

Spotlight on Health

Expanded Carrier Screening

Inherited genetic disorders occur in about 0.4% of live births.¹ Collectively, they account for a significant impact on hospitalizations and healthcare costs.² Carriers of genetic disorders can be identified by screening, which can help couples with family planning. The field of carrier screening is constantly evolving, and expanded carrier screening (ECS) panels have become available in recent years. However, guidance on designing and selecting these panels has been limited.

In March 2017, the American College of Obstetricians and Gynecologists (ACOG) published guidelines on the use of ECS in light of new technologies and an ethnically diverse population. This newsletter will discuss the benefits of ECS in the context of the updated guidelines.

Targeted vs Expanded Carrier Screening

Carrier screening is a tool used to help identify carriers of inherited genetic disorders. It can identify disorders associated with autosomal recessive and X-linked gene variants. These variants are typically associated with known medical disorders. Some disorders are more prevalent in certain races or ethnicities.³

Traditional targeted carrier screening generally involves testing single genes associated with single inherited conditions. Test selection is generally based on a person's family history or ethnicity. However, some people may not know their ethnic background, or they may provide inaccurate information. And some people with mixed ethnicity may be difficult to categorize. As a result, targeted screening based on ethnicity can fail to identify some carriers.⁴

Next-generation sequencing (NGS) is helping to overcome this obstacle by making ECS possible. NGS is an important advance in genetic testing. Its use in carrier screening enables testing for a wider range of clinically relevant genes at the same time. Despite the advantages of ECS, it has introduced new issues. Screening panels are available for hundreds of conditions, but may offer limited clinical utility. This approach can lead to more than half of tested people being identified as carriers.⁵ Identifying people as carriers of extremely rare conditions can lead to unnecessary anxiety. Some disorders are so rare that it is not possible to calculate their residual risk.⁵ Fortunately, new guidelines are available to offer direction for the best use of ECS.

New Guidelines

In March 2017, ACOG published 2 committee opinions that specifically address carrier screening.^{5,6} The new guidance offers criteria for selecting which disorders to screen. In short, screening should be selected to target the most common, debilitating, or actionable disorders. The selection criteria are highlighted in the sidebar. Other key guideline recommendations include:



ACOG Disorder Screening Selection Criteria⁵

Disorders included on ECS panels should meet several of the following criteria:

- Screening accuracy
- Carrier frequency ≥ 1 in 100
- Well-defined phenotype
- Detrimental effect on quality of life
- Associated with cognitive or physical impairment
- Necessity of surgical or medical intervention
- Early onset
- Improved perinatal outcomes
- Optimized newborn outcomes

- Every pregnant woman should be provided information about carrier screening.
- Carrier screening and counseling are ideal before pregnancy.
- All women who are pregnant or considering pregnancy should be offered screening for the following disorders:
 - Cystic fibrosis
 - Spinal muscular atrophy
 - Hemoglobinopathies (eg, sickle cell disease)
 - Thalassemias (eg, α -thalassemia, β -thalassemia)
 - Fragile X, for women with a family history or with ovarian insufficiency

The guidelines state that additional screening may be indicated based on family history or ethnicity. They also recognize that ancestry is increasingly difficult to define and genetic disorders are less likely than in the past to be confined to high-risk ethnic groups. To that end, the guidance recognizes ethnic, panethnic, and expanded screening as acceptable strategies.

Counseling

The new ACOG guidelines emphasize counseling as an essential element of ECS. They recommend that counseling address the following general concepts⁵:

- Some conditions do not have clearly observable traits.
- Negative screen results may reduce likelihood, but a residual risk always remains.
 - Some conditions are so rare that prevalence estimates, and thus residual risk estimates, may not be reliable.
- Screening panels may be variable and change over time, but rescreening is not recommended.

Counseling can support informed reproductive decision making, as well as optimized pregnancy outcomes. Counseling is also an opportunity to assess a person's ability to understand and handle test results.⁷ Ultimately, carrier screening is meant to provide meaningful information to people. This information, coupled with counseling, should lead to informed decision making that supports an individual's personal values.

How the Laboratory Can Help

Quest Diagnostics offers the QHerit™ Expanded Carrier Screen, which tests for variants associated with 22 clinically actionable inherited disorders consistent with current guidelines.^{5,6} Quest also offers ethnicity-based carrier screening, as well as a wide variety of individual genetic tests. Quest offers board-certified genetic counselors who are available for consultation with healthcare providers at 1.866.436.3463 or GenInfo@QuestDiagnostics.com.

References

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