



UR
MEDICINE

GOLISANO
CHILDREN'S HOSPITAL

Cystic Fibrosis: An Overview

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APP Grand Rounds/Enduring Presentation

Summer 2019

MEDICINE *of* THE HIGHEST ORDER

Objectives

1. Understand the genetic abnormality causing cystic fibrosis (CF) and the newborn screen process
2. Recognize the multiple organ systems affected by CF
3. Identify common treatments /medications and management strategies for CF (both inpatient and outpatient)
4. Understand the CFTR modulators available and a general overview of how they work
5. Understand the unique infection control issues related to CF
6. Recognize the psychosocial implications of CF

DEFINITION:

Cystic fibrosis is a progressive, genetic disease that causes persistent lung infections and limits the ability to breathe over time. In people with CF, mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene cause the CFTR protein to become dysfunctional...

Epidemiology/Demographics of Cystic Fibrosis

- Autosomal recessive transmission
- Over 1700 mutations on CFTR gene known to date
- ~ 1 per 31 Americans are symptom free carriers of a defective CFTR gene
 - 1 in 29 Caucasian-Americans
 - 1 in 46 Hispanic-Americans
 - 1 in 65 African-Americans
 - 1 in 90 Asian-Americans

Epidemiology of Cystic Fibrosis (cont'd)

- ~ 30,000 individuals living with CF in the US (about 70,000 individuals worldwide)
 - 1 in 2,500-3,500 Caucasian-Americans
 - 1 in 4,000-10,000 Hispanic-Americans (steady increase over the past 15 years reflecting national population trends)
 - 1 in 15,000-20,000 African-Americans
 - 1 in 100,000 Asian-Americans
- ~ 1,000 new cases of CF are diagnosed each year
 - More than 75% of new diagnoses are made by age 2 years
 - Median predicted age of survival has increased from 33.4 years in 2003 to 40.7 years in 2013 to 46.2 in 2017

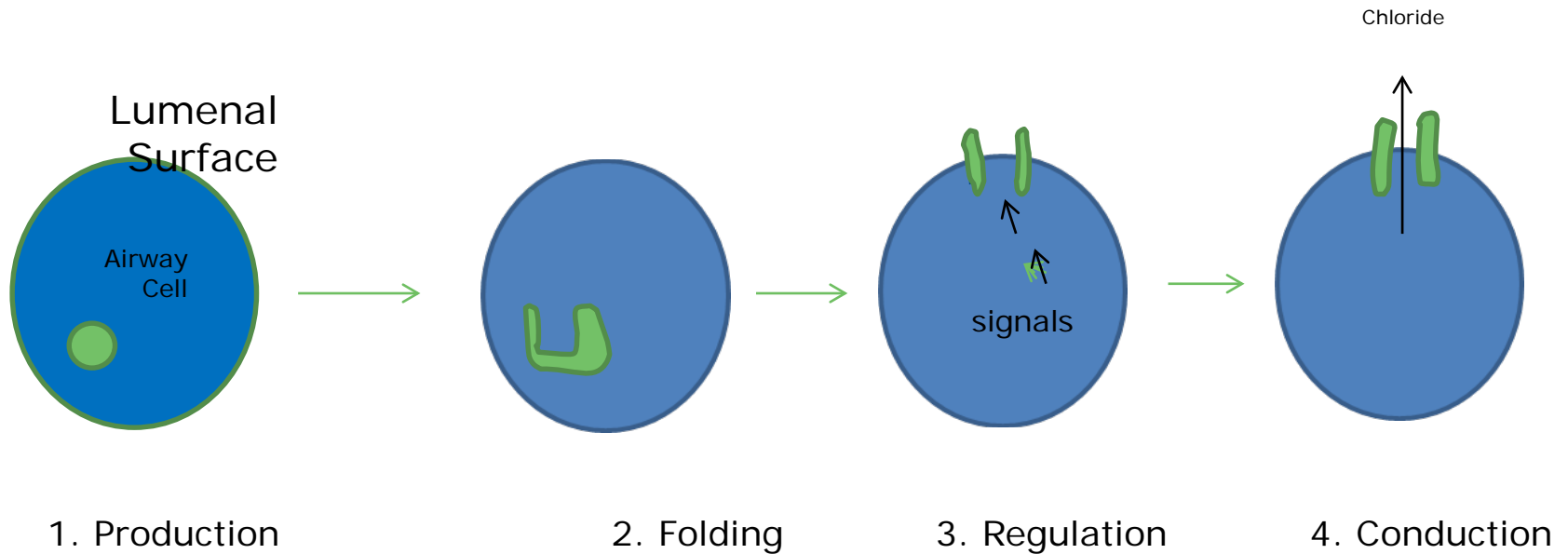
CFTR: What is it?

Cystic fibrosis transmembrane conductance regulator

- A protein found in the cells that line various organs (like the lungs and pancreas)
- This protein is responsible for regulating the flow of salt and fluids in and out of the cells in different parts of the body
- Plays a key role in maintenance of airway surface liquid layer

How CFTR works in healthy cells

(Adapted from Orenstein, 2004)



CFTR Abnormality

Defective protein

Mutations in the CFTR gene cause the CFTR protein to malfunction or not be made at all

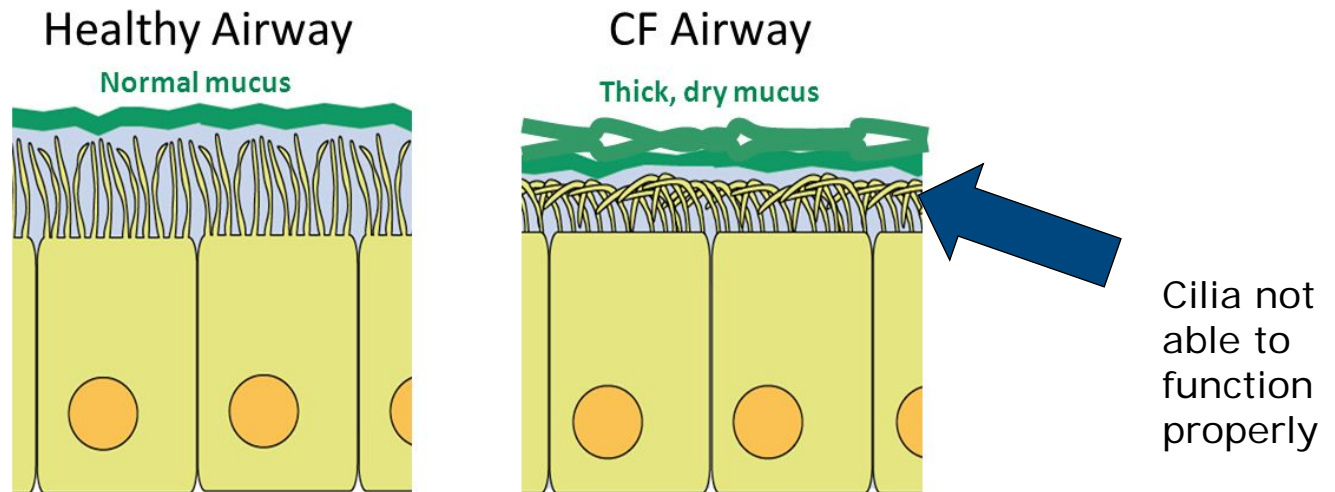
When the protein is not working correctly, it's unable to help move chloride -- a component of salt -- to the cell surface. Without the chloride to attract water to the cell surface, the mucus in various organs becomes thick and sticky

The salt balance in the body is disturbed. Without CFTR:

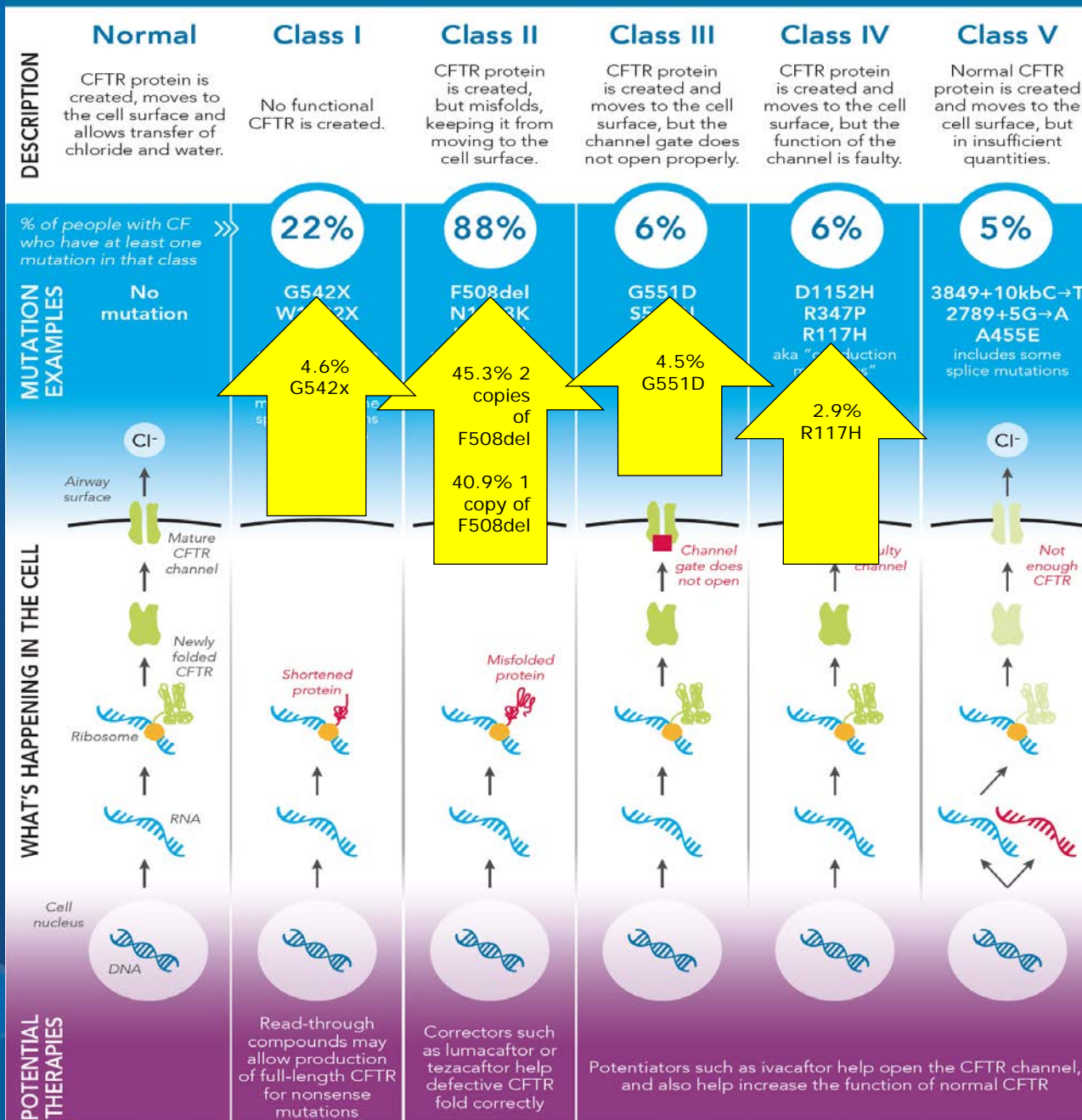
- Airway surface liquid is depleted
- Mucociliary clearance is reduced
- Mucus viscosity is increased
- Failure to resorb NaCl

CF patients do not make more mucus than non-CF

Cystic Fibrosis patients' airways are dehydrated and cannot clear mucus.



CFTR MUTATION CLASSES



Arrows indicate % of all people with CF in 2017 who have a specific mutation

Newborn Screen (NBS) Process for Cystic Fibrosis

NY State started NBS in 2002 (nationwide since 2010)

NYS revised screening protocol in 12/2017 to include DNA testing on eligible samples

CF included on NBS panel because:

- Better nutritional outcomes which ultimately leads to improved pulmonary health

CF NBS is a screening tool, not a diagnostic one

Sweat test / Sweat Chloride Measurement ****BEST METHOD**

- Quantitative pilocarpine iontophoresis
- Loss of CFTR function → failure to reabsorb NaCl and therefore high Cl levels in patients with CF

Symptoms at Diagnosis

In individuals <1 year if age:

- Meconium ileus or intestinal obstruction: 13.1
- Failure to Thrive: 5.1%
- Steatorrhea/abnormal stools/malabsorption: 2.8%
- Acute or persistent respiratory abnormalities: 1.3%

In individuals >1 year of age:

- Acute or persistent respiratory abnormalities: 45%
- Failure to Thrive: 11.2%
- Nasal polyps/sinus disease: 10.8%
- CBVAD or infertility/GU abnormalities: 7.4%
- Steatorrhea/abnormal stools/malabsorption: 6.7%

The Cystic Fibrosis Foundation



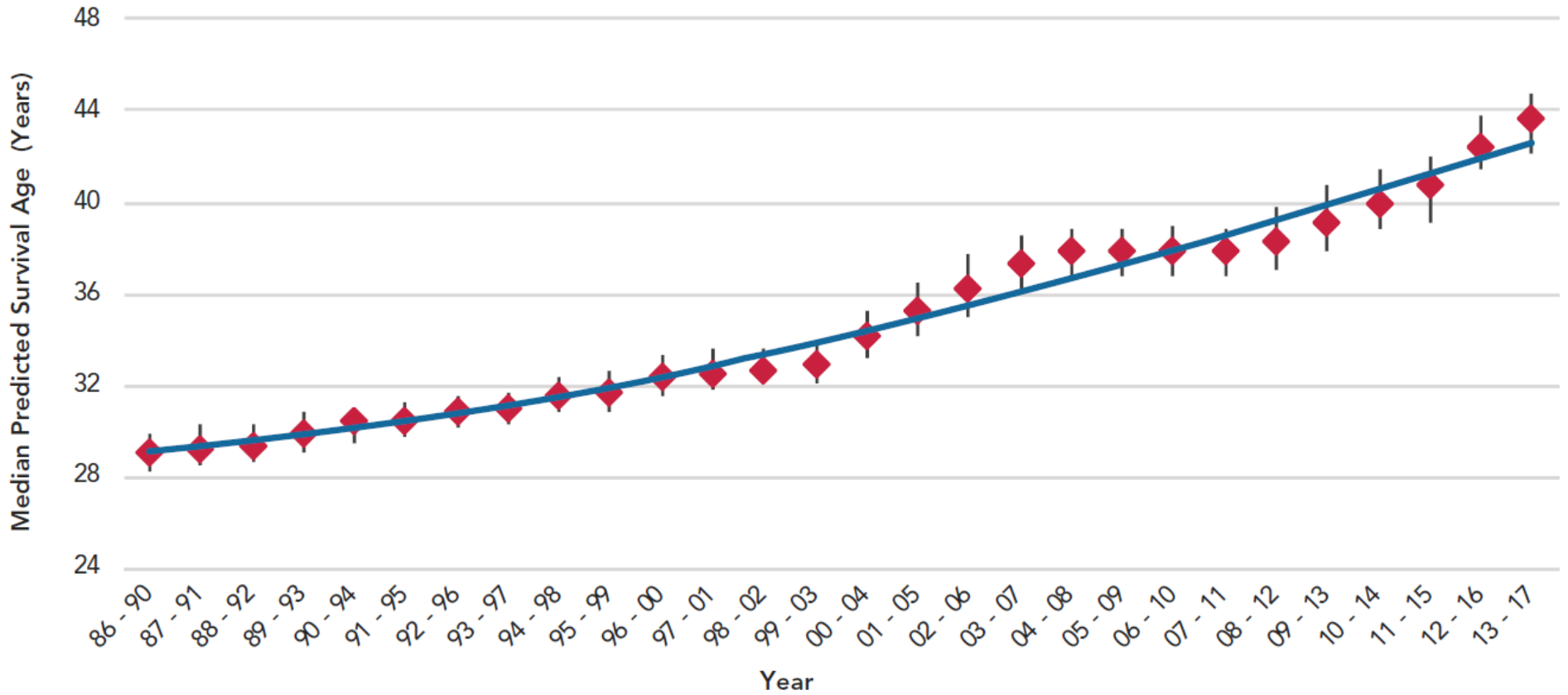
Founded in 1955 by parents of kids with CF

Mission: to assure the development of the means to cure and control cystic fibrosis and to improve the quality of life for those with the disease

Accredits a network of >120 Care Centers in US

- Grants for care and research
- QI Training
- CF Care Guidelines
- Education and advocacy resources
- Patient Registry (houses data from 29,887 CF patients)

Median Predicted Survival Age, 1986–2017 In Five Year Increments

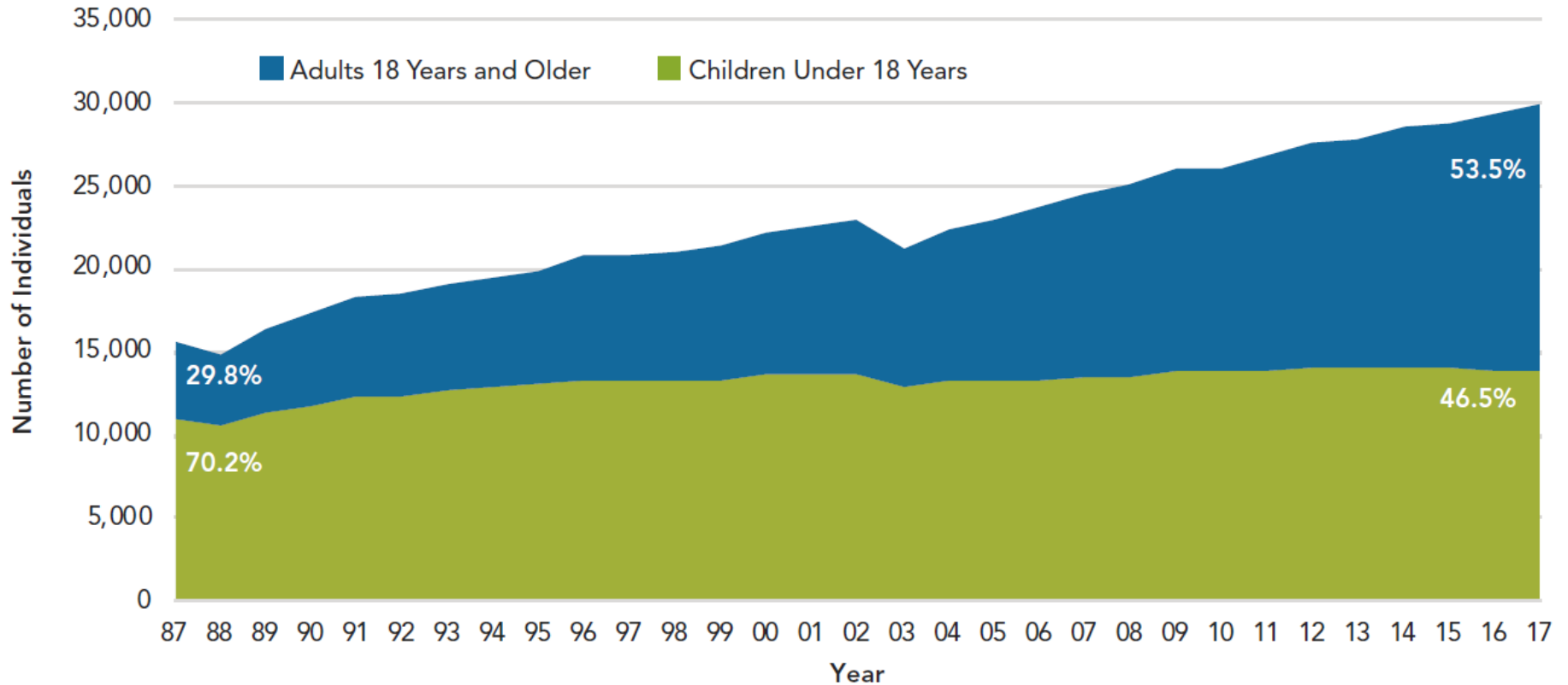


Primary Cause of Death in 2017

Cause	Number of Individuals	Percent
Respiratory/cardiorespiratory	239	62.9
Transplant-related	61	16.1
Other	38	10.0
Unknown	24	6.3
Liver Disease/Liver Failure	13	3.4
Suicide or Trauma	5	1.3

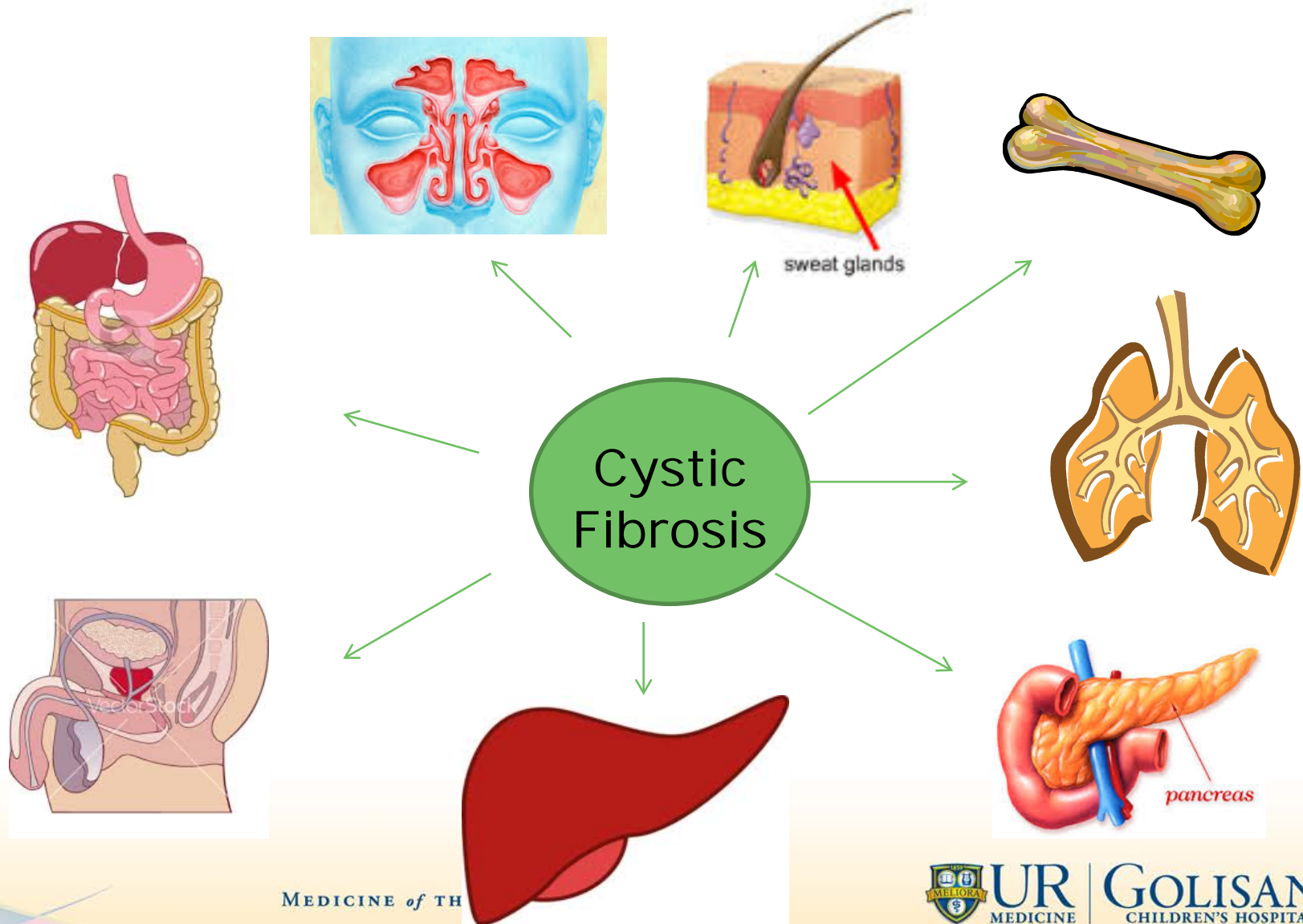
- 380 deaths total in 2017
- Of those, 47.6 percent occurred in individuals with 2 copies of delF508

Number of Children and Adults with CF, 1987–2017



Note: the decrease in the number of individuals in 2003 is due to a delay in obtaining informed consent forms before the close of the calendar year at some CF care centers.

Multiple organ systems affected



Complications of CF, 2017

(taken from CFF Registry Report, 2017)

	Age < 18 (%)
Number of Individuals (n)	13,831
Percent with no complications	24.2
Percent with complications not reported ^A	1.2
Cystic Fibrosis-Related Diabetes	
Cystic fibrosis-related diabetes (CFRD) ^B	5.3
Hepatobiliary	
Gall stones ^C	0.1
Gall stones, requiring surgery/procedure ^C	0.1
Liver disease, cirrhosis ^D	2.4
Liver disease, non-cirrhosis ^C	3.4
Acute hepatitis ^C	0.1
Hepatic steatosis	0.6
Liver disease, other ^C	1.9
Bone/Joints	
Arthritis/arthropathy	0.5
Bone fracture ^C	0.2
Osteopenia	1.4
Osteoporosis	0.5
Pulmonary	
Allergic bronchopulmonary aspergillosis (ABPA)	2.6
Asthma	30.5
Hemoptysis	0.8
Hemoptysis, massive ^C	<0.1
Pneumothorax requiring chest tube ^C	0.1

GI	Age < 18 (%)
Distal intestinal obstruction syndrome (DIOS) ^C	2.0
Fibrosing colonopathy/colonic stricture ^C	<0.1
Gastroesophageal reflux disease (GERD)	36.1
GI bleed requiring hospitalization (non-variceal) ^C	<0.1
History of intestinal or colon surgery	3.6
Pancreatitis ^C	0.5
Peptic ulcer disease ^C	<0.1
Rectal prolapse ^C	0.5
Mental Health	
Anxiety disorder	4.1
Depression	3.6
Other Complications	
Cancer confirmed by histology ^C	0.0
Hearing loss	1.3
Hypertension	0.4
Kidney stones ^C	0.2
Nasal polyps requiring surgery ^C	1.9
Renal failure requiring dialysis ^E	<0.1
Sinus disease	22.7

Upper Respiratory Tract

Nasal polyp frequency in CF: 31 – 56%

Most commonly reported in ages 5–14 years

Role of allergy not clear

Pansinusitis common (identified by sinus CT)

Conservative management / 1st line treatment:

- Nasal irrigation (NeilMed sinus rinse) and topical steroids
- New rinse kit available by request for inpatient; stocked in clean utility room w/ premixed packets; use w/ sterile water
- ENT referral for surgical management of persistent and symptomatic polyps may improve lung function
- If performed, typically at the end of an inpt tune-up

Lower Respiratory Tract: Pathogenesis of Cystic Fibrosis

Defective CFTR
↓
Abnormal (Airway) Surface Environment

↓
Bronchial Obstruction

↓
Infection

↓
Inflammation

↓
Bronchiectasis

Lower
Respiratory
Tract

- Lung disease begins within the first few months of life without symptoms
- Cigarette smoke exposure a risk factor
- Airway clearance recommended for all patients with CF

Airway Clearance Techniques

Chest Percussion and Postural Drainage

High Frequency Extrathoracic Oscillation

- “The Vest” which ↑sputum mobilization

Intraluminal Percussive Devices

- Examples are the Flutter or The Acapella

Positive Expiratory Pressure Devices

- Examples are PEP valve or AerobiKA

Exercise

Huff Cough



Airway Clearance Devices

High Frequency Chest Wall Oscillation

Intraluminal Oscillation

DID YOU KNOW?

Most people with cystic fibrosis use chest physical therapy (CPT or Chest PT) as an airway clearance technique to drain mucus (postural drainage) from the lungs. This may include percussion (clapping), vibration, deep breathing, and huffing or coughing. High-frequency chest wall oscillation (HFCWO) vests, otherwise known as airway clearance systems, are a common part of people with CF's daily routines.

#cysticfibrosisawarenessmonth



CYSTIC FIBROSIS FOUNDATION[®] cff_sc



Oscillating PEP Device (positive airway pressure)

Oscillations create short bursts of increased expiratory resistance to thin, dislodge and move mucus to the upper airways where it can be coughed out.

Aids in lung hygiene and helps prevent infections

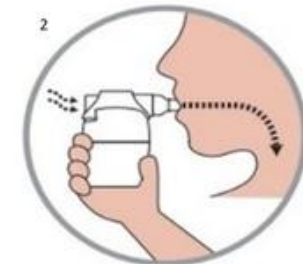
Improves gas transfer and lowers air trapping

Oscillations start at the beginning of each exhalation and continue through the end for maximum effect

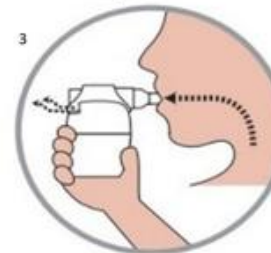
Recommended treatment is 2 times a day for 10 minutes. Increase to 3-4 times per day if producing a lot of mucus.



1
Close lips around mouthpiece



2
Inhale and Hold 2 - 3 seconds



3
Exhale slowly, steady and firmly. After at least 10 breaths, perform 2-3 huff coughs to clear your airway.



4
Repeat and cough as directed

Huff Cough Technique

1. Sit up straight with chin tilted slightly up and mouth open
2. Take a slow deep breath to fill lungs about three quarters full
3. Hold breath for two or three seconds
4. Exhale forcefully but slowly followed by a continuous exhalation to help move mucus from the smaller to larger airways
5. Repeat maneuver two more times then follow with one strong effective regular cough to clear mucus from larger airways
6. Do 4-5 huff coughs during and after airway clearance

Medications that enhance airway clearance techniques

Hypertonic Saline

- hydrates thick, sticky mucus in the airways
- high osmolality draws water from the airway to re-establish the aqueous surface layer that is deficient in CF (where salt goes, water goes)
- Albuterol before dose to limit bronchospasm
- Trial in PFT lab for first dose

Medications that enhance airway clearance techniques

Pulmozyme (dornase alpha)

- uniquely targets extracellular DNA, a cause of thick, sticky mucus
- acts like “scissors” in the mucus



- Cuts up the DNA strands outside the cell that can make CF mucus thick and sticky
- DNA is from the white blood cells that work to fight lung infections. (present even if no lung infection)



Cff.org and pulmozyme.com

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CF Pulmonary Exacerbation

Increased bacterial burden

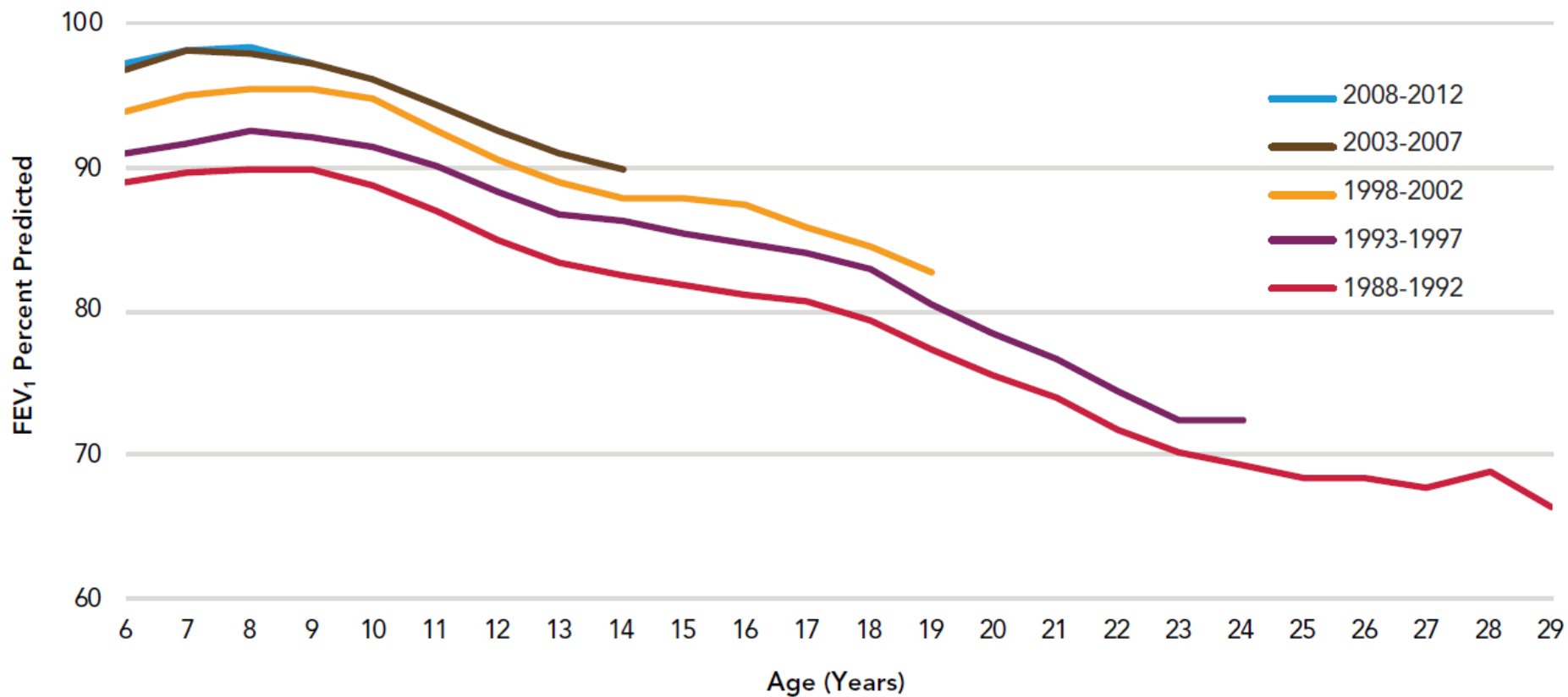
- Respiratory infection
- Build up over time
- Difficulty keeping up with prescribed respiratory plan of care

Increased inflammatory response

Clinical features

- Increased cough and sputum
- Sputum turns greener
- Fatigue
- Weight loss
- Decline in lung function (FEV1)

Median FEV₁ Percent Predicted, by Age and Birth Cohort



Spirometry/lung function testing



- Measures how much air is blown out and how fast it is blown out
- FEV1 % predicted (forced expiratory volume in 1 second) is common value used to report lung function

CF Pulmonary Exacerbation: Treatment

3-way approach

- Airway Clearance to combat mucous obstruction
- Antibiotics to combat lung infection
- Aggressive nutrition to provide ample energy to fight infection and inflammation

Same approach outpatient vs inpatient, but obviously more stringent / stronger interventions when inpatient

Pulmonary Exacerbation: Outpatient Antibiotics

Outpatient

- Look at last sputum culture (routinely obtained every 3 months)
 - Often a 21-day course with a 1 month follow-up
 - Those with *pseudomonas aeruginosa* on sputum/deep throat culture qualify for inhaled antibiotics
 - TOBI via nebulized solution or Podhaler (BID x 28 days)
- AND/OR
- Cayston via nebulized solution (TID x 28 days)
 - Length depends on frequency of colonization
 - i.e for one cycle or ongoing alternate month therapy

Pulmonary Exacerbation: Inpatient Antibiotics

Intravenous most commonly via PICC

- Prefer peripheral access if “good veins”
- PICC risk factors: clot development, infection

Most commonly Tobramycin and Cefepime

- Need tobramycin levels drawn to determine therapeutic range; will also check kidney function
- Requires audiology exam prior to discharge due to Tobramycin

Other variations: allergy status & previous results

Sometimes, tune-up started inpatient and completed at home

The finer details of Inpatient Airway Clearance

- EZ Pap or Aerobika or DR Burton VPAP can be ordered with neb treatments based on pt status/ability; ordered by physician as an RT order; RT does the 1st treatment to set the flow
- A separate neb cup is used for each med; after each treatment, wash the cup with soap & water; rinse with sterile water; turn upside down on a paper towel to air dry until the next treatment
- Hypertonic saline and pulmozyme are typically ordered BID during hospitalization; suggested order is hypertonic saline, pulmozyme, hypertonic saline, pulmozyme throughout the day so that the pulmozyme will “dwell” in lungs overnight



Inpatient Tune-Up

Goals: IV antibiotics, intensive airway clearance (every 4 hours while awake; goal 4-5 times daily), nutritional support (dietician consult including calorie count, every other day weight, management of nutritional supplements)

Excellent time to model effective airway clearance techniques (i.e. active participation vs passive while laying in bed)

Typically 2 weeks in time

Monitor lung function (FEV1) weekly

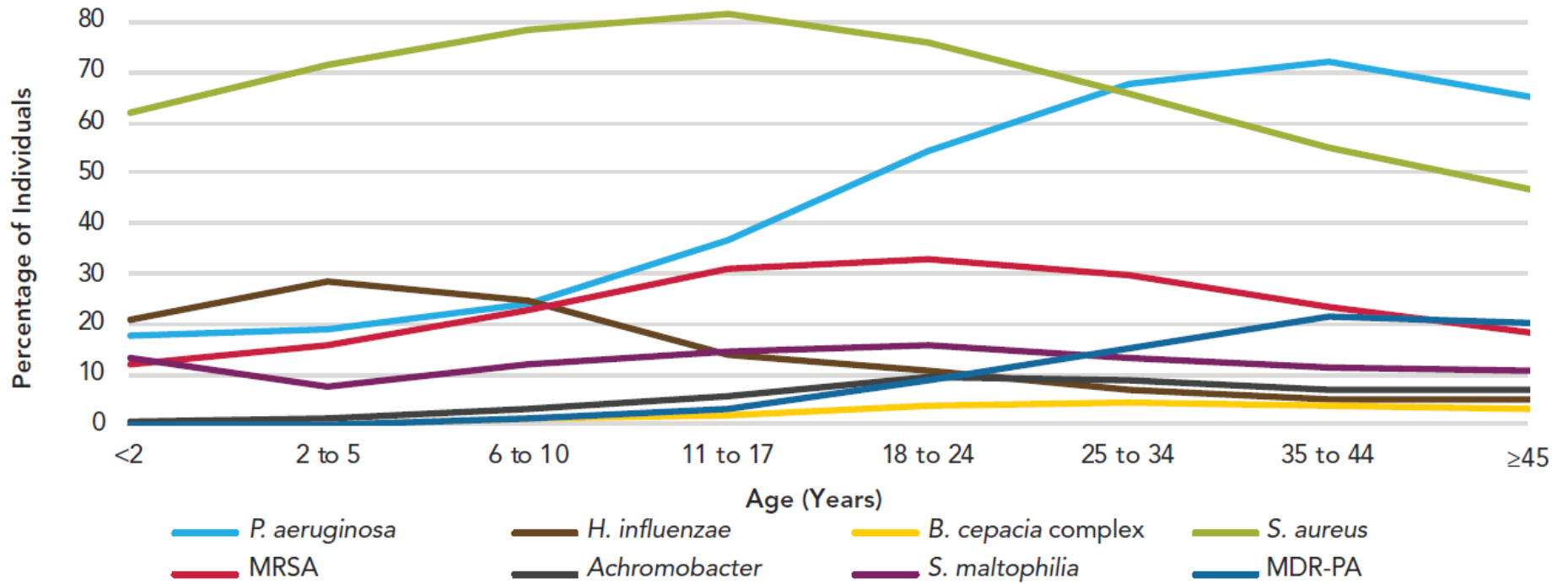
Goals for discharge: improvement in symptoms, weight gain, improvement in FEV1

Typically seen in CF clinic 1 month post-discharge

**Should be emphasized that an inpatient tune-up is work and not a respite







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Prevalence of Respiratory Microorganisms by Age Cohort, 2017



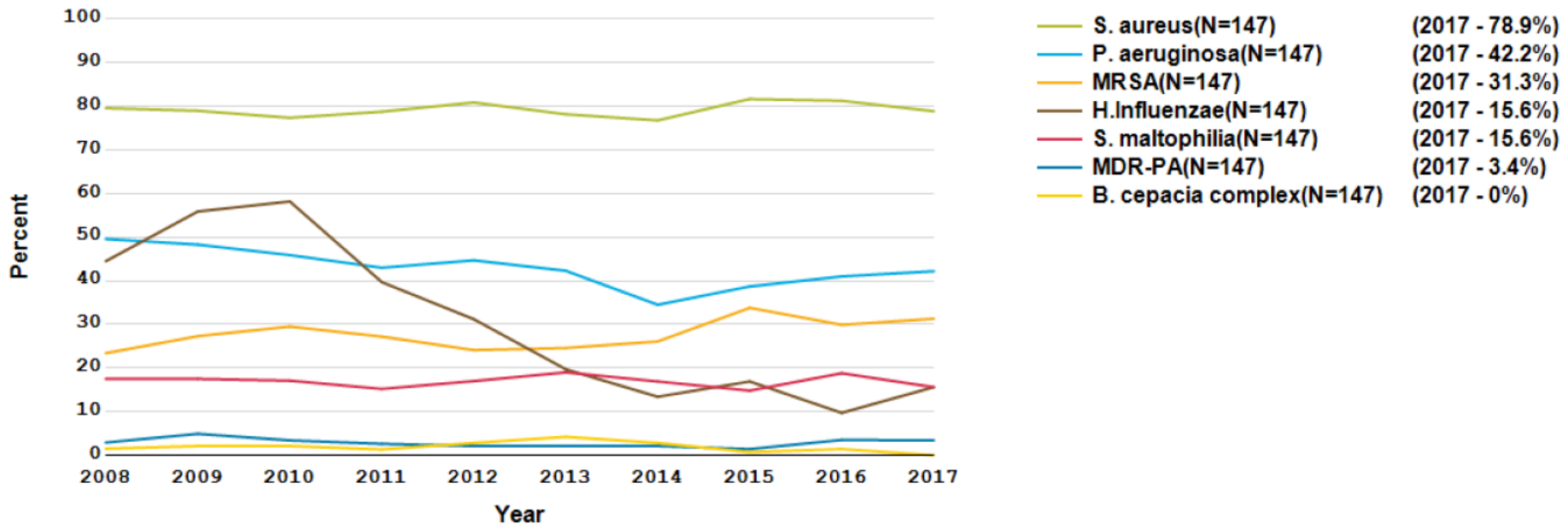
Culture Data on Pathogens Seen in 2017

As of 1/2019 at URM, 1 pt with CF with this bacteria; requires **strict implementation of infection control measures** in an effort to prevent transmission to other CF pts

		Percent with Infection	Median Age in Years at First Infection	Distinctive Features in CF
	<i>P. aeruginosa</i>	44.6	5.2	<ul style="list-style-type: none"> • A leading cause of airway infection • Associated with a decline in lung function • 17.9% of strains are multidrug-resistant
	<i>B. cepacia</i> complex	2.4	19.4	<ul style="list-style-type: none"> • Small proportion of people with CF infected • Can lead to rapid deterioration • Multidrug-resistant
	MRSA	25.2	11.1	<ul style="list-style-type: none"> • Prevalent among people with and without CF • Multidrug-resistant • Health care and community-associated strains
	<i>S. maltophilia</i>	12.6	9.4	<ul style="list-style-type: none"> • Found in water, soil, plants, animals, and hospital environments • Often multidrug-resistant
	<i>Achromobacter xylosoxidans</i>	5.8	13.8	<ul style="list-style-type: none"> • Inhabits natural environment, including soil and water • Often multidrug-resistant
	Non-tuberculous mycobacteria	12.6	20.7	<ul style="list-style-type: none"> • Found in water and soil • Sporadic reports of person-to-person spread • Treatment is rigorous and often poorly tolerated

URMC Data (both Pediatric and Adult) from 2017 CF Registry Center Specific Full Report

Microbiology



CF Pulmonary Complications

Allergic Bronchopulmonary Aspergillosis (ABPA)

- Allergic hypersensitivity caused by *Aspergillus fumigatus*; screened for and diagnosed by labs
- Treatment: prolonged oral corticosteroids +/- antifungal

Hemoptysis

- Erosion of blood vessels
- Scant (<5ml), Mild-moderate (5-240 ml), massive (>240 ml)
- Notify pulmonary team if patient becomes symptomatic

Pneumothorax

- 5-8 % of all CF pts will have (↑risk age/severity)
- Symptoms include sudden onset chest pain, SOB

Other Pulmonary Treatments: Anti-inflammatory Therapy

Oral corticosteroids

- Helps delay progression of lung disease
- Associated with significant side effect (check BGs)
- Used primarily for short-term effects or severe lung disease

Inhaled corticosteroids

- Widely used if airway reactivity or wheezing present
- Many patients with CF have a co-morbidity of asthma

Azithromycin (given orally three times weekly)

High dose ibuprofen

The Gastrointestinal System

Pancreatic insufficiency (PI) or dysfunction present at birth in 60% of infants dx by NBS

- ~90% have at 1 year of age
- Leads to malabsorption and fat soluble vitamin loss (ADEK) → may lead to FTT and low vitamin levels

Most common diagnostic tool

- fecal elastase

Treatment: Daily ADEK supplement and...

The Gastrointestinal System

Pancreatic Enzyme Replacement Therapy (PERT)

- start in infancy if 2 known mutations or objective evidence of pancreatic insufficiency (weight loss/GI sx)
- Should be given prior to all meals/snacks
 - In infancy, this includes all formula/breast feeds
- Dose is weight based
- Teach signs of malabsorption (greasy/shiny stools, foul odor, cramping, fatty floaters, frequent bulky stools)

Pancreatic Enzyme Replacement Therapy

open capsule and mix beads

with an acidic food; make no beads left in

Swallow whole or

mouth



Pancreatic Enzyme Replacement Therapy

- Single-use, point-of-care digestive enzyme cartridge
- Connects in-line with enteral feeding pump tubing & patient extension sets
- Designed to digest fats contained in enteral formulas, mimicking the function of the digestive lipase that is normally secreted by the pancreas
- Used with continuous or overnight feeds (not used with bolus feeds)
- Used for patients > age 5 years
- Continue to give PO enzymes before oral meals/snacks
- Currently one brand on the market



CF and GI Complications

- Meconium Ileus
 - Presenting sign of CF in 10-20% of pts / 99% of MI due to CF
 - intestinal obstruction from thick meconium → present acutely
 - Broad range of clinical severity; typically requires surgery
- Distal ileal obstruction syndrome (DIOS)
 - Thick intestinal mucous and dehydrated stool contents
 - Clinical Presentation: ↓BMs, abdominal pain/cramps, emesis
 - May be able to palpate mass
 - Work-up includes abd films & labs: LFTs, amylase/lipase
 - Early and aggressive treatment with bowel clean-out
 - More severe cases require inpt stay, NG tube, enemas & surgical consult → risk of recurrence

CF and GI Complications

CF patients with GI complaints (i.e. abdominal pain) require

- Increased index of suspicion
 - More extensive work-up
 - More aggressive therapy
- Other complications
 - Pancreatitis
 - Appendicitis
 - Intussusception
 - Gallstones
 - Rectal prolapse

CF and Other GI Disease

CF liver disease

- incidence: ~11%
- bile sludging leads to biliary cirrhosis
- Screen with annual LFTs; if elevated, referred to GI
- Treat with Actigall; end state disease → liver transplant

Cystic Fibrosis Related Diabetes (CFRD)

Cystic Fibrosis Related Diabetes (CFRD)

- Occurs in ~20% of the adolescent population
- Imbalance of insulin needs:
 - Insulin requirement > Insulin production
- The best therapy for CFRD is insulin
- Annual OGTT recommended starting at age 10
- On initial inpt admission, typically check 2 days of post-prandial and fasting BGs; stop if normal
- If on prednisone burst inpatient, check BGs post-prandial and fasting for the first 2-3 days of therapy & stop if WNL
- Management referred to Endocrine Group
- Psychological burden - a 2nd chronic disease

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Nutrition in Cystic Fibrosis

A crucial element of maintenance and treatment

Calories, Calories, Calories!!

Malabsorption = ↓ calorie/ nutritional absorption

Chronic cough/presence of infection = ↑calorie use

Socioeconomic / education / behavioral issues

- Inadequate knowledge, maladaptive feeding behaviors, financial barriers to obtaining food, maladaptive family functioning

Poor appetite

- Constipation, reflux, chronic ingestion of sputum

Salt supplement:

- Newborn to 6 months: 1/8 tsp /day divided among feeds
- Age 6 months until on regular diet: ¼ tsp/day

Nutrition in Cystic Fibrosis

Goal is a weight for length at the 50%ile (< 2 years)

Goal is for a BMI at the 50%ile (age 2 and up)

When inpatient, typically weighed 3x/week (but if < 2 y.o., then weigh daily)

Early nutritional treatment is key

- A higher BMI%ile at age 2 years is associated with better lung function later in childhood

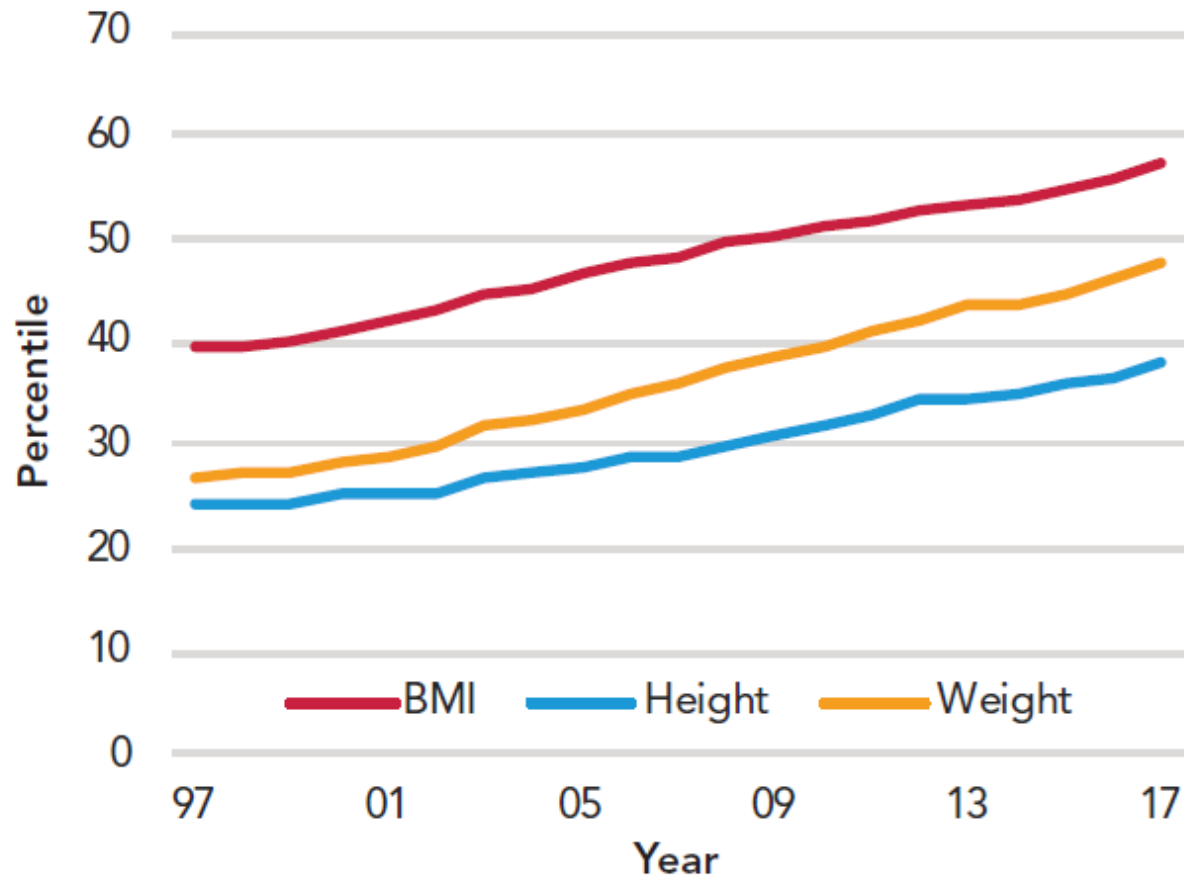
Oral supplements are commonly needed

With continued FTT, G-Tube a strong consideration

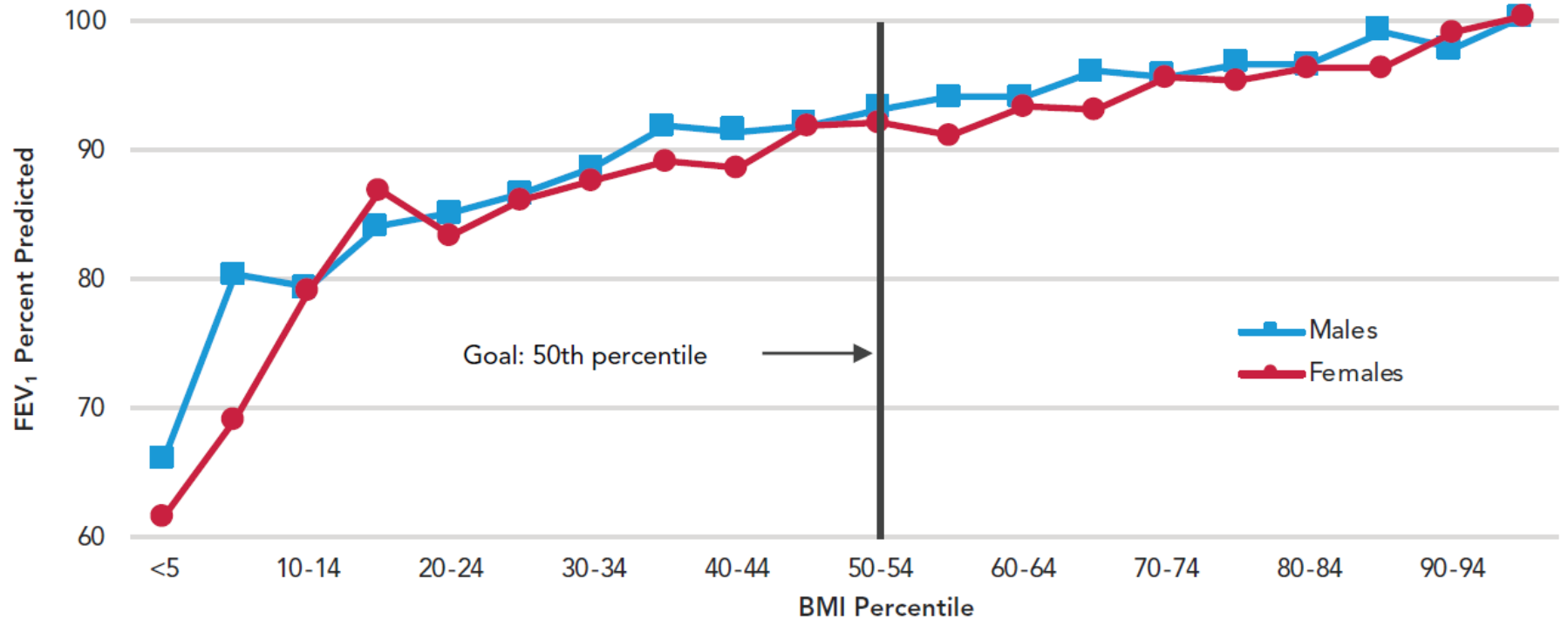
Behavioral issues should be addressed early

- Parental involvement and consistency are keys

Median Nutritional Outcomes Percentiles for Individuals 2 to 19 Years, 1997–2017



FEV₁ Percent Predicted vs. BMI Percentile for Children 6 to 19 Years in 2017



CF Related Bone Health and Disease

Prone to osteopenia / osteoporosis

- Malabsorption / malnutrition affects vitamin D levels and calcium absorption and low bone minerals
- Delayed puberty contributes to less bone being made
- Inflammation related to lung infection leads to bone loss

More common in late teen and adult years; screening begins at age 8 years for those eligible for DEXA scan to assess

Broken bones can affect lung health because of pain associated with airway clearance

Affects eligibility for organ transplants

Treat with Ca and Vit D supplements

Female Reproductive System in CF

Possible delay in menstruation b/c of nutrition

Be aware of yeast infection w/ antibiotic use

Should see GYN for birth control—risk of clots if have a PICC or port;
do antibiotics change effectiveness?

Thick vaginal mucous may affect conception

Pregnancy:

- Nutritional status and lung health contribute
- Physical and psychologic health affected
- However, able to give birth to a healthy infant

Male Reproductive System in CF

	Males Without CF	Males With CF
Normal sexual performance	Yes	Yes
Make sperm	Yes	Yes
Amount of ejaculate	Normal	Possibly slightly less than normal
At risk for sexually transmitted infections	Yes	Yes
Ability to father a child	Typically Yes	Yes, but usually only with a special procedure

Vas deferens is either missing or blocked

Sperm is made in testicles but not transported to the penis

95-98% of males with CF do not have sperm in their ejaculate

Normal sexual function, pleasure / performance

Lung Transplant

A consideration for severe lung disease

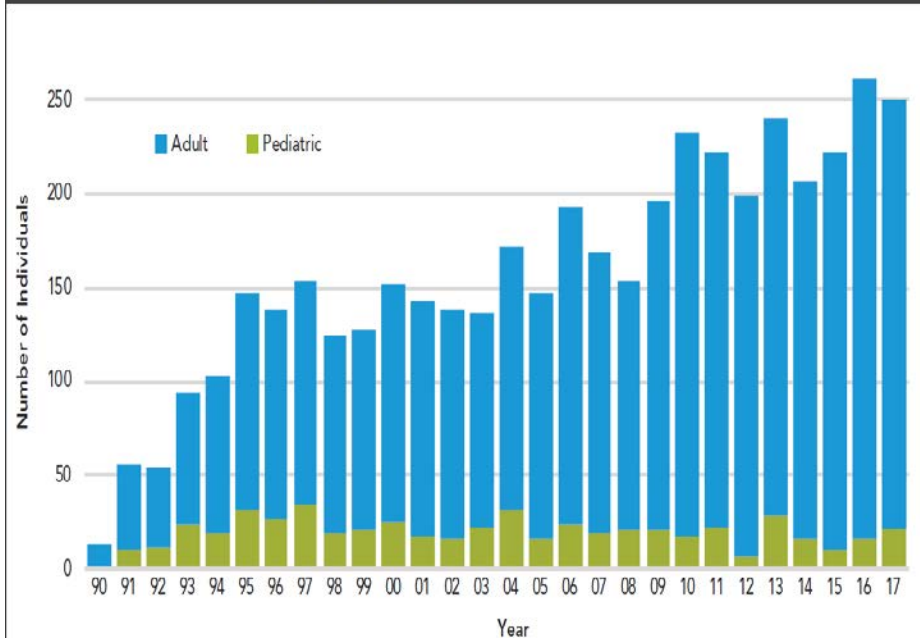
Initial referral to a lung transplant center should be considered when FEV1 ~30%

In the last 5 years, about 200 to 250 people with CF have received lung transplants per year

Survival in CF:

- over 80 percent are alive 1 year after transplant
- and over 50 percent are alive after 5 years.

Number of Individuals Receiving a Lung Transplant, 1990-2017



Cystic Fibrosis Foundation Therapeutics Pipeline

In 2015, this was a 1-page document

Today in 2017, an entire section of the CFF website dedicated to this in the following topics (<https://www.cff.org/trials/pipeline>):

- Restore CFTR Function
- Mucociliary Clearance
- Anti-Inflammatory
- Anti-Infective
- Nutritional-GI-Other

All studies classified as:

- Pre-clinical
- Phase One
- Phase Two
- Phase Three
- To Patients

Research Highlights

The Science of Adding Tomorrows

- 1993: Pulmozyme thins mucous in the lungs
- 1996: TOBI (nebulized medication) is FDA approved
- 2002: azithromycin improves lung health
- 2004: hypertonic saline helps clear lung mucous
- 2010: Cayston is FDA approved
- 2012 Kalydeco™ (ivacaftor) for G551D mutation (ages 6 and older) is FDA approved
- 2012: FDA approval of TOBI Podhaler
- 2014: FDA approval of Kalydeco™ for R117H mutation (ages 6 and older) plus 8 other gating mutations (covers 10 mutations total)
- 2015: FDA approval of Orkambi (ivacaftor/lumacaftor) for ages 12yrs+ for homozygous delF508
- 2015: FDA approval of Kalydeco for ages 2 – 5 yrs (total of 10 mutations)
- 2016: FDA approval of Orkambi for ages 6 years – 11 years
- 2017 (May): FDA approval to increase Kalydeco mutation coverage to 33
- 2017 (Aug): FDA approval to increase Kalydeco mutation coverage to 38
- 2017: FDA approval of Relizorb (digestive enzyme cartridge) for \geq 5 years on enteral feeds
- 2018: FDA approval of Orkambi for ages 2 years – 5 years
- 2018: FDA approval of Kalydeco for ages 12 months - < 24 months
- 2018: FDA approval of Symdeko (ivacaftor/tezacaftor) for homozygous delF508 ages 12yr +

CFTR Modulation

designed to correct function of defective CFTR protein

- goal is for Cl and Na (salt) to move properly in and out of cells lining the lungs and other organs

currently, modulation therapy focuses on:

- corrector therapy (lumacaftor or tezacaftor):
 - to unfold protein
- potentiator therapy (ivacaftor):
 - to move CFTR to the surface
 - works on gating defect /mutation to fix faulty channel or dysfunction of protein in cell surface
- Or combo of corrector / potentiator therapy



CFTR Modulator Types

Potentiators

- Help chloride flow through CFTR protein channel at the cell surface
- The CFTR protein is shaped like a tunnel that can be closed by a gate
- Potentiators hold the gate open so chloride can go through
- Example: ivacaftor (Kalydeco®)

Correctors

- Help the CFTR protein to form the right 3-D shape so that it is able to move– or traffic– to the cell surface
- These drugs help the CFTR protein form the right shape, traffic to the cell surface, and stay there longer
- Example: lumacaftor or tezacaftor

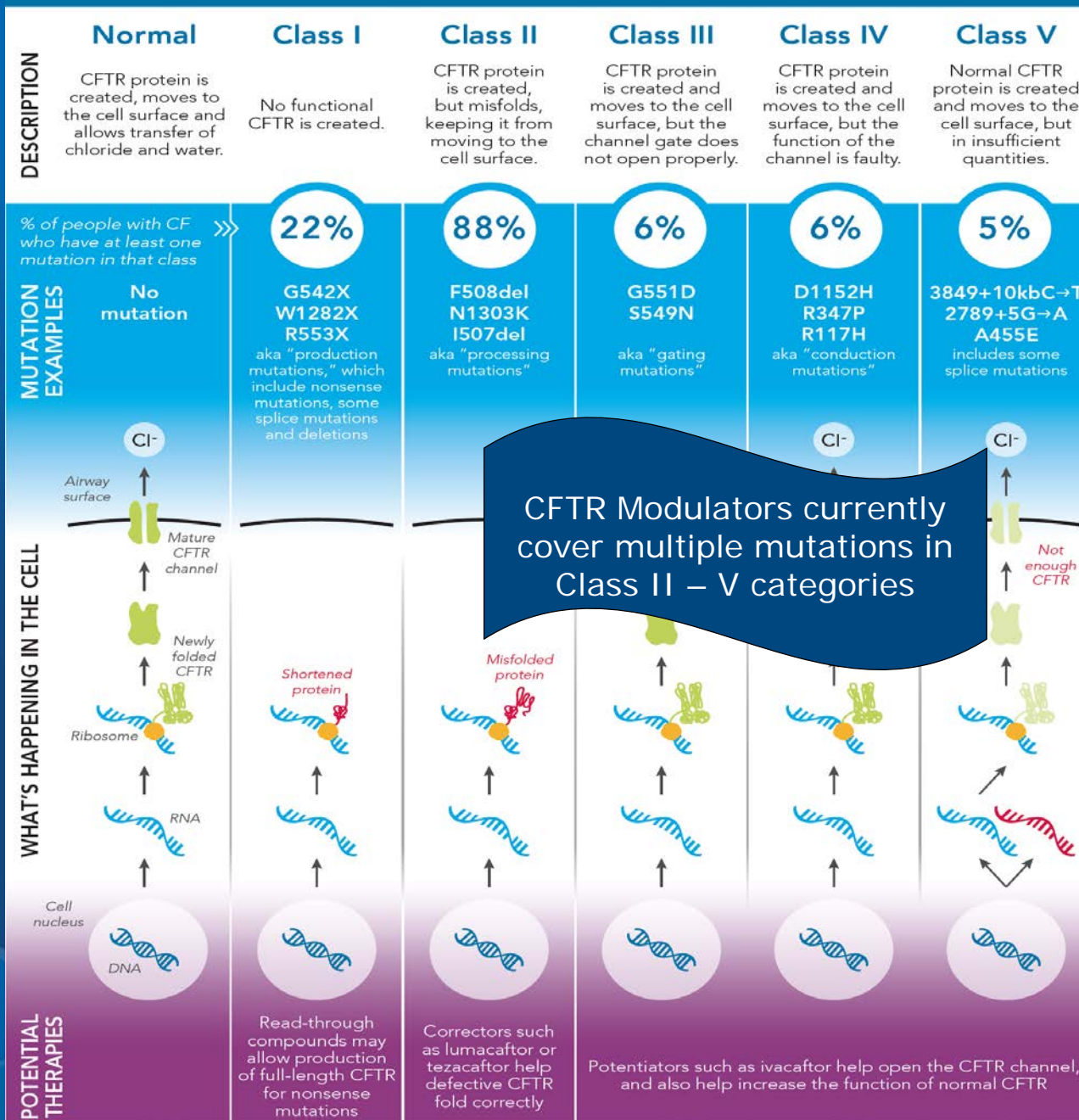
Combination of Potentiator/Correctors

- Hold the gate of the CFTR protein open so enough chloride can pass through to reduce the symptoms of CF
- Example: tezacaftor/ivacaftor (Symdeko®) or lumacaftor/ivacaftor (Orkambi®)

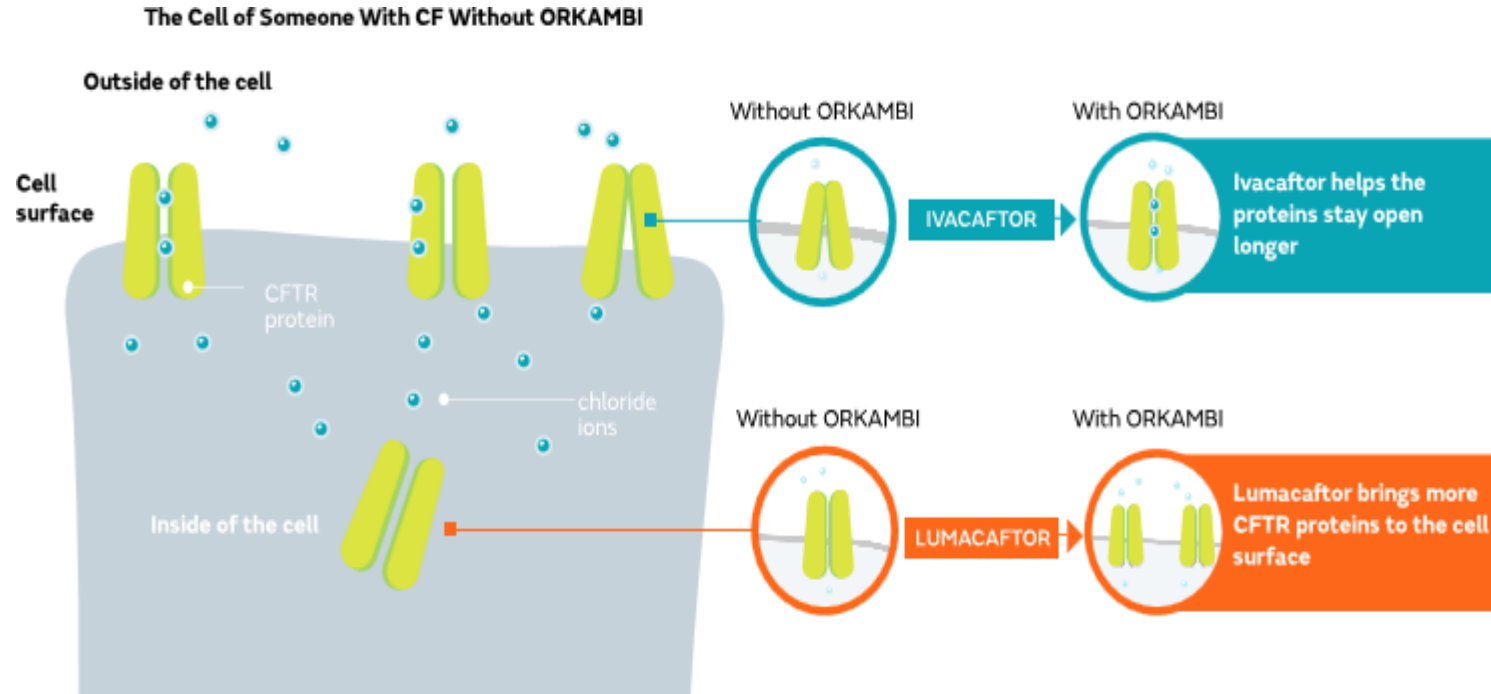
Amplifiers

- Increase the amount of CFTR protein that the cell makes
- Currently under development and are being tested; not yet available to patients

CFTR MUTATION CLASSES



How CFTR modulators work in a person with homozygous F508del (a potentiator and a corrector)



Infection Prevention & Control

In 2013 CFF released new guidelines b/c of evidence that individuals with CF are a risk to each other by transmission of CF pathogens

Experimental evidence in CF:

- Droplets can travel ~ 6 ft (previously thought ~3 ft)
- Droplets remain suspended 45 minutes – 2 hours after a patient leaves the room

Transmission can occur in both healthcare and non-healthcare settings

Infection Prevention and Control: Inpatient Units at UR

Modified Pulmonary Contact Precautions

Private room

Patient to perform hand hygiene and wear a mask when leaving room

Hospital staff will wear a gown and gloves with patient interactions and clean stethoscope (with alcohol wipe or Cavi-wipe) prior to and after patient contact

Parents, family/friends should wash hands when they enter or leave room

Patient should stay in room with fever, runny nose or when coughing up mucus

Staff will partner with pt/family to schedule time in common rooms (like the playroom) so patients with CF can be coordinated

Staff will partner with pt/family to make sure that things a pt with CF touches outside of exam rooms get wiped with CaviWipes

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Infection Prevention and Control: Outpatient Clinic at UR

Modified Pulmonary Contact Precautions

Patient with CF wears a mask and performs hand hygiene upon entry into waiting area

Mask stays on until in a private exam room

All staff wear gown/gloves during pt interaction and provider cleans stethoscope with either alcohol wipe or Cavi-wipe prior to and following patient contact

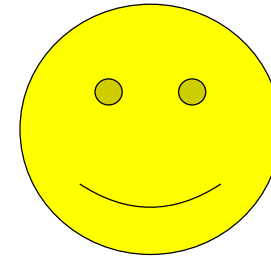
Upon exit from exam room, patient with CF performs hand hygiene and again wears a mask until exit from building

**Visitors with CF to an inpatient unit or an outpatient clinic should perform hand hygiene and wear a mask; mask changed every 30 minutes or if damp

Infection Prevention and Control



Vog and Cambridge masks are NOT approved by the CFF as effective methods of infection control b/c of inability to disinfect



Disposable masks are recommended by the CFF and approved at URM as part of Modified Pulmonary Precautions; should be discarded/replaced after 30 minutes and when soiled

Psychosocial Factors: The Short List

Parental guilt /genetic component

Chronic illness / shortened lifespan

Time it takes for DAILY maintenance therapies (and stepped up therapies with illness)

The focus on eating / nutrition

- One thing the patient can control; a known “trigger” to make caregivers upset

Compliance: Different issues early childhood vs adolescence

Stigma associated with infection control measures

Diagnosis disclosure

Depression, Anxiety and CF

People with CF and parents who take care of children with CF are two to three times more likely to experience depression, anxiety or both compared to people in the general population

- If left untreated, people with CF may have lower lung function & BMI, more inpt stays, lower quality of life, higher health care costs, and inability to manage treatment plans effectively

In 2015, the CFF developed guidelines to address this

Annual (at least) screens for Depression (PHQ-9) and Anxiety (GAD-7) performed in outpatient clinic by social worker

Patients age 12 years and up are screened

Parents of patients age 17 years or younger have the option to be screened

Referred for formal mental health evaluation/services as appropriate

Patient Independence/Transition of Care

Ages 6-9 years:

- Begin to answer questions about symptoms and health with help from parent
- Begin to learn the names of medications and purpose for each (age appropriate slang terms)
- Begin to understand reason for airway clearance, and technique/frequency used
- Begin to discuss recognition of respiratory/GI baseline and symptoms that indicate a change
- Begin to discuss school issues (telling teachers and friends about CF, enzyme use during school, field trips, bathroom use, importance of access water and salty snacks)
- Begin to discuss why some people have CF and others do not; explaining CF to friends

Ages 10-12 years:

- Patient answers questions independently about symptoms and health
- Use proper names for medications and purpose for each
- Begin to independently set up/use airway clearance; continue discussion of why this is important
- Continue discussion of respiratory/GI baseline and symptoms that indicate a change
- Continue discussion of school issues (telling teachers and friends about CF, enzyme use during school, field trips, bathroom use, importance of access water and salty snacks)
- Continue discussion of why some people have CF and others do not; explaining CF to friends

Taken from Note Templates used for Patients with CF in the Outpatient Clinic

Patient Independence/Transition of Care

Ages 13-15 years:

- Patient to independently answer questions about symptoms and health
- Portions of visit independently with parent in waiting room
- Names of medications and purpose for each
- Monitor medications and supplies and inform parent of needs
- Airway clearance: independently set-up/perform, able to verbalize purpose, technique and frequency
- Patient to begin to understand yearly tests (blood, sputum, CXR)
- Patient to begin to understand purpose of quarterly visits to CF Center
- Lifestyle Choices: Smoking, drinking, drugs related to CF

Ages 16-19 years:

- Independent clinic visits with parent/caregiver involved at the time of visit summary
- Names of medications and purpose for each
- Monitor medications and supplies and work with parent to obtain refills, etc
- Airway clearance: able to verbalize purpose, technique and frequency
- Patient to begin to understand yearly tests (blood, sputum, CXR)
- Encourage direct communication via phone or MyChart with CF Care Team; be aware of date of clinic appointments
- Lifestyle Choices: job/occupation; collegeSmoking, drinking, drugs related to CF

Taken from Note Templates used for Patients with CF in the Outpatient Clinic

Transition to Adult Care

Similar issues to other chronic conditions

Growing number of adults with CF

Locally, Adult CF Center is housed in the Complex Care Center (next to Culver Medical Group)

Prepare for transition with education, expectations, transition check-list and annual transition meetings with the adult group

CCC can arrange a tour for patients and their families who are interested

Special Considerations

Constantly offer hope

Patient and Family Education

Anticipatory Guidance

At least quarterly visits to the CF Center

Open communication with PCP and school if needed

Team approach

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