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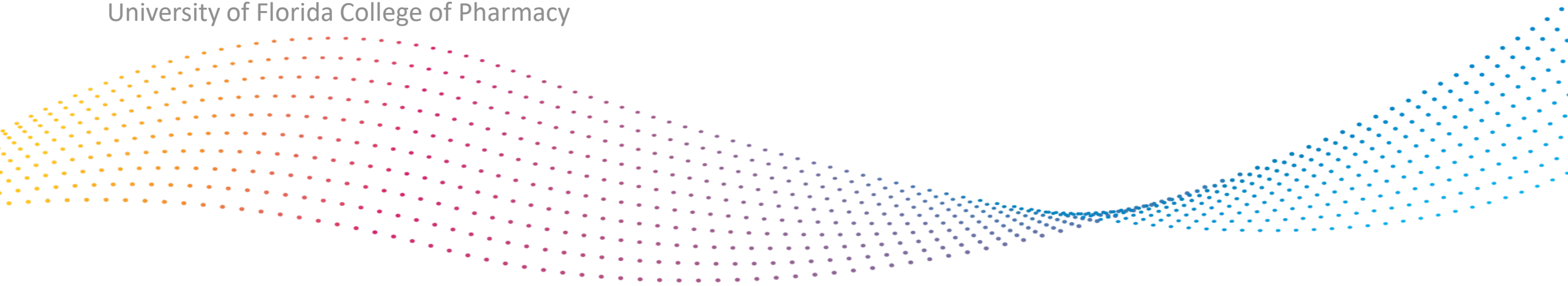
Hypertonic Saline Use in Cystic Fibrosis

Melissa Thivierge, PharmD Candidate

University of Florida College of Pharmacy



Objectives

1. Define Cystic Fibrosis
2. Review Clinical Presentation
3. Review Diagnosis Procedures
4. Review Pulmonary Symptom Progression Monitoring
5. Review Non-Pharmacologic Treatment Options
6. Review Pharmacologic Treatment Options
7. Analyze the use of Hypertonic Saline as a Pharmacologic Option

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INTRODUCTION

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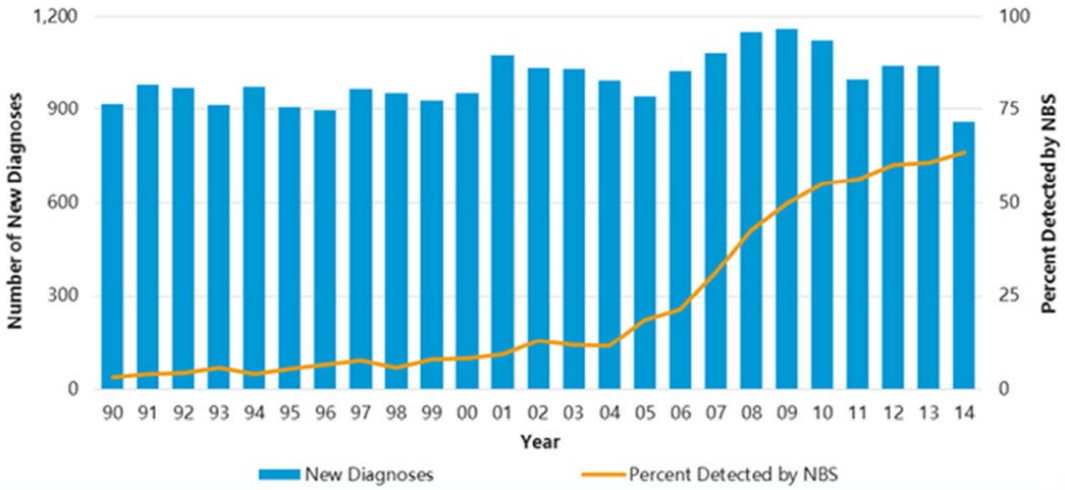
What is Cystic Fibrosis?

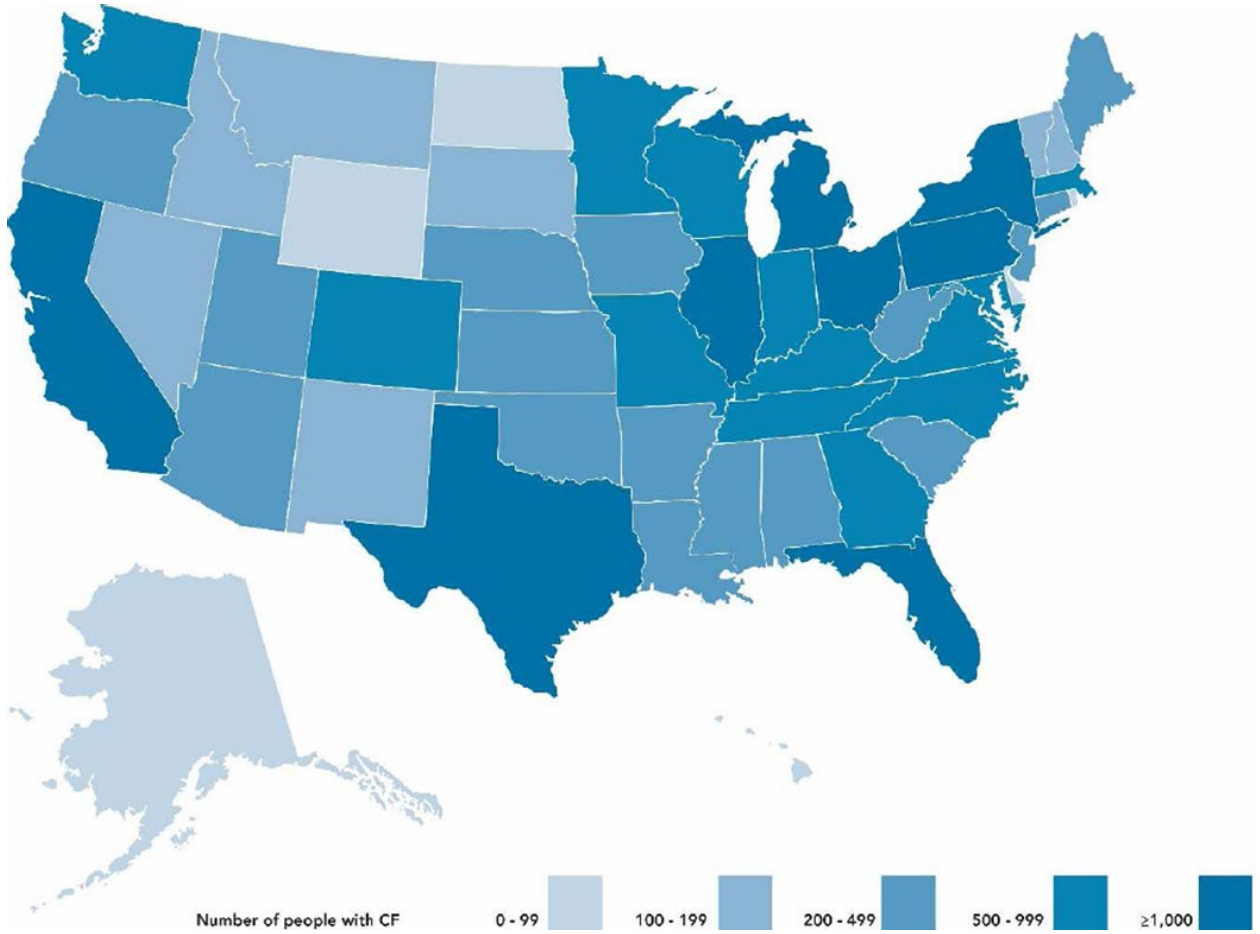
- An **irreversible** multisystem disorder caused by pathogenic mutations of the CF Transmembrane Conductance Regulator (CFTR) gene.
- Typical signs and symptoms include persistent pulmonary infections, pancreatic insufficiency, and elevated sweat chloride levels.
- Three Categories of Cystic Fibrosis: Classical, CFTR-Related and CRMS/CFSPID

Prevalence of Cystic Fibrosis

American Population	Prevalence
White Americans	1:3200
Hispanic Americans	1:10,000
Native Americans	1:10,500
African Americans	1:15,000
Asian Americans	1:30,000



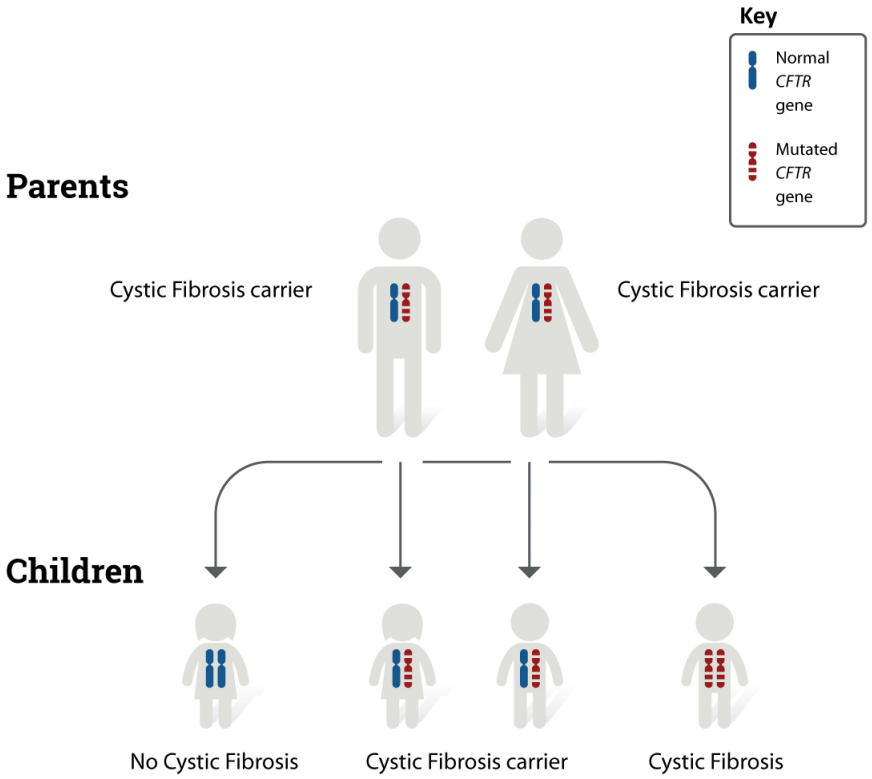
Cystic Fibrosis Foundation. *Patient Registry 2014 Annual Report*. Bethesda 2015



Cystic Fibrosis Foundation. *Patient Registry 2014 Annual Report*. Bethesda 2015

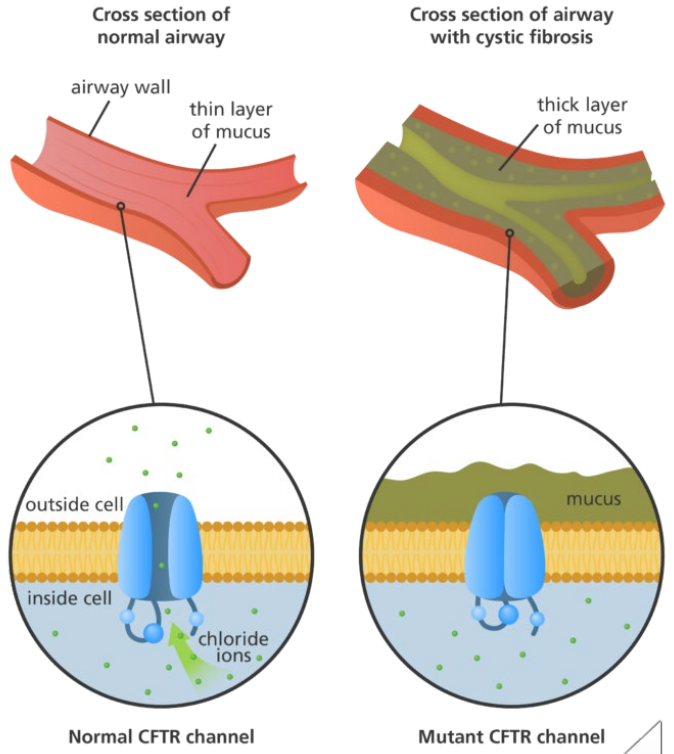
Pathophysiology

Cystic Fibrosis is caused by a mutation in the CFTR gene located on Chromosome 7. A deletion of F508 (Phenylalanine) is the most common mutation (70%) .



Class	Mutation defect	Specific effect of mutation class
I	Lack of CFTR synthesis	No functioning CFTR chloride channels
II	Defective protein processing	CFTR is destroyed in the cell. CFTR does not reach cell surface
III	Defective channel regulation	CFTR reaches cell surface but does not properly open for chloride transport
IV	Defective chloride conduction	CFTR function is poor and chloride conduction is defective
V	Reduced amount of CFTR protein	Decreased production of CFTR
VI	Increased turnover of CFTR at cell surface	CFTR is functional but unstable at cell surface, and is removed and destroyed

To date, more than 2,000 different CFTR mutations have been identified and fall into six classes based on how the defect changes the functionality of the gene.



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CLINICAL PRESENTATION

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Clinical Presentation

Cystic Fibrosis is a multifaceted disease affecting one or more organ systems

Pulmonary

Gastrointestinal

Pancreatic

Hepatic

Renal

Musculoskeletal

Genitourinary

Clinical Presentation

General
Family History of CF Salty-Tasting Skin Clubbing of Fingers and Toes Productive Cough Pseudomonas aeruginosa isolated from airway secretions Hypochloremia metabolic alkalosis

Neonatal	Infancy
Meconium Ileus Prolonged Neonatal Jaundice Abdominal or Scrotal Calcifications (secondary to meconium peritonitis) Intestinal Atresia	Persistent Infiltrate on Chest X-Ray Failure to Thrive Anasarca or Hypoproteinemia Chronic Diarrhea Abdominal Distension Cholestasis Staphylococcus aureus Pneumonia Pseudotumor Cerebri (vitamin A deficiency) Hemolytic Anemia (vitamin E deficiency)
Childhood	**Adolescent/Adult**
Chronic Pansinusitis Nasal Polyps Steatorrhea Rectal Prolapse Distal Intestinal Obstruction Syndrome Recurrent or Chronic Pancreatitis Liver Disease	Allergic Bronchopulmonary Aspergillosis Chronic Pansinusitis or Nasal Polyps Bronchiectasis Hemoptysis Recurrent or Chronic Pancreatitis Portal Hypertension Delayed Puberty Congenital Bilateral Absence of the Vas Deferens

Adapted from O'Sullivan. Cystic fibrosis. Lancet 2009;373:1891–904

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DIAGNOSIS

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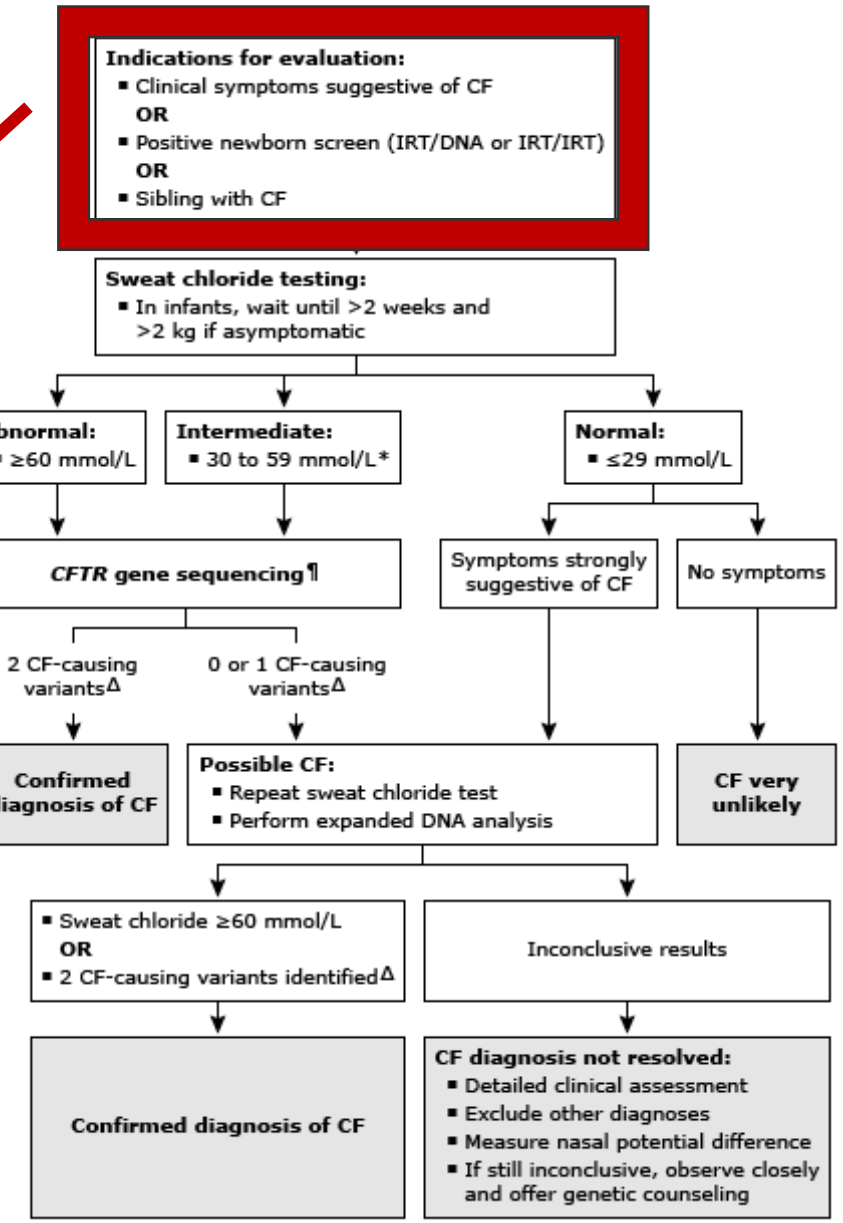
Diagnosis of Cystic Fibrosis

Multi-Step Process

Indications for evaluation:
- Clinical symptoms suggestive of CF
  OR
- Positive newborn screen (IRT/DNA or IRT/IRT)
  OR
- Sibling with CF



Newborn Screening

IRT	DNA
Identifies a patient with 1 or 2 copies of CTFR gene mutation **DOES NOT** identify **IF** the patient has 1 or both or both copies of CTFR gene mutations	Identifies if a patient has 1 or both copies of CTFR gene mutation 1 mutation = Carrier of CF 2 mutations = Diagnosis of CF

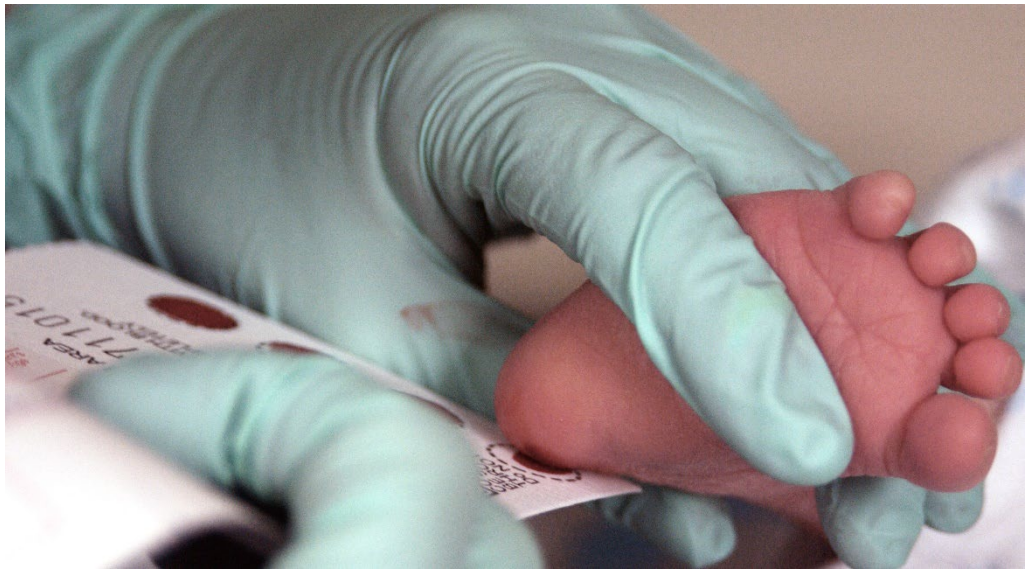
IRT = Immunoreactive Trypsinogen Assay
DNA = Deoxyribonucleic Acid Assay

2 Testing Algorithms

1. IRT/DNA (Sensitivity = 80%)
2. IRT/IRT1/DNA (Sensitivity = 99.5%)

In both Algorithms, an IRT value >60 ng/mL is considered clinically significant and triggers a repeat test in 2 weeks.

Infants with a positive result should undergo sweat testing when at least 2 weeks of age and >2 kg

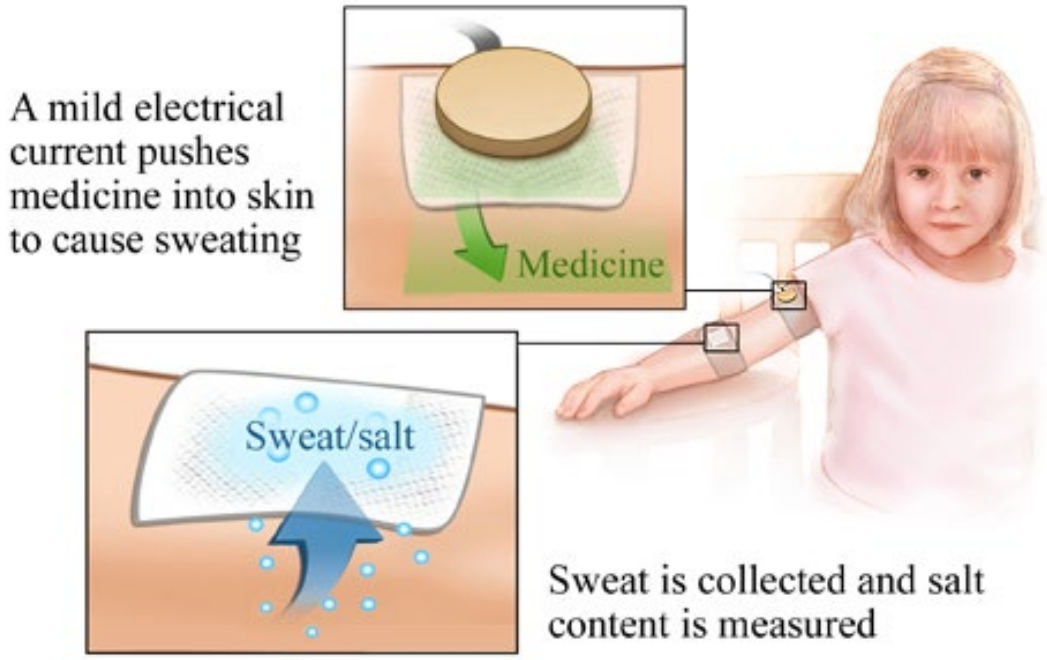


Sontag MK, Wright D, Beebe J, et al. A new cystic fibrosis newborn screening algorithm: IRT/IRT1 ↑/DNA. *J Pediatr*. 2009;155(5):618–622.

Sweat Testing

GOLD STANDARD for diagnosis of CF

Collection of sweat via pilocarpine ionophoresis



Sweat chloride concentration	Result	Interpretation
≤29 mmol/L	Normal	CF very unlikely
30 to 59 mmol/L	Intermediate	Possible CF, additional testing recommended*
≥60 mmol/L	Abnormal	Diagnosis of CF, if confirmed by a second test and if clinical symptoms consistent with CF are present¶

Asymptomatic infants with equivocal results of the diagnostic process (sweat chloride test and DNA analysis) are given a provisional diagnosis of CRMS, also known as CFSPID.[1]

CF: cystic fibrosis; CRMS: cystic fibrosis-related metabolic syndrome; CFSPID: cystic fibrosis screen positive, inconclusive diagnosis.

* Additional testing usually consists of molecular diagnosis (DNA analysis) and a second sweat test.

¶ Clinical symptoms of CF are not required among newborns identified through a screening program, or among siblings of patients with CF who are diagnosed by shared genotype.

Cystic Fibrosis Foundation, Borowitz D, Parad RB, et al. Cystic Fibrosis Foundation practice guidelines for the management of infants with cystic fibrosis transmembrane conductance regulator-related metabolic syndrome during the first two years of life and beyond. J Pediatr 2009; 15[illegible].

Cystic Fibrosis Categories

Classical Disease	CFTR-Related	CRMS/CFSPID
• Patient demonstrates disease in one or more organ systems • Elevated sweat chloride levels ≥60 mmol/L	• Classical disease limited to one organ system • Some evidence of CFTR dysfunction that does not meet full genetic criteria for CF diagnosis • Should have complete gene sequencing to confirm CFTR gene duplications or deletions	• Asymptomatic infant with a positive Newborn Screening results and either …. • Intermediate sweat chloride levels (30 – 59 mmol/L) on two separate occasions **OR** • Normal sweat chloride levels (≤29 mmol/L) on two separate occasions **AND** two CFTR mutations

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PROGRESSION MONITORING

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Pulmonary Radiographs

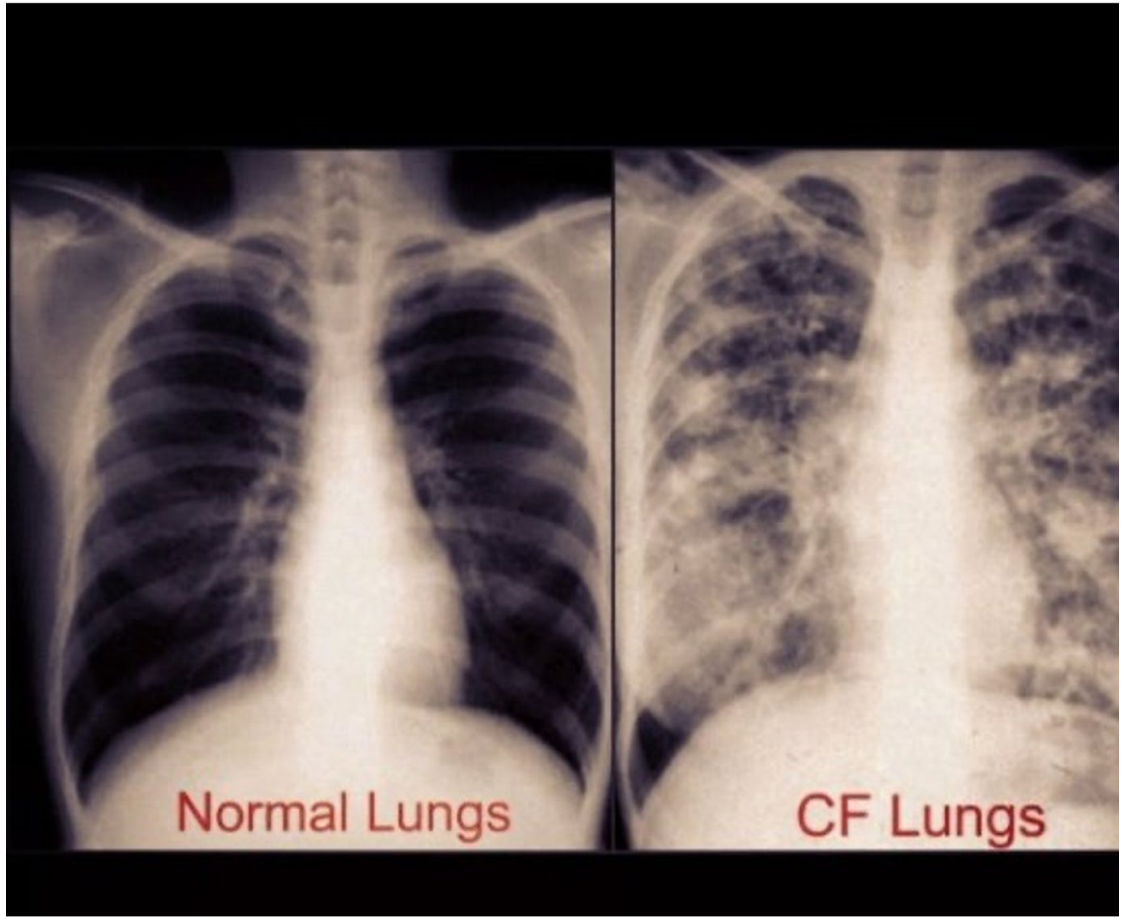
Diagnostic of chronic infection

Assist in preventing and managing pulmonary exacerbations by showing bilateral infiltrates on radiographic images

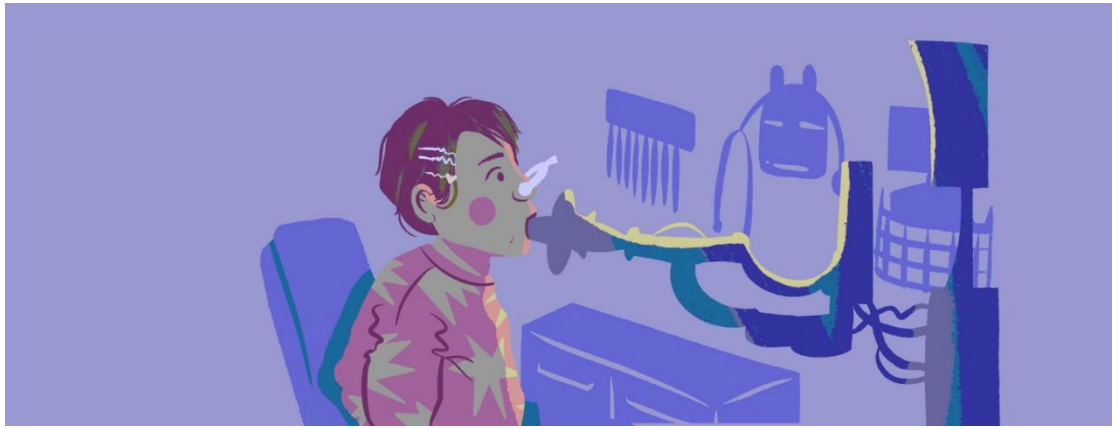
Uses less radiation than CT scans

Early disease may show hyperinflations and minimal bronchial thickening

Advanced disease will show bronchiectasis, air trapping and hyperinflation



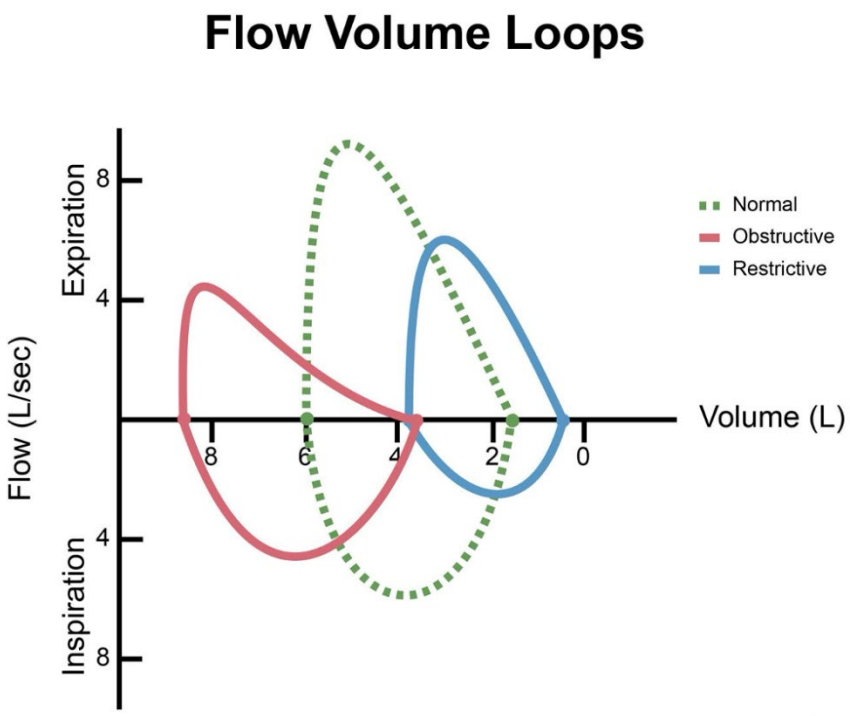
Pulmonary Function Test (PFT)



In CF progression, PFT will show a decline in lung function

Patient will experience:

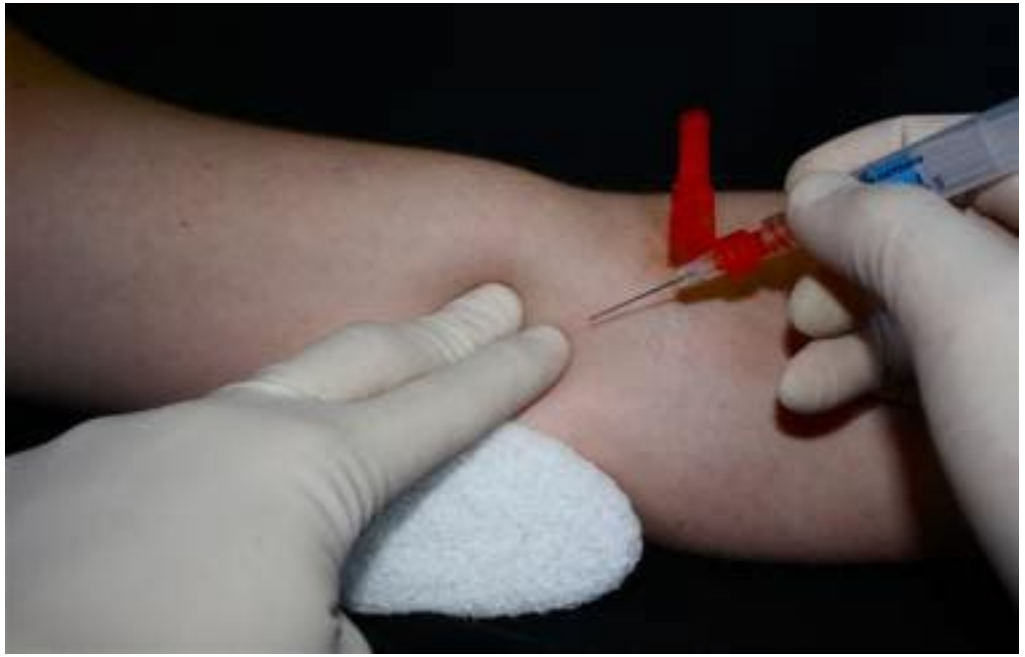
1. pulmonary exacerbations
2. increased sputum production
3. chronic cough



Arterial Blood Gas (ABG)

Useful in early diagnosis and determining severity of exacerbations

Declining lung function may exhibit hypoxemia leading to respiratory acidosis



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PULMONARY NON-PHARMACOLOGICAL OPTIONS

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Non-Pharmacological Options

Table 2

Nonpharmacologic Airway Clearance Therapy

Airway Clearance Therapy	Outcome
Percussion and postural drainage	Loosens and clears mucus
Positive expiratory pressure	Opens airways
Active cycle of breathing technique	Relaxes airways, gets air behind mucus, and clears mucus out of the lungs
Autogenic drainage	Moves mucus out of the lungs
High-frequency chest wall oscillation machine	Vibrates the chest, loosens and thins mucus
Physical activity (exercise)	Improves lung function

Source: Reference 30.

Flume PA, Robinson KA, O'Sullivan BP, et. al. Cystic fibrosis pulmonary guidelines: airway clearance therapies. *Respir Care*. 2009;54(4):522-537.

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PULMONARY PHARMACOLOGICAL OPTIONS

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Pulmonary Treatment Options

1. CFTR Modulators
2. **Airway Clearance Therapies**
3. Infection Prevention
4. Bronchodilators
5. Anti-inflammatory Therapy
6. Acute Exacerbation Prevention
7. Acute Exacerbation Treatment

Table 3

Pharmacologic Treatment of CF
With High/Substantial or High/Moderate Net Benefit

Drug	Recommend-ation Category	Dose	Common Side Effects
Inhaled hypertonic saline (7% nebu-lized solution)	B[a]	4 mL/dose via oral inhalation twice daily	Cough, bronchospasm/chest tightness, pharyngitis, hemoptysis, sinusitis, sneezing
Dornase alfa	A[b], B[a]	2.5-mg oral inhalation 1-2 times daily	Chest pain, conjunctivitis, pharyngitis, hoarseness/voice alterations
Aztreonam	A[b], B[a]	Age ≥7 y: 75 mg nebulized 3 times daily for 28 days	Cough, nasal congestion, wheezing, pharyngolaryngeal pain, chest discomfort, bronchospasm
Tobramycin	A[b], B[a]	300 mg (one ampule) inhaled twice daily for 28 days	Nephrotoxicity, ototoxicity cough, pharyngitis, rhinitis, dyspnea, hemoptysis, asthma, sinusitis, epistaxis, hyperventilation, rales, wheezing, laryngitis, bronchitis
Azithromycin	B[a] (with *P aeruginosa*)[c]	250 mg orally 3 days per week (MWF)	Diarrhea, nausea, vomiting
Ivacaftor	A[b]	Age ≥6 y: 150 mg orally Age 2-5 y, 50-75 mg orally, every 12 h	Abdominal pain, diarrhea, elevated liver enzymes, headache, nasal congestion, nausea, pharyngitis, rash
Lumacaftor/ Ivacaftor	No published grade recommendation to date	Age 12 y and older: 2 tablets (200/125) twice daily with fat-containing food Ages 6-11 y: 2 tablets (100/125) twice daily with fat-containing food	Abdominal pain, diarrhea, elevated hepatic enzymes, headache, nasal congestion, nausea, pharyngitis, amenorrhea, cough, dyspnea
Ibuprofen	B[a,c]	20-30 mg/kg twice daily. Maximum daily dose 3,200 mg/day	Abdominal pain, constipation, edema, neutropenia, prolonged bleeding time,

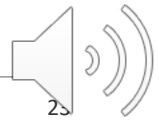
[a] mild disease; [b] moderate-to-severe disease; [c] off-label. CF: cystic fibrosis.
Source: References 19, 20, 22, 24, 25, 31-34.

DeSimone E, Tillerman J, et. al Cystic Fibrosis: Update on Treatment Guidelines and New Recommendations. *U.S. Pharmacist*. 2018 May https://www.uspharmacist.com/article/cystic-fibrosis-update-on-treatment-guidelines-and-new-recommendations

Airway Clearance Therapy

- Difficulty clearing secretions form the airways is a common complaint among CF patients with moderate to severe lung disease.

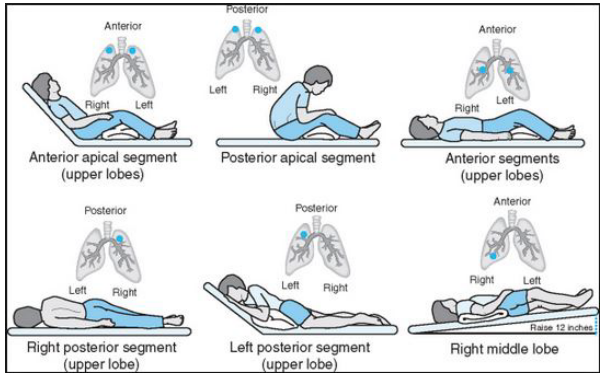
- High viscosity of CF-sputum is caused by dehydration and the interaction of several macromolecules
  - Mucus glycoproteins
  - Denatured DNA
  - Protein polymers (actin filaments)



Airway Clearance Therapy

- Airway clearance can be promoted by a combination of inhaled drugs to loosen and liquefy the mucus.

- Chest physiotherapy helps the patient expectorate the secretions



Airway Clearance Therapy

1. Dornase alpha (First Line Option)
2. **Hypertonic 7% Saline**
3. Mannitol (Second Line Option)

Inhaled Therapy BID Administration Sequence
1. Albuterol (Reduces risk of bronchospasm) 2. Hypertonic 7% Saline 3. Dornase alpha (once daily administration) 4. Chest physiotherapy/exercise 5. Other inhaled treatments (aerosolized antibiotics)

Inhaled medications should not be mixed in the same nebulizer, because the consequences of doing so are unknown.

DNase is inactivated if it is mixed with Hypertonic 7% saline.

Similarly, these agents should not be mixed with tobramycin or other inhaled antibiotics.

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HYPERTONIC SALINE USE

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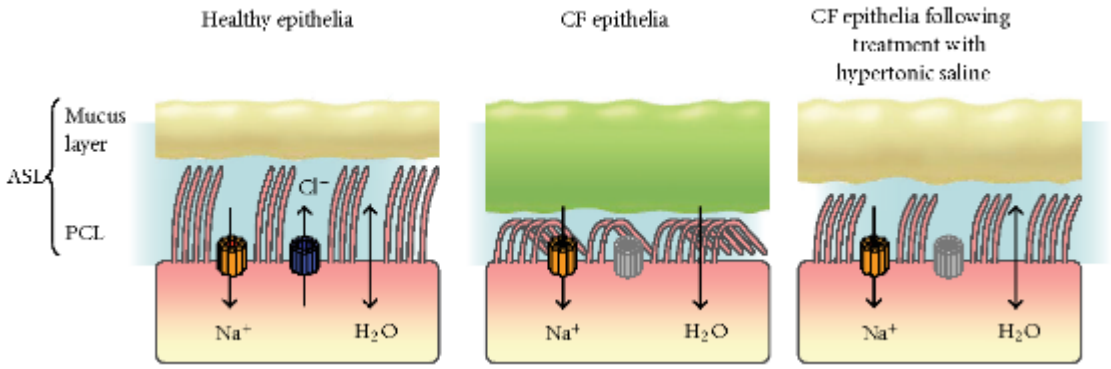
Hypertonic Saline Use

Inhaled hypertonic saline helps to hydrate the mucus that is present in the airways of patients with CF.

It is presumed that high osmolarity of the solution draws water from the airway to temporarily reestablish the aqueous surface layer that is deficient in CF



1. Donaldson SH, Bennett WD, Zeman KL, Knowles MR, Tarran R, Boucher RC. Mucus clearance and lung function in cystic fibrosis with hypertonic saline. N Engl J Med. 2006 Jan 19;354(3):241-50. doi: 10.1056/NEJMoa043891. PMID: 16421365.
2. Reeves, Emer P. et al. "Hypertonic Saline in Treatment of Pulmonary Disease in Cystic Fibrosis." *The Scientific World Journal* 2012 (2012): n. pag.

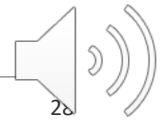
Hypertonic Saline Use

Adult & Children Dosing:

Inhale 4 mL hypertonic 7% saline solution twice daily via nebulizer

*** Pretreat with an inhaled bronchodilator (albuterol) to prevent bronchospasm

*** Inhaled 3% solution may be used if patients cannot tolerate 7% (institutional protocol specific)



Hypertonic Saline Use

Inhaled Dornase alpha and hypertonic saline have been recommended to promote airway clearance per CFF guidelines (2007-2016)

- CFF guidelines were published prior to the use of CFTR triple therapy elexacaftor-tezacaftor-ivacaftor (ETI)
  - FDA approval in children ≥ 12 years October 2019
  - FDA approval in children ≥ 2 years April 2023

- SIMPLIFY study may show that that use of hypertonic saline may not be necessary for some patients

1. Federal Drug Administration. *FDA approves new breakthrough therapy for cystic fibrosis.* October 21, 2019. Accessed August 12, 2024 https://www.fda.gov/news-events/press-announcements/fda-approves-new-breakthrough-therapy-cystic-fibrosis
2. Cystic Fibrosis Foundation. *FDA Approves Trikafta for Children Ages 2 Through 5 Years with Certain CF Mutations.* April 26, 2023. Accessed August 12, 2024 https://www.cff.org/news/2023-04/trikafta-approval-ages-2-5-mutations

SIMPLIFY Study

Why the SIMPLIFY Study?

- ETI therapy substantially restores CFTR protein function and improves mucociliary clearance
- Reduces mucus accumulation and airway obstruction
- Unknown if hypertonic saline and dornase alfa is clinically necessary in individuals treated with ETI
- No large randomized, controlled trials testing the effects of withdrawing chronic daily therapy of hypertonic saline and dornase alfa after establishing treatment with CFTR modulators

Mayer-Hamblett N, Ratjen F, Russell R, Donaldson SH, Riekert KA, Sawicki GS, Odem-Davis K, Young JK, Rosenbluth D, Taylor-Cousar JL, Goss CH, Retsch-Bogart G, Clancy JP, Genatossio A, O'Sullivan BP, Berlinski A, Millard SL, Omlor G, Wyatt CA, Moffett K, Nichols DP, Gifford AH; SIMPLIFY Study Group. Discontinuation versus continuation of hypertonic saline or dornase alfa in modulator treated people with cystic fibrosis (SIMPLIFY): results from two parallel, multicentre, open-label, randomised, controlled, non-inferiority trials. Lancet Respir Med. 2023 Apr;11(4):329-340. doi: 10.1016/S2213-2600(22)00434-9. Epub 2022 Nov 4. PMID: 36343646; PMCID: PMC10065895.

SIMPLIFY Study

Value of This Study:

- SIMPLIFY is the first study to assess the impact of discontinuing standard of care therapy after establishing ETI patients ≥ 12 years of age

- Tested whether discontinuation of hypertonic saline or dornase alpha is non-inferior to continuation of therapy over a 6-week study period
  - Primary Outcome – Change in percent predicted FEV_1
  - Secondary Outcome – Meaningful changes in lung clearance index (LCI), safety, and patient reported outcomes

Mayer-Hamblett N, Ratjen F, Russell R, Donaldson SH, Riekert KA, Sawicki GS, Odem-Davis K, Young JK, Rosenbluth D, Taylor-Cousar JL, Goss CH, Retsch-Bogart G, Clancy JP, Genatossio A, O'Sullivan BP, Berlinski A, Millard SL, Omlor G, Wyatt CA, Moffett K, Nichols DP, Gifford AH; SIMPLIFY Study Group. Discontinuation versus continuation of hypertonic saline or dornase alfa in modulator treated people with cystic fibrosis (SIMPLIFY): results from two parallel, multicentre, open-label, randomised, controlled, non-inferiority trials. Lancet Respir Med. 2023 Apr;11(4):329-340. doi: 10.1016/S2213-2600(22)00434-9. Epub 2022 Nov 4. PMID: 36343646; PMCID: PMC10065895.

SIMPLIFY Study

Results of SIMPLIFY Study:

- Study was not powered to detect significant differences between subgroups
- However, the confidence intervals consistently exceeded the non-inferiority margin

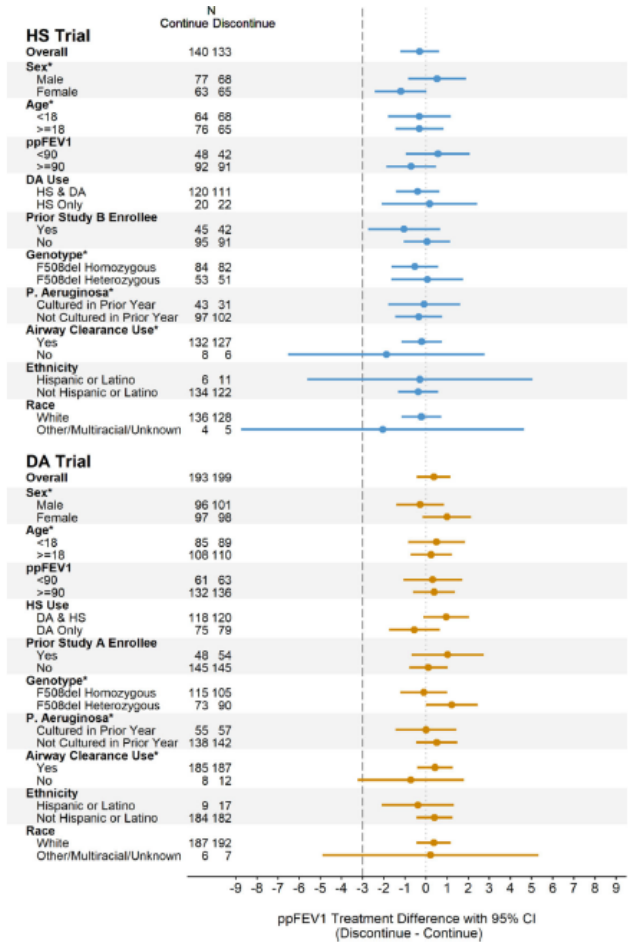


Figure 3.
Difference between the discontinuation and continuation treatment arms in the 6-week change in $ppFEV_1$ among subgroups in the PP population in the HS trial and DA trial. Treatment differences adjusted for randomization strata. Pre-defined subgroups noted with *. Sensitivity analyses in the ITT population provided in Figure S2.

Mayer-Hamblett N, Ratjen F, Russell R, Donaldson SH, Riekert KA, Sawicki GS, Odem-Davis K, Young JK, Rosenbluth D, Taylor-Cousar JL, Goss CH, Retsch-Bogart G, Clancy JP, Genatossio A, O'Sullivan BP, Berlinski A, Millard SL, Omlor G, Wyatt CA, Moffett K, Nichols DP, Gifford AH; SIMPLIFY Study Group. Discontinuation versus continuation of hypertonic saline or dornase alfa in modulator treated people with cystic fibrosis (SIMPLIFY): results from two parallel, multicentre, open-label, randomised, controlled, non-inferiority trials. Lancet Respir Med. 2023 Apr;11(4):329-340. doi: 10.1016/S2213-2600(22)00434-9. Epub 2022 Nov 4. PMID: 36343646; PMCID: PMC10065895.

SIMPLIFY Study

Adverse Effect Results:

- CRISS & CFQ-R (respiratory domain) used to assess symptoms
  - Large numbers in CRISS = More symptoms
  - Large number in CFQ-R = Fewer symptoms

- No significant differences between treatment arms in CRISS or CFQ-R score changes after 6 weeks
- Incidents of protocol defined pulmonary exacerbations and hospitalizations were infrequent and comparable between treatment groups.

Table 2.

Overview of Safety Outcomes

	Hypertonic Saline (HS) Trial		Dornase Alfa (DA) Trial	
	Continue N=186	Discontinue N=184	Continue N=237	Discontinue N=240
Participants with any SAE, n (%)	1 (0.5%)	2 (1.1%)	0 (0.0%)	0 (0.0%)
Abdominal Pain	0 (0.0%)	1 (0.5%)	0 (0.0%)	0 (0.0%)
Infective Pulmonary Exacerbation	1 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Suicidal ideation	0 (0.0%)	1 (0.5%)	0 (0.0%)	0 (0.0%)
Participants with any AE, n (%)	44 (23.7%)	64 (34.8%)	55 (23.2%)	89 (37.1%)
Maximum AE Severity, n (%) *				
Mild	23 (52.3%)	41 (64.1%)	36 (65.5%)	62 (69.7%)
Moderate	20 (45.5%)	18 (28.1%)	15 (27.3%)	24 (27.0%)
Severe †	1 (2.3%)	4 (6.3%)	4 (7.3%)	3 (3.4%)
Life Threatening ‡	0 (0.0%)	1 (1.6%)	0 (0.0%)	0 (0.0%)
Participants with at least one respiratory AE, n (%)	22 (11.8%)	30 (16.3%)	24 (10.1%)	47 (19.6%)
Participants with AE leading to Treatment Regimen Modification, n (%)	1 (0.5%)	5 (2.7%)	2 (0.8%)	7 (2.9%)
Participants with AE leading to Physician Directed Modification, n (%)	1 (0.5%)	0 (0.0%)	1 (0.4%)	4 (1.7%)
Participants with Most Common AEs, n (%) §				
Cough	7 (3.8%)	7 (3.8%)	10 (4.2%)	16 (6.7%)
Nasal Congestion	10 (5.4%)	5 (2.7%)	4 (1.7%)	11 (4.6%)
Chest Discomfort	1 (0.5%)	6 (3.3%)	1 (0.4%)	11 (4.6%)
Sputum Increased	3 (1.6%)	3 (1.6%)	2 (0.8%)	9 (3.8%)
COVID-19	2 (1.1%)	6 (3.3%)	1 (0.4%)	6 (2.5%)
Infective Pulmonary Exacerbation	5 (2.7%)	3 (1.6%)	3 (1.3%)	7 (2.9%)
Myalgia	2 (1.1%)	1 (0.5%)	1 (0.4%)	6 (2.5%)
Headache	3 (1.6%)	4 (2.2%)	6 (2.5%)	4 (1.7%)

Data are n (%).

*Percentages out of participants with any AE.

†The AEs classified as severe were the following, participants could have more than one severe event: Hypertonic Saline Continue: infective pulmonary exacerbation; Hypertonic Saline Discontinue: abdominal pain, chest discomfort, juvenile idiopathic arthritis, nasal congestion, pulmonary congestion; Dornase Alfa Continue: diarrhoea, eye infection bacterial, rib fracture, upper respiratory tract infection, wrist fracture; Dornase Alfa Discontinue: chest pain, immunization reaction, infective pulmonary exacerbation.

‡The AE classified as life threatening was suicidal ideation.

§Most common AEs defined as those occurring in at least 2.5% of participants in any treatment group across studies.

Mayer-Hamblett N, Ratjen F, Russell R, Donaldson SH, Riekert KA, Sawicki GS, Odem-Davis K, Young JK, Rosenbluth D, Taylor-Cousar JL, Goss CH, Retsch-Bogart G, Clancy JP, Genatossio A, O'Sullivan BP, Berlinski A, Millard SL, Omlor G, Wyatt CA, Moffett K, Nichols DP, Gifford AH; SIMPLIFY Study Group. Discontinuation versus continuation of hypertonic saline or dornase alfa in modulator treated people with cystic fibrosis (SIMPLIFY): results from two parallel, multicentre, open-label, randomised, controlled, non-inferiority trials. Lancet Respir Med. 2023 Apr;11(4):329-340. doi: 10.1016/S2213-2600(22)00434-9. Epub 2022 Nov 4. PMID: 36343646; PMCID: PMC10065895.

SIMPLIFY Study

Study Conclusion:

- Among patients > 12 years with CF and established on ETI and **relatively good lung function**:
  - Discontinuation of either hypertonic saline or dornase alpha did not result in clinically meaningful changes in $ppFEV_1$ and LCI
  - No significant safety concerns were identified
  - Low rates of adverse events

- **Higher rates of adverse events in patients with lower lung function**

Mayer-Hamblett N, Ratjen F, Russell R, Donaldson SH, Riekert KA, Sawicki GS, Odem-Davis K, Young JK, Rosenbluth D, Taylor-Cousar JL, Goss CH, Retsch-Bogart G, Clancy JP, Genatossio A, O'Sullivan BP, Berlinski A, Millard SL, Omlor G, Wyatt CA, Moffett K, Nichols DP, Gifford AH; SIMPLIFY Study Group. Discontinuation versus continuation of hypertonic saline or dornase alfa in modulator treated people with cystic fibrosis (SIMPLIFY): results from two parallel, multicentre, open-label, randomised, controlled, non-inferiority trials. Lancet Respir Med. 2023 Apr;11(4):329-340. doi: 10.1016/S2213-2600(22)00434-9. Epub 2022 Nov 4. PMID: 36343646; PMCID: PMC10065895.

Hypertonic Saline Use

Recommended Treatment for Patients ≥ 12 years on ETI

Mild or No Lung Disease	Moderate to Severe
No longer routinely recommend dornase alpha or hypertonic saline	Recommend use of **BOTH** dornase alpha and hypertonic saline

*** SIMPLIFY study did not enroll patients < 12 years old

- Recommended to maintain hypertonic saline and dornase alpha use while on ETI therapy.

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Hypertonic Saline Use in Cystic Fibrosis

Melissa Thivierge, PharmD Candidate 2025

University of Florida College of Pharmacy