WAKE FOREST
UNIVERSITY
HEALTH SCIENCES

Cystic Fibrosis Screening / Genotyping

Clinical indicators of individuals for whom molecular genetic testing should be considered:

- To establish or confirm the diagnosis of CF in symptomatic individuals
- For carrier detection:
  - In population screening programs
  - In at-risk relatives, their reproductive partners, and in certain other individuals
  - In prenatal testing of at-risk pregnancies and for pregnancies in which fetal echogenic bowel has been identified

Cystic fibrosis needs to be considered in the following:

- Infants with meconium ileus occurs in 10-20% of newborns diagnosed with CF
- Infants with salt-loss syndromes (acute salt depletion, chronic metabolic alkalosis) hyponatremia and hypochloremia of unknown etiology with compensatory metabolic alkalosis
- Infants with hypoproteinemia and anemia
- Children with rectal prolapse
- Children with failure to thrive, poor growth and weight gain, nutritional problems, chronic diarrhea, or malabsorption. Pancreatic insufficiency with malabsorption occurs in the great majority of patients with CF.
- Children with refractory asthma (particularly at a young age), recurrent pneumonia, recurrent sinusitis, and/or nasal polyps. Alternatively, such children may have a spectrum of disorders not related to CF, including immunologic abnormalities, ciliary dysfunction, broncopulmonary anatomic abnormalities, and allergies. Though they may be present as sequelae of any of these conditions, gastroesophageal reflux and chronic tracheal aspiration also deserve to be considered as primary causes of such symptoms.
- Adolescents or adults with recurrent pancreatitis
- Adults with recurrent sinusitis/bronchitis or bronchiectasis, nasal polyps, recurrent pancreatitis
- More than 95% of males with CF are infertile due to azoospermia resulting from absent, atrophic or fibrotic Wolffian duct structures.

Molecular genetic testing:

CFTR is the only gene associated with the *CFTR*-related disorders, cystic fibrosis and CBAVD. Over 1000 mutations have been identified in the *CFTR* gene although the vast majority are rare mutations and have only been detected in one family.

Mutation panel. A 32 mutation panel is used which includes the 23 mutations recommended by the American College of Medical Genetics and the American College of Obstetricians and Gynecologists. The mutation detection rate for this 32 mutation panel varies depending on an individual's ethnic background. In some symptomatic

individuals, only one or neither mutation is detectable; in some carriers, the disease-causing mutation is not detectable. Mutations analyzed: deltaF508; deltaI507; G542X; G551D; W1282X; N1303K; R553X; 621+1G->T; R117H; 1717-1G->A; A455E; R560T; R1162X; G85E; R334W; R347P; R347H; 711+1G->T; 1898+1G->A; 2184delA; 1078delT; 3849+10kbC->T; 2789+5G->A; 3659delC; I148T; 3120+1G->A; V520F; S549N; S549R; 3905insT; 394delTT; 3876delA.

Poly T tract analysis. The Poly T tract, a string of thymidine bases located in intron 8 of the *CFTR* gene, can be associated with *CFTR*-related disorders depending on its size. The three common variants of the poly T tract are 5T, 7T, and 9T. Both 7T and 9T are considered polymorphic variants and 5T is considered a variably penetrant mutation. Poly-T testing is appropriate as a reflex test when a R117H mutation is detected or an adult male is being evaluated for CBAVD. Males with CBAVD or suspected CBAVD and individuals with non-classic CF are all appropriate for T tract typing.

Billing Information:

Initial CF Screening/Genotyping

- cpt codes: 83907, 83890, 83909, 83900, 83901x14, 83914x30, 83912

Reflex test for R117H mutation - PolyT status

- cpt codes: 83900, 83901x14, 83914, 83909, 83912

Reflex test for I148T mutation - sequence analysis

- cpt codes: 83894, 83909x2, 83898, 83904x2, 83912

Reflex test for 506/507 polymorphism

- cpt codes: 83900, 83901x14, 83914x2, 83909, 83912

Turn around time: 7-10 days