians and Gynecologists; Committee on Genetics, American College of Obstetricians and Gynecologists. ACOG Committee Opinion no. 410: ethical issues in genetic testing. *Obstet Gynecol*. 2008;111:1495-1502.
3. Centers for Disease Control and Prevention. Family history collection tools. 2009. www.cdc.gov/genomics/famhistory/resources/tools.html. Accessed October 25, 2010.

Genetic Counseling... *Continued from page 19*

cancer, she is not considered to be at increased risk for hereditary breast or ovarian cancer.

Frank and colleagues found that a woman with this family history has a 1.5% risk of having a genetic mutation involving the *BRCA1* or *BRCA2* gene.[6] If more information for this patient reveals cancer diagnoses in the family, a reevaluation would be appropriate.

Advances in the Understanding of Heritable Diseases

The advancements made in our understanding of the human genome have led to greater understanding in the progression of heritable diseases. The creation of a family pedigree has become the model for visualizing and interpreting familial diseases (Figures 1-3). A detailed family history can help healthcare professionals to determine when genetic testing is appropriate for the individual patient.[3]

Documenting a family history also provides a starting point for medical intervention for an entire family.[7] It allows for referral to appropriate specialists, where the patients can obtain information that can help them make informed choices about their health and the health of their future children.

Conclusion

Factors to consider when taking a family history in the context of human reproduction include previous pregnancies, degree of relatedness between the woman and her partner, genetic relationship to affected family members, mode of inheritance, and consanguinity. If a patient is at high risk for a hereditary disease, she or he should be referred to a genetic counselor. If healthcare professionals place a greater emphasis on this component of patient consultation, we will be able to provide more comprehensive care for patients and their families. ■

References

1. Acton RT, Go RC, Roseman JM. Genetics and cardiovascular disease. *Ethn Dis*. 2004;14:S2-8-S2-16.
2. Rich EC, Burke W, Heaton CJ, et al. Reconsidering the family history in primary care. *J Gen Intern Med*. 2004;19:273-280.
3. Scheuner MT, Wang SJ, Raffel LJ, et al. Family history: a comprehensive genetic risk assessment method for the chronic conditions of adulthood. *Am J Med Genet*. 1997;71:315-324.
4. Zlotogora J, Shalev SA. The consequences of consanguinity on the rates of malformations and major medical conditions at birth and in early childhood in inbred populations. *Am J Med Genet A*. 2010;152A:2023-2028.
5. Bennett RL, Motulsky AG, Bittles A, et al. Genetic counseling and screening of consanguineous couples and their offspring: recommendations of the National Society of Genetic Counselors. *J Genet Couns*. 2002;11:97-119.
6. Frank TS, Deffenbaugh AM, Reid JE, et al. Clinical characteristics of individuals with germline mutations in *BRCA1* and *BRCA2*: analysis of 10,000 individuals. *J Clin Oncol*. 2002;20:1480-1490.
7. Hunt SC, Gwinn M, Adams TD. Family history assessment: strategies for prevention of cardiovascular disease. *Am J Prev Med*. 2003;24:136-141.