Carrier screening: an evolving resource for couples planning a family

Gabriel Lazarin, MS, CGC

Gabriel Lazarin is a board-certified genetic counselor and Vice President of Medical Science Liaisons at Counsyl, a DNA testing and genetic counseling company.

Carrier screening is routinely performed in the obstetrics field. This genetic testing identifies couples at risk of conceiving a pregnancy affected with a recessive genetic disease. Although utilized less in family practice settings, there is reason to consider a change.

Over the past two decades, genetic disease screening practices for women and their partners have changed dramatically, owing to shifting population demographics and advancing testing technologies. In 2001, population-based cystic fibrosis testing was introduced for Caucasians and Ashkenazi Jewish, and later in all groups, due to its prevalence and clinical impact. Since then, carrier screening has expanded, both in purpose and in diseases tested.

Given the rapid pace of change, keeping abreast of new data and laboratory offerings is a challenge for any provider. For simplification, here we present three things you should know about carrier screening today.

1. Preconception carrier screening is superior to screening during pregnancy.

The ideal time to offer carrier screening is before pregnancy, according to consensus expert opinion. This was recently affirmed in a joint statement from the American College of Obstetricians and Gynecologists, American College of Medical Genetics and Genomics, National Society of Genetic Counselors, Perinatal Quality Foundation, and Society of Maternal-Fetal Medicine (“Joint Statement”, p.5). Preconception identification of at-risk couples avails access to more reproductive options, including preimplantation genetic diagnosis, adoption, and use of donor gametes. Once pregnant, two options remain - either invasive diagnostic testing (and its accompanying risk for fetal loss) or watchful waiting.

Despite the advantages of preconception screening, only 1 in 6 family physicians provide such preconception care. There is significant potential benefit to changing this practice: 63% of reproductive-aged women visit a family physician on an annual basis and 66% of those only visit their FP. The well-woman visit is an opportune time for a discussion on carrier screening.

2. Carrier screening isn’t only for untreatable pediatric-onset diseases.

Historically, carrier screening served to identify risks for having children affected with severe diseases, such as Tay-Sachs disease and cystic fibrosis.

As the number of diseases tested has expanded, so have the objectives of carrier screening. In contrast to guidelines and opinions that have focused on the birth of severely affected children,
the Joint Statement broadens that scope, stating, “the goal of preconception and prenatal carrier screening is to provide couples with information to optimize pregnancy outcomes based on their personal values and preferences.”

This broader description considers the interest of patients in screening for diseases that benefit from early interventions. Medium chain-acyl coA dehydrogenase deficiency (MCADD) is a metabolic disorder that causes hypoglycemia and, in some cases, death. Since a modified diet and supplementation is an effective treatment, MCADD is included for newborn screening in all states. Yet, 5% of MCADD-related pediatric deaths occur within 72 hours after birth, leaving a short window of opportunity to detect and address the disease. Carrier screening provides the opportunity for earlier preparation and avoidance of morbidity and mortality for many other diseases like MCADD.

Yet another consideration of carrier screening is for diseases causing prenatal lethality. For example, Smith-Lemli-Opitz syndrome (SLOS) is a disease that has emerged as having an expected birth incidence similar to other commonly screened diseases, yet is uncommon due to high fetal mortality rates. Because of this, SLOS testing may already be appropriate in any case of spontaneous abortion or stillbirth.

3. Expanded carrier screening identifies carriers for more diseases in the diverse US population.

In recent years, carrier screening has evolved from an ethnicity-based protocol for a handful of diseases to pan-ethnic testing for dozens to hundreds of disease. Decreasing costs for genetic analysis have enabled this possibility, but population demographics and the distribution of genetic disease lend considerable merit to expanded carrier screening.

Certain diseases, such as beta-hemoglobinopathies and Tay-Sachs disease, are perceived to occur within specific groups. Yet, due to increasing admixture, such diseases are frequently found in other populations. The 2010 US Census confirms that the multiracial population is growing quickly, which will further diminish the effectiveness of ethnicity-based protocols.

Lastly, the expansion of diseases tested captures a greater portion of genetic disease burden. Approximately 20% of infant mortality and 18% of infant hospitalizations are due to single-gene diseases. This may be surprising since there are few “common” and recognized recessive diseases akin to cystic fibrosis and sickle cell disease. In fact, it is the large collection of rare occurrences that accumulate to a high frequency. Data from population-based expanded carrier screening finds that the collective frequency of 89 severe recessive diseases is higher than that of Down syndrome or open neural tube defects.

Expanded carrier screening is relatively new practice in obstetrics, but appears to be gaining acceptance among genetic counselors and obstetricians. Expert opinion statements provide guidance to family practitioners who adopt it.