



Case Study Rationales:

Detection & Diagnosis of Cystic Fibrosis in Diverse Populations

Case 1: Hispanic Newborn with Normal Newborn Screening

Patient: A 2-week-old Hispanic newborn with prolonged jaundice, poor feeding, and weight loss. Newborn screening was normal.

Discussion and Clinical Insights:

This newborn may have undiagnosed CF due to lower detection rates and limited variant coverage in standard newborn screening panels, particularly in racially and ethnically diverse populations. Many CFTR variants that are more common in Hispanic individuals are not included in commonly used panels, increasing the risk of false-negative results. Neonatal signs that raise suspicion of CF, including failure to thrive, jaundice, and feeding difficulty, should prompt diagnostic testing for CF regardless of newborn screening results.

Case 2: Eastern European Teen with Chronic Respiratory Symptoms

Patient: A 15-year-old white male who recently immigrated from Eastern Europe with chronic cough, wheezing, and a history of recurrent pneumonia.

Discussion and Clinical Insights:

This adolescent may have undiagnosed CF given the absence of newborn screening for CF in many Eastern European countries and his persistent pulmonary symptoms consistent with the disease. Immigrant populations may carry region-specific or rare CFTR variants that are not covered by standard U.S. screening panels. Although CF is often perceived as a disease primarily affecting white individuals of European descent, diagnostic bias may lead providers to assume the diagnosis has already been considered or excluded, even when a newborn screening result is unavailable. His history of chronic cough and recurrent lower respiratory infections should prompt diagnostic testing for CF.

Case 3: African American Adult Female with Gastrointestinal Symptoms and Colorectal Cancer

Patient: A 45-year-old Black woman with a history of irritable bowel syndrome, chronic constipation, and nutritional insufficiency despite stable intake, who was recently diagnosed with colorectal cancer.

Discussion and Clinical Insights:

This patient may have undiagnosed CF given racial diagnostic bias and a non-classic extrapulmonary presentation. In adults, gastrointestinal manifestations of CF are frequently misdiagnosed as irritable bowel syndrome or other functional gastrointestinal disorders, which can delay accurate diagnosis. Symptoms such as malabsorption, chronic constipation, and colorectal complications may indicate CF-related pancreatic or gastrointestinal involvement. Her recent diagnosis of colorectal cancer may also warrant further evaluation, as gastrointestinal malignancies have been reported at increased rates in adults with cystic fibrosis.

Moreover, CF remains significantly underdiagnosed in Black patients, in part because CFTR variants more commonly found in people of color are excluded from most genetic testing and newborn screening panels. This gap, combined with a persistent lack of clinical suspicion for CF when evaluating patients of color, contributes to diagnostic delays. When gastrointestinal symptoms such as malabsorption, chronic constipation, or colorectal complications remain unexplained following a thorough workup, diagnostic testing specific for CF should be pursued to support timely identification and effective clinical management.

Case 4: South Asian American Male with Upper Airway and Gastrointestinal Symptoms

Patient: A 21-year-old South Asian American male with chronic sinus congestion, low BMI, and rectal bleeding, who was previously diagnosed with anxiety and hemorrhoids.

Discussion and Clinical Insights:

This patient may have undiagnosed CF given the presence of atypical extrapulmonary symptoms and a clinical history that includes multiple alternative diagnoses, which may have diverted attention away from CF as a potential underlying cause. His chronic sinus congestion, low body mass index, and rectal bleeding may reflect CF-related upper airway involvement, malabsorption, or gastrointestinal complications. These symptoms were previously attributed to anxiety and hemorrhoids, which may have delayed further evaluation, particularly in a patient perceived to be at low risk for CF based on ethnicity. However, CF is increasingly recognized in South Asian populations, with studies suggesting a higher prevalence than previously reported, especially compared to other regions of Asia. In patients with similar clinical features, CF should be included in the differential diagnosis, and timely diagnostic evaluation should be initiated when symptoms remain unexplained.