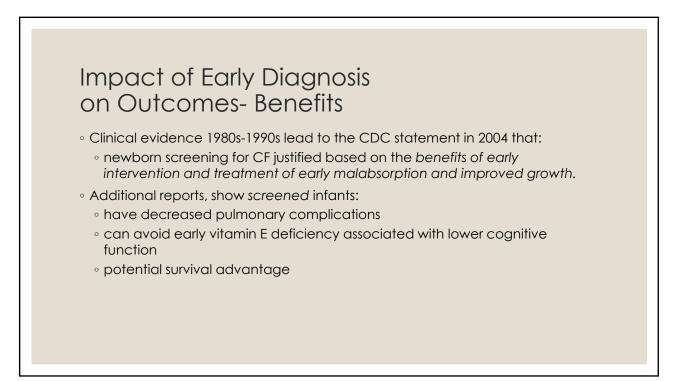


 Definitive treatment has not been available that would stop disease progression in infancy

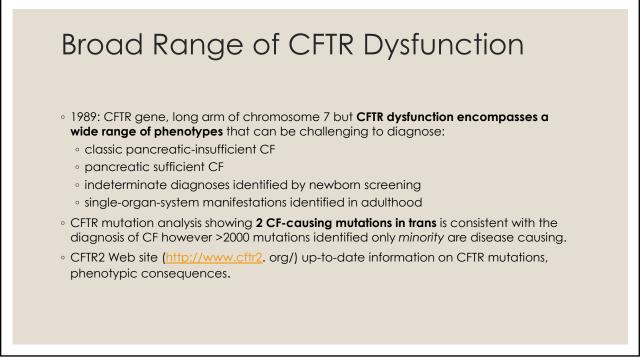
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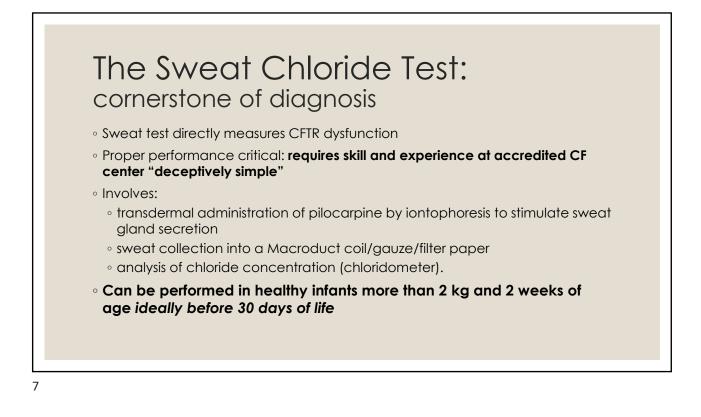


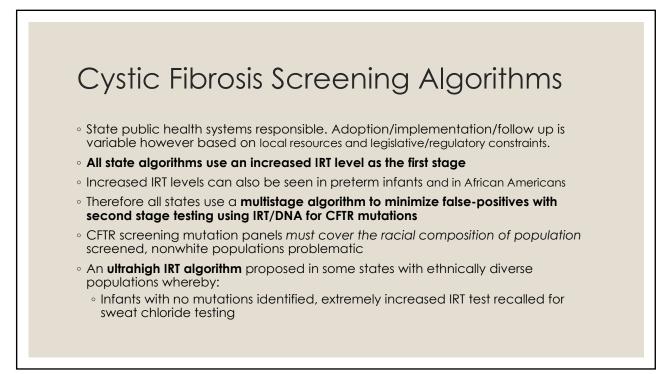
# Nutritional and Pulmonary Outcomes in the First Year

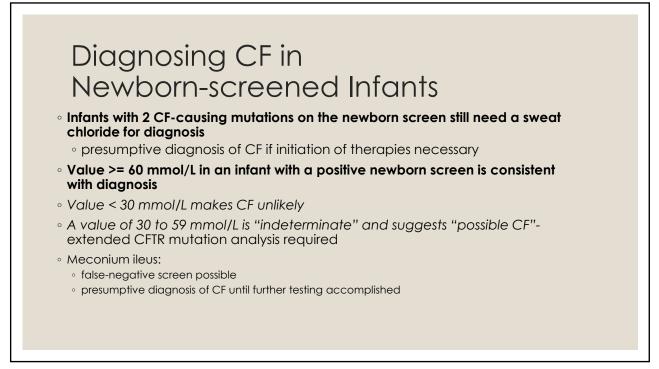
- Despite catch-up growth in weight following newborn screening **linear growth impairment continues to occur during the first year** 
  - earlier, more aggressive nutritional therapy necessary for normal growth.
- Guidelines for infant care and a more aggressive approach to preventative care are in place however:
  - lung disease known to be present in the first months of life
  - ability to change the early course of lung disease in CF remains limited
  - need for early therapies before onset of irreversible lung damage
  - long-term pulmonary benefits of CF newborn screening controversial
- Hope that CFTR modulators may offer hope



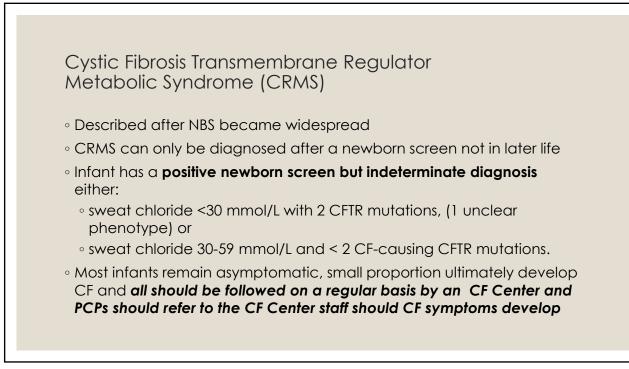


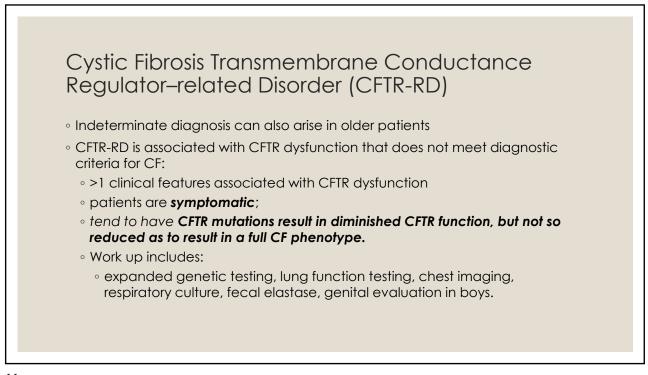




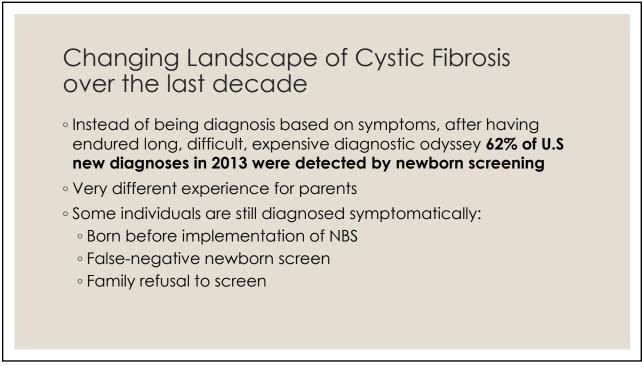












### Diagnosing Cystic Fibrosis: Symptomatic Individuals

### Any child with signs/symptoms of CF or positive family history should have sweat testing regardless of CF newborn screen

 sweat chloride level less <39 mmol/L unlikely to be CF</li>
 indeterminate sweat chloride requires extended genetic testing

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#### Signs and symptoms suggestive of CFTR dysfunction in children and adolescents

Nutritional and gastrointestinal:

- Nutritional/metabolic: failure to thrive, hypoproteinemia, hypochloremic dehydration, chronic metabolic alkalosis
- Intestinal: meconium ileus, rectal prolapse, distal intestinal obstructive syndrome, steatorrhea
- Pancreatic: exocrine pancreatic insufficiency, recurrent pancreatitis
- Hepatic: protracted neonatal jaundice, biliary cirrhosis

#### Sinopulmonary:

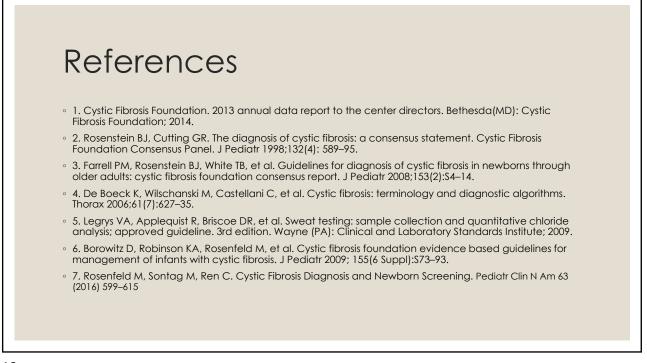
- Chronic wet or productive cough
- Bronchiectasis on chest imaging
- Respiratory infection with *Pseudomonas aeruginosa* or other atypical gram-negative organisms
- Nasal polyposis in children
- Digital clubbing
- Allergic bronchopulmonary aspergillosis

Obstructive azoospermia in boys

## Summary

- The diagnosis of CF is straightforward in most patients.
- Rapid advances in CFTR genetics/CF NBS make clear the varying clinical manifestations of CFTR dysfunction that complicate diagnosis
- We balance the benefits of early detection and treatment of a life-shortening illness with the risks of inconclusive diagnoses in infants who are likely to remain healthy, but in whom there is a small risk of progression to CF.
- CF newborn screening/ diagnosis algorithms are likely to change in next decade based on advances in tandem mass spectrometry/extended genetic analysis, better understanding of genotype-phenotype.
- Critical to keep risks/benefits of detection of the wide range of CFTR dysfunctions in mind.

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