Before, Between & Beyond Pregnancy
The National Preconception Curriculum and Resources Guide for Clinicians

Guidance for Preconception Cystic Fibrosis Carrier Screening

Colleen Landy Schmitt. MS, CGC
Genetic Counselor
Department of Obstetrics & Gynecology
University of North Carolina at Chapel Hill

This guidance should not substitute for clinical judgments or expert consultation

Summary of:
ACOG Committee Opinion
Update on Carrier Screening for Cystic Fibrosis
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Recommendations:

1. Information about cystic fibrosis screening should be made available to all couples. It is reasonable to offer cystic fibrosis carrier screening to all couples regardless of race or ethnicity as an alternative to selective screening.

    - ❖ Initial guidelines (2001) recommended screening be offered to all Caucasian couples planning a pregnancy or seeking prenatal care. In practice, two thirds of obstetricians offer carrier screening to all patients regardless of ethnicity. This is reasonable if patients are adequately counseled on their risk of carrier status and the limitations of the testing based on their ethnicity. It is the responsibility of the ordering physician to ensure the patient has been properly counseling regarding limitations of the testing its results.

2. Cystic fibrosis carrier screening should be offered before conception or early in pregnancy when both partners are Caucasian or of European or Ashkenazi Jewish ethnicity. Patients may elect to use either sequential or concurrent carrier screening; the latter option may be preferred if there are time constraints for decisions regarding prenatal diagnostic testing or termination of an affected pregnancy.

    - ❖ In general screening, it is most cost-effective and practical to perform initial screening on the patient and follow-up with her partner if a mutation is identified.

- ❖ Preconception carrier screening is beneficial, as knowledge of their carrier status may affect a couple's decision to conceive, use donor gametes, or consider preimplantation genetic diagnosis (PGD) or prenatal testing.

3. For individuals with a family history of cystic fibrosis, medical records indicating the CFTR mutations in the affected family member should be obtained whenever possible. If the mutation has not been identified, screening with an expanded panel of mutations or, in some cases, complete analysis of the CFTR gene by sequencing may be indicated. Genetic counseling in this situation is beneficial.
4. Individuals who have a reproductive partner with cystic fibrosis or congenital absence of the vas deferens may benefit from screening with an expanded panel of mutations or, in some cases, a complete analysis of the CFTR gene by sequencing.

    - ❖ Sequencing of the CFTR gene is not appropriate for routine carrier screening, but may be useful for patients with cystic fibrosis, a family history, infertile males with congenital absence of the vas deferens, or a positive newborn screening test result when an expanded panel of mutations is negative.

5. When both partners are cystic fibrosis carriers, genetic counseling is recommended to review prenatal testing and reproductive options. Prenatal diagnosis by chorionic villus sampling or amniocentesis, using DNA-based testing of fetal cells, should be offered. If the partner is unavailable for testing, genetic counseling may be helpful.
6. Cystic fibrosis carrier screening may identify individuals with two cystic fibrosis mutations who have not previously received a diagnosis of cystic fibrosis. These individuals may have a milder form of cystic fibrosis and should be referred to a specialist in cystic fibrosis for further evaluation. Genetic counseling is also beneficial.

ACOG Recommendations for Choosing a Cystic Fibrosis Screening Panel

- While over 1300 mutations have been identified in the CFTR gene, 23 are currently recommended. The mutations appear in multiple ethnic populations, have been shown to lead to classic cystic fibrosis and are present in at least 0.1% of patients with the disorder.
- Initial guidelines (2001) recommended a panel of 25 mutations found in at least 0.1% of patients with cystic fibrosis. Two (I148T and 1078delT) have been removed because they do not cause classic cystic fibrosis or occur less frequently that 0.1%.
- Additional mutations were not recommended at this time because they would not substantially increase the test sensitivity. Larger mutations panels or, in some cases, CFTR gene sequencing may be reasonable in clinical situations noted above.

- Testing for the 5T/7T/9T variant is recommended only as a reflex in the presence of the R117H mutation.