Episode 83 – Cystic Fibrosis April 28, 2023

Introduction

Cystic fibrosis (CF)[1] is a life-threatening genetic metabolic disorder of the exocrine glands, which affects the gastrointestinal and respiratory systems and other organs. Mucus secreted by cells in lung airways, pancreatic ducts, gastrointestinal tract, and the reproductive system is normally thin and slippery and acts as a lubricant, but in CF it becomes thickened and blocks these structures, leading to frequent infections and loss of function. [1] [2]

The following can result from CF:

- Thick bronchial secretions block small airways of the lungs, which become inflamed and infected. As the disease progresses, bronchial walls thicken, airways fill with infected secretions, causing lung damage and breathing difficulties.
- Thick secretions block the bile ducts of the liver.
- Thick secretions may block the pancreas preventing digestive enzymes (lipase, protease, amylase) from reaching the small intestine, where nutrient breakdown and absorption occurs.
- Pancreas may produce less insulin.
- Intestines can become blocked by thick secretions.
- Fertility can be impacted as reproductive organs are affected in various ways.
- Sweat glands in the skin secrete fluid containing more salt than normal. [3]

Typical complications caused by CF include:

- Difficulty digesting fats and proteins.
- Malnutrition and vitamin deficiencies due to inability to absorb nutrients.
- Progressive lung damage from chronic infections and aberrant inflammation, including bronchitis, bronchiectasis, pneumonia, hemoptysis, and pneumothorax.
- Cystic fibrosis-related diabetes, usually occurring in adolescence or adulthood.
- Sinus infections and nasal polyps. [2] [4]

Cystic fibrosis severity differs from person to person. However, persistent, and ongoing lung infection, with destruction of lungs and loss of lung function, eventually leads to death in the majority of those with CF. At present, there is no cure, but treatment is available. Treatment aims to ease symptoms, reduce complications, and improve quality of life. Close monitoring and early, aggressive intervention is recommended to slow the progression of CF, which can lead to a longer life.

[1] Cystic fibrosis (CF) is also called mucoviscidosis.

Tremendous advancements in specialized CF care have added years and improved the quality of the lives of individuals with CF. The average life expectancy has steadily increased since the 1950s. During the 1950s, a child with CF rarely lived long enough to attend elementary school. Today, many individuals with CF are attending school, pursuing careers, getting married, and having children. [2] [4] [5] [6]

Epidemiology

Cystic fibrosis was not recognized as a separate disease until 1938, and was classified as a childhood disease because high mortality among affected infants and children. However, by the mid-1980s, more than half of all children with CF survived into adulthood because of aggressive therapeutic measures. Significant advances in CF management in recent decades have dramatically changed the epidemiology and prognosis of CF, which is no longer exclusively a pediatric disease. [1] [6]

Cystic fibrosis is an inherited disorder mainly affecting Caucasian people of European ancestry. It is estimated to occur in one per 2,500 to 4,500 newborns in these populations, and is particularly concentrated in people of northwestern European descent. It is much less common among people of African ancestry (about one per 17,000) and is very rare in people of Asian ancestry (about one in 31,000). [1] [7]

Cystic fibrosis affects over 4,300 Canadians or roughly one in 3,850 live births. The total Canadian population with CF has steady increased and has grown by ~28% since 2002. Just over 1,400 Ontarians live with CF (67% adults; 33% children). [4] [8] [9]

Stephenson et al. (2017) analyzed CF registry statistics, comparing 110 CF care centres in the US with 42 Canadian CF clinics. The study found the median age of survival in Canada was 10 years greater than in the US (50.9 vs. 40.6 years, respectively). The difference in life expectancy seemed to be connected to access to lung transplants, post-transplant care, and differences in the two countries' healthcare systems. [10]

The *Canadian Cystic Fibrosis Registry 2021 Annual Data Report* noted a substantial increase in the median age of survival for Canadians living with CF from 55.4 years in 2020 to 57.3 years in 2021. This means ~50% of children born with CF today are expected to live beyond 57.3 years. Also, 50% of individuals receiving lung transplants are expected to live beyond 10.7 years following transplantation. This steady growth in the median age of survival is an indicator of the quality of CF care, research, and treatments in Canada as well as the efforts that those with CF and their caregivers put into maintaining their health. [8] [11]

Etiology

In 1989 the defective gene responsible for CF was isolated. The gene, called cystic fibrosis transmembrane conductance regulator (*CFTR*), lies in the middle of chromosome 7 and encodes the CFTR protein (a chloride channel on the surface of epithelial cells in multiple organs that regulates chloride, sodium, bicarbonate, and water transport across epithelial and other cell membranes). These functions are critical for maintaining and adjusting the fluidity of mucous secretions. CFTR protein is in every

organ that makes mucus, including the lungs, liver, pancreas, intestines, and sweat glands. It is also present in many other cells in the body.

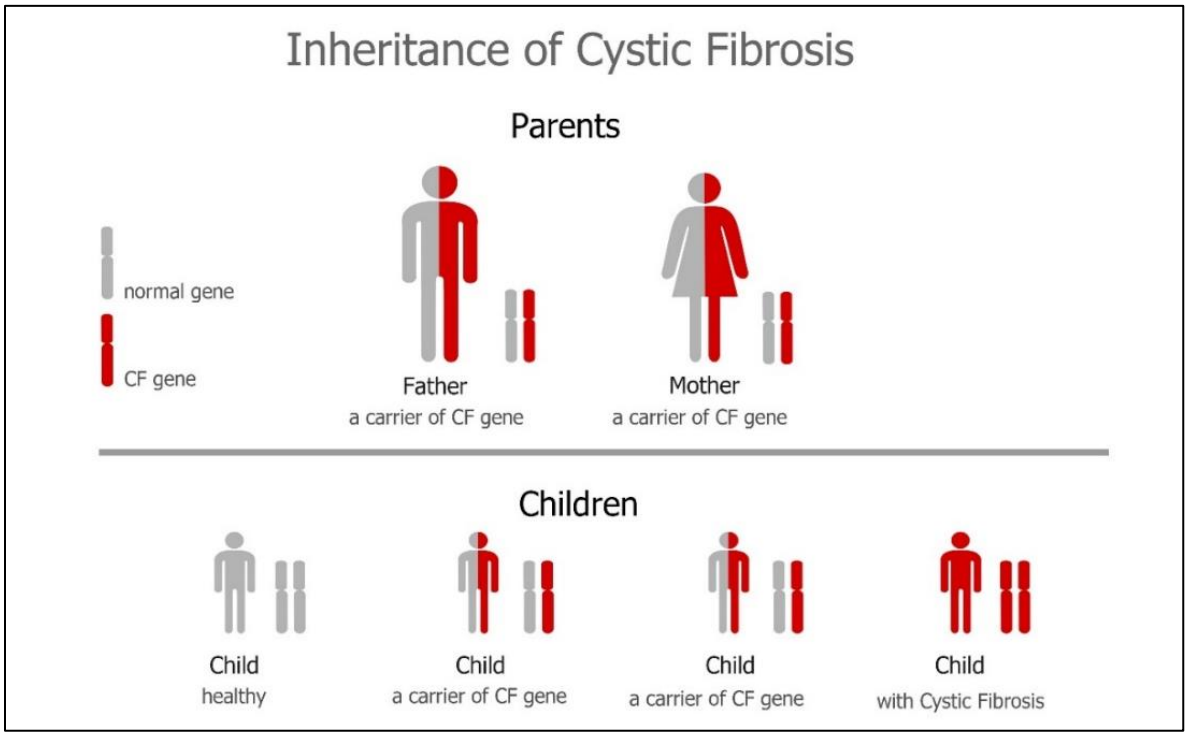
CFTR gene mutation causes the CFTR protein to malfunction. As a result, chloride and sodium ions accumulate in cells, thereby drawing fluid into the cells and causing dehydration of the mucus, resulting in thick, sticky mucus in the respiratory, digestive, and reproductive systems, as well as increased salt in sweat. This impairs function of affected organs.

Everyone with CF has two faulty or mutated CF genes, called variants. Over 2,000 *CFTR* variants have been identified. The two inherited genes could be the same variant, or two different variants. The genes an individual carries are known as their genotype. The most common variant is *F508del*, which occurs in 85% of cases. The type of variants and other factors dictates disease severity, and which organs will be affected. Knowing the type of variants (i.e., a person's genotype) is important as it may impact treatment. [1] [2] [5] [12] [13] [14]

Cystic fibrosis is an autosomal recessive disorder (i.e., the disease only occurs when a child inherits two defective copies of the gene, one from each parent). Females and males are equally affected. Approximately, one in 25 Canadians carry one defective copy of the gene. Carriers do not have CF, nor do they exhibit any related symptoms.

When both parents are carriers, there is a:

- 25% chance their child will be born with CF,
- 50% chance their child will be a carrier, but will not have CF; and
- 25% chance their child will not be a carrier, and will not have CF. [1] [4]



Pathophysiology

Nearly all exocrine glands are affected. Glands may:

- Become obstructed by sticky or solid material in the lumen (e.g., pancreas, intestinal glands, intrahepatic bile ducts, gallbladder, submaxillary glands).
- Appear histologically abnormal and produce excessive secretions (e.g., tracheobronchial and Brunner (duodenal) glands.[2]
- Appear histologically normal but secrete excessive sodium and chloride (e.g., sweat, parotid, small salivary glands).

Lungs

- Lungs are normal at birth, but problems often develop in infancy or early childhood, as thick mucus adheres to airway surfaces and begins to block small airways (i.e., mucus plugging).
- Mucus plugging leads to chronic bacterial infections and inflammation causing bronchiectasis[3] and respiratory insufficiency. Breathing becomes increasingly difficult and reduce the lungs' ability to transfer oxygen to the blood.
- Bronchiectasis can occur next to blood vessels in the lungs. The combination of airway damage and infection can result in hemoptysis (coughing up blood). Often only a small amount of blood, but it can be life-threatening.
- In advanced lung disease, chronic hypoxemia (low blood oxygen) results in muscular hypertrophy of the pulmonary arteries, pulmonary hypertension,[4] and right ventricular hypertrophy.[5] Untreated right ventricular hypertrophy can lead to heart failure.[6]
- Lungs of most individuals are chronically colonized by pathogenic bacteria because the thick mucus provides an ideal breeding ground. Early in the disease course, *Staphylococcus aureus* is the most common pathogen, but as the disease progresses, *Pseudomonas aeruginosa*, including multidrug-resistant strains, is frequently isolated. *S. aureus* and *P. aeruginosa* are the two most prevalent pulmonary pathogens among individuals with CF.
- Other pulmonary pathogens may include methicillin-resistant *S. aureus* (MRSA); *Burkholderia cepacia* complex; nontuberculous mycobacteria; *Stenotrophomonas maltophilia*; *Achromobacter* species; and Aspergillus species.
- Adolescents and adults may experience rupture of the alveoli into the pleural space. This rupture can allow air to enter into the pleural space (pneumothorax), which collapses the lung.
- Respiratory failure due to progressive damage to lungs and is the most common cause of death. [3] [5] [8] [12] [14]

[2] Brunner glands are located in the duodenum, the first part of the small intestine after the stomach.
[3] Bronchiectasis is abnormal widening and scarring of the bronchi caused by chronic infection and inflammation, leading to permanent damage.
[4] Pulmonary hypertension is increased pressure in the pulmonary circulation.
[5] Right ventricular hypertrophy causes the muscular wall of right ventricle to become thick because the heart is overworked.
[6] Refer to Episodes 79, 80, and 81 for more information on cardiovascular disease.

Sinuses

- Sinus infections are common since thick mucus creates a breeding ground. Nasal polyps can develop because of chronic mucosal nasal inflammation and swelling. [5]

Pancreas

- Thickened secretions obstruct pancreas ducts preventing digestive enzymes from reaching the intestine.
- Lack of enzymes leads to malabsorption of fats, proteins, and vitamins, which can lead to nutritional deficiencies, poor or delayed growth, weight loss, and pancreatitis.
- Pancreas can eventually become scarred and no longer produce sufficient insulin. About 2% of children, 20% of adolescents, and up to 50% of adults with CF develop insulin-dependent diabetes.
- Pancreatic function is compromised in 85-95% of individuals with CF. [3] [5] [12]

Intestines

- Intestines can become blocked by thick secretions.
- Blockage is common immediately after birth because meconium in the fetus's digestive tract is abnormally thick. Meconium ileus (blockage in the small intestine) and meconium plug syndrome (blockage in the large intestine) may require surgery.
- Older children and adults may have intermittent or chronic constipation and intestinal obstruction by thickened stool and mucus, termed distal intestinal obstruction syndrome (DIOS).
- DIOS is similar to constipation. However, the back-up of stool and mucus is higher up in the intestines, usually occurring where the small intestine joins the large intestine. DIOS can be a complete or partial bowel obstruction and requires urgent treatment. Symptoms of DIOS include abdominal pain, distention, and vomiting.
- Intussusception[7] can cause intestinal obstruction. It is a serious condition because it can cut off blood supply to the affected portion of the intestine. If left untreated, it can lead to tissue death, intestinal perforation, and peritonitis.[8] [3] [5] [12] [15]

Liver and gallbladder

- Bile ducts that carry bile from the liver and gallbladder to the small intestines can be blocked and inflamed, which may lead to CF-related liver disease, such as jaundice, fatty liver disease, and liver fibrosis and cirrhosis. Severe liver disease may require a liver transplant.
- Gallstones may develop, but only a small percentage develops symptoms. Surgical removal of the gallbladder is rarely needed. [3] [5] [16]

Reproductive organs

- Reproductive organs can be blocked by thick secretions, which can cause infertility.
- Almost all males (98%) are infertile. Infertility is much less common in females.
- Infertility in males is due to blocked or absence of vas deferens.

[7] Intussusception is a condition in which a segment of the intestine slides inside an adjacent section of the intestine like a collapsible telescope.
[8] Peritonitis is inflammation of the peritoneum, the tissue lining the abdominal cavity.

- Decreased fertility in females is due to thicker vaginal mucus which makes it more difficult for sperm to travel and fertilize the egg.
- Females with CF are often able to conceive naturally, although it may take longer. Also, many have carried pregnancies to term. Outcome of the pregnancy for both the pregnant individual and the newborn is related to the pregnant individual's health status during pregnancy.
- For males with CF, conception can be achieved through assisted reproductive technologies. Otherwise, sexual function is not impaired in males or females.
- CF can cause delayed puberty, about 18 months later than average. Delayed puberty is associated with inadequate nutrition, low body weight, poor lung function, hormonal issues, and other health concerns. [9] [12] [17] [18] [19]

Sweat glands

- Sweat glands secrete fluid containing more salt than normal, increasing the risk of dehydration, especially with exercise or in hot weather. Signs and symptoms include increased heart rate, fatigue, weakness, and low blood pressure. [3] [5]

Other complications of CF may include:

- Bleeding disorders, night blindness, osteopenia, and osteoporosis due to inadequate absorption of fat-soluble vitamins A, D,[9] E, and K. Other risk factors for osteopenia and osteoporosis[10] include poor nutritional status, physical inactivity, corticosteroid therapy, and delayed maturation in puberty.
- Depression and anxiety due to dealing with a chronic illness.
- Chronic pain, such as arthralgia (joint pain), arthritis, and myalgia (muscle pain).
- Obstructive sleep apnea and other sleep disorders (e.g., problems sleeping). Obstructive sleep apnea increases risk of hypertension, coronary artery disease, arrythmia, myocardial infarction, heart failure, and stroke.[11] Sleep bruxism[12] can be associated with sleep apnea, because the clenching of teeth may serve as a compensating behaviour through the pushing of the mandible forward in an attempt to open the airway. Thus, individuals with OSA may display signs of bruxism, including worn tooth enamel, fractured teeth, tooth pain and sensitivity, and/or masseter muscle soreness.
- Dialysis-dependent chronic kidney disease, possibly related to treatments as well as to CF
- Kidney stones
- Iron deficiency anemia
- Hearing loss and tinnitus caused by exposure to ototoxic drugs (especially aminoglycosides, a class of antibiotic)
- Increased risk of cancer of the bile ducts, pancreas, and intestines.
- Heart failure [3] [5] [12] [20] [21] [22] [23]

[9] For additional information on vitamin D, refer to Episode 22.
[10] For additional information on osteoporosis, refer to Episodes 41 and 42.
[11] Refer to Episodes 79, 80, and 81 for additional information on cardiovascular disease.
[12] Refer to Episode 82 for discussion on bruxism and tooth wear.

Risk factors

Family history is the only risk factor for acquiring CF (i.e., two parents who carry abnormal CF genes and pass the abnormal gene on to their child). However, some factors impact disease severity, such as the genotype, lifestyle, and age.

Genotype: *CFTR* gene mutations can be divided into five main classes based on the function of the CFTR protein (see chart below). Class I, II, or III variants are generally considered more severe resulting in little or no CFTR function and causes classic CF symptoms. Class IV, or V variants are considered milder resulting in residual CFTR function (e.g., pancreatic function is unaffected) and may have later onset of symptoms. Also, other genes (called modifier genes) can affect an individual's symptoms and outcome. However, there is no strict relationship between specific variants and disease manifestation, so clinical testing (i.e., testing organ function) rather than genotyping is a better guide to prognosis.

Lifestyle: Lifestyle factors that can impact CF include diet, physical activity, tobacco and alcohol consumption. Individuals with CF need to consume a very large number of calories to grow and maintain weight, which can be difficult to achieve. Physical activity is important to help keep lungs healthy. Individuals with CF should not smoke, vape, or be exposed to secondhand smoke, as it will worsen lung disease. Vaping and smoking cannabis should also be avoided as it can result in increased frequency of respiratory exacerbations, hospitalizations, and accelerated lung function decline. Those with CF should be careful with alcohol intake and avoid it altogether if they have liver disease.

Age: CF worsens with age. Individuals with CF usually experience a small decline in lung function each year. [2] [12] [24] [25]

Classification of *CFTR* gene mutation based on impact of CFTR protein [8]

Class	Impact on CFTR protein
I	No functional CFTR protein is made
II	CFTR protein is abnormal and destroyed by the cell before it reaches the cell membrane
III	CFTR protein reaches the cell membrane but the channel is blocked
IV	CFTR protein reaches the cell membrane but the channel does not move chloride properly
V	CFTR protein is made and works properly but the quantity of protein made is insufficient

Signs and symptoms

Signs and symptoms vary depending on disease severity and the individual's age. Symptoms may worsen or improve over time. Some individuals may not experience symptoms until their teenage years or adulthood. Individuals who are not diagnosed until adulthood usually have milder disease and are more likely to have atypical symptoms (e.g., recurring bouts of pancreatitis, infertility, recurring pneumonia). Symptoms can be classified into two main categories: respiratory and digestive. [3] [5]

Respiratory signs and symptoms may include:

- Persistent cough that produces thick mucus (sputum)
- Wheezing or shortness of breath

- Exercise intolerance
- Repeated lung infections, including pneumonia or bronchitis
- Disease progression may lead to barrel-shaped chest due to hyperinflation of the lungs; and clubbing of fingertips or toes due to insufficient oxygen.
- Inflamed nasal passages, stuffy nose, or nasal polyps
- Recurrent sinusitis (sinus infections) [5] [15] [26] [27] [28]

Gastrointestinal signs and symptoms may include:
- Foul-smelling, greasy stools
- Poor weight gain and growth in infants and children despite normal or large appetite.
- Adolescents often have slowed growth.
- Intestinal blockage, particularly in newborns (meconium ileus), which causes vomiting, abdomen bloating (distention), and absence of bowel movements.
- Chronic or severe constipation, which may include frequent straining while trying to pass stool, eventually causing rectal prolapse
- Gastroesophageal reflux disease (GERD)[13] is relatively common among children and adults, which can exacerbate respiratory disease. [3] [5] [26]

Other symptoms include:
- Salty tasting sweat. Parents may notice the formation of salt crystals on their child's skin or often can taste salt when they kiss their child.
- Infertility in males, and decreased fertility in females. Delayed puberty in adolescents. [9] [12] [17] [29]

Diagnosis

CF is diagnosed through newborn screening, sweat testing, genetic testing, carrier screening, and other tests. [3]

Newborn screening

Infants with CF usually have no signs of the disease at birth. Newborn screening helps to diagnose CF early, which can help delay or prevent serious health problems related to CF. In Ontario, a heel prick is used to take a few drops of blood from each infant shortly after birth. The blood is tested for more than 25 treatable diseases, including CF. Blood is screened for CF by testing for immunoreactive trypsinogen (IRT), a chemical made by the pancreas. IRT is normally found in small levels in the body. In individuals who have CF, IRT levels tend to be high. But, IRT levels can also be high if a newborn is premature, had a stressful delivery, or for other reasons. [30] [31] [32]

A positive result means the infant could have CF, or develop some of the same health problems individuals with CF have when they get older. However, more tests are needed to determine if the infant has CF (e.g., sweat test, genetic testing). [30] [31]

[13] Refer to Episode 60 and 82 for discussion on GERD, including impact on oral health.

Sweat test

A sweat test measures the amount of chloride present in sweat. Cystic fibrosis is the most common cause of an elevated sweat chloride level. Children with CF can have two to five times the normal amount of chloride in their sweat.

A sweat test is done when there is a positive newborn screen for CF, a family history of CF, or symptoms of the disorder. It may also be done in children and adults who were not screened at birth but have symptoms suggestive of CF. The most common symptoms in children include chronic coughing, not gaining weight, and abnormal bowel movements. Symptoms in adults may include recurring bouts of pancreatitis, nasal polyps, chronic sinus or lung infections, bronchiectasis, or male infertility.

No special preparation is needed for the test. It is painless and takes about an hour. The test is done by collecting a small amount of sweat from a small area of skin on the forearm (or thigh for an infant). Localized sweating is stimulated with pilocarpine gel. Electrodes are placed on the area. A weak current is used to help the medication enter the skin. Some children feel a tingling or tickling sensation from the electric current. The electrodes are removed and a special sweat collection device is attached to the area. Sweat is collected for 30 minutes. Collected sweat is sent to a lab for testing. It can take a few days to weeks to confirm CF. The test will have to be repeated if not enough sweat was collected to obtain a result. [5] [26] [30] [31] [33]

Sweat test results:

- Abnormal: (≥60 mmol/L) CF is most likely. However, some children with CF have borderline or even normal sweat chloride levels.
- Borderline: (30 to 59 mmol/L) CF is possible. More testing is needed.
- Normal: (<30 mmol/L) CF is unlikely. [34]

Genetic testing

Genetic testing for an abnormal *CFTR* gene can help diagnose CF in a newborn with a positive newborn screening test result, in an individual with one or more symptoms, or in an individual who has a sibling with CF. A cheek swab or blood sample is required for genetic testing. [3] [31]

CF can also be diagnosed prenatally by genetic testing on the fetus using chorionic villus sampling[14] or amniocentesis. This is done if both parents carry a *CFTR* variant. [3]

Carrier screening

Carrier screening for the *CFTR* gene can be done for individuals with a relative with CF to help determine if they are at increased risk of having children with CF. Unless both potential parents have at least one *CFTR* variant, their children will not have CF. [3]

[14] In chorionic villus sampling, a small sample of the chorionic villi is removed, which are tiny projections that make up part of the placenta. A sample of the chorionic villi can be removed through the cervix (transcervically) or the abdominal wall (transabdominally). [91]

Other tests

Nasal potential difference and intestinal current measurements are used to help diagnose CF when sweat and genetic tests are inconclusive. For nasal transepithelial potential difference, a small electrical current is run across the nasal epithelium. Different solutions are applied to the nasal lining and the electrical current is measured. Individuals with CF respond very differently than those without CF to this test. Intestinal current measurement assesses CFTR chloride channel function in rectal tissues or other intestinal epithelia. For this test, small superficial biopsies of the rectal mucosa are obtained by forceps or suction biopsy. Biopsy collection is painless, does not require sedation, and is safe and easy to perform at any age. [12] [26] [35] [36]

Treatment

Presently, there is no cure for CF. Treatment depends upon stage of the disease and specific organs involved. Treatment for CF requires comprehensive and multidisciplinary support. The multidisciplinary team may include physicians, nurses, dietitians, physical and respiratory therapists, mental health professionals, pharmacists, and social workers. Goals of therapy are to maintain normal nutritional status, prevent or aggressively treat pulmonary and other complications, encourage physical activity, and provide psychosocial support. The treatment regimen is complex and may take up to two hours each day.

Treatment may include:

- Airway clearance techniques (ACTs)[15] to move the thick mucus out of the airways. Loosened mucus is then expectorated and not swallowed. Coughing is the most basic ACT and should not be suppressed. Coughing moves mucus out of the large airways. However, moving mucus out of the small airways requires other ACTs. Other ACTs include postural drainage, chest percussion and vibration, coughing, and huffing.

- Aerobic exercise to increase heavy breathing to help loosen airway mucus prior to expectoration.

- Pancreatic enzyme supplements to help digest food. Enzymes must be taken before every meal or snack, including nutritional supplements, breast milk, and formula. Some foods and drinks do not need enzymes because they are easily digested and absorbed (e.g., clear popsicle, hard candy, fruit juice, fruits, soft drinks, sport drinks, tea and coffee without dairy, etc.).

  Most enzyme supplements come in capsule form. Each capsule contains enteric coating granules that allow granules to dissolve in the small intestine to help digest carbohydrates, proteins, and fats. Enzymes work for about 45 to 60 minutes after taking them. If meals are longer than 30 minutes, some individuals split the enzyme dose, taking half at the start of the meal and the other half partway through.

[15] Refer to the video 'Airway Clearance Techniques (ACTs)' by the Cystic Fibrosis Foundation for descriptions of various ACTs. https://youtu.be/1Ufj3oU_M2w

Doses vary greatly between individuals. Not taking enzymes or the proper dose can lead to poorly digested food that can sit in the intestines and cause gas, pain, and unpleasant odours. Poorly digested food can also cause problems ranging from constipation and DIOS, to loose, floating, greasy, frequent stools.

Capsules are taken with liquid and swallowed whole. If a child or someone is not able to swallow capsules, the capsules are opened and sprinkled on a small amount of an acidic food (e.g., applesauce) that can be swallowed. Granules do not have a taste. Mixing enzymes with milk-based foods (e.g., pudding) should be avoided because they may damage the enteric coating. Granules should not be crushed or chewed because it impacts their effectiveness. Also, granules should not be kept in the mouth for prolonged periods since it can cause oral mucosal irritation.

- Vitamin supplements (e.g., fat-soluble A, D, E, and K vitamins) and nutritional supplements.

- High-calorie diet which include high-fat and high-carbohydrate meals and snacks. Extra salt in the diet is needed as individuals with CF lose a lot of salt in their sweat, especially during exercise and hot weather. Sometimes supplemental enteral tube feedings via the stomach or small intestine for individuals who cannot absorb enough nutrients is required.

- Medications such as antibiotics, bronchodilators, mucolytics (drugs to thin lung mucus), and/or in some cases, to correct the nonworking protein made by the CF gene. See below for more information on medications for CF.

- Specific medications for diabetes (e.g., insulin), liver disease, and osteoporosis (e.g., bisphosphonates)[16] if required.

- GERD medications such as proton pump inhibitors (e.g., omeprazole [Prilosec], lansoprazole [Prevacid], esomeprazole [Nexium]) and H2 blockers (e.g., ranitidine [Zantac], famotidine [Pepcid], nizatidine [Axid]). Over the counter antacids (e.g., simethicone [Maalox]) are sometimes used along with proton pump inhibitors. In addition to treating GERD, H2 blockers and proton pump inhibitors also can help reduce acid in the intestines to help the enzymes work better.

- Oxygen therapy is indicated for severe pulmonary insufficiency and hypoxemia.

- Continuous positive airway pressure (CPAP) may be beneficial for those with obstructive sleep apnea.

- Drinking plenty of fluids and over-the-counter medication polyethylene glycol (e.g., Restoralax) to prevent constipation or bowel obstruction. Stool softeners may also be prescribed.

[16] Refer to Episodes 41 and 42 for discussion on osteoporosis and bisphosphonates, including medication-related osteonecrosis of the jaw (MRONJ).

- Bowel surgery to remove bowel blockages or to repair intussusception of the bowel.

- Lung transplantation may be an option for advanced lung disease, life-threatening lung complications, or increasing resistance to antibiotics for lung infections. Both lungs are usually transplanted to reduce the risk of infection spreading to the new lung. Lung transplantation is not a cure for CF, as individuals with CF are still affected by the disease, including complications in their digestive tract and upper respiratory tract, and mental health issues associated with chronic illness. However, lung transplantation can increase length and quality of life.

- Liver transplantation for severe cystic fibrosis-related liver disease, such as cirrhosis, may be an option.

- Heart transplantation for end-stage heart failure when medications and other treatments no longer work. Sometimes individuals may receive one organ or a combination (e.g., lung and liver; heart and lung). The vast majority of organ transplants in Canada for CF are lung transplants. [3] [5] [8] [12] [20] [30] [37] [38] [39] [40] [41] [42] [43]

Medications
Treatment for the lungs is focused on preventing airway blockage and controlling infection. Several medications may be prescribed.

Bronchodilators (e.g., salbutamol [Ventolin]) help prevent airways from narrowing and are usually administered usually through inhalation. Those with severe lung problems and low blood oxygen levels may need supplemental oxygen therapy. [3]

Mucolytics are drugs that thin mucus in airways, such as dornase alfa (e.g., Pulmozyme) or hypertonic saline, which are inhaled through a nebulizer. Dornase alfa is an enzyme that cleaves the DNA in the sputum. Hypertonic saline is a highly concentrated sterile saline solution of different concentrations (3%, 3.5%, 7%). Hypertonic saline works by increasing the amount of sodium in the airways, the sodium attracts water into the airways. Both these drugs thin the mucus; make it easier to cough up sputum; improve lung function; and may reduce risk of respiratory tract infections. [3]

Corticosteroids (e.g., prednisone or dexamethasone) are given orally to relieve symptoms in infants with severe bronchial inflammation; in individuals who have narrowed airways that cannot be opened with bronchodilators; and in individuals who have allergic bronchopulmonary aspergillosis (ABPA), an allergic lung reaction to a type of fungus (most commonly *Aspergillus fumigatus*). ABPA is also treated with an antifungal drug given orally, intravenously, or both, in conjunction with the systemic corticosteroid. [3] [44]

Ibuprofen, a nonsteroidal anti-inflammatory drug (NSAID), is sometimes used to slow the deterioration of lung function. [3]

Drugs to treat sinusitis are often needed as chronic sinusitis is a very common problem. Treatment options include nasal saline irrigation, inhaling dornase alfa into the nose using a nebulizer, and irrigating the nose and sinuses with antibiotics. A corticosteroid nasal spray is recommended to treat allergic rhinitis (inflammation and swelling of nasal mucous membranes).

Antibiotics are started as early as possible at the first sign of a respiratory tract infection. A sample of coughed-up sputum or a swab of a sample from the back of the throat and tonsils is collected and tested so the correct drug is prescribed. *Staphylococcus aureus*, including methicillin-resistant or methicillin-sensitive strains, and *Pseudomonas* species (e.g., *P. aeruginosa*) are commonly found. Many different antibiotics can be given orally to treat staphylococcal infections. To treat a *Pseudomonas* infection, the inhaled form of tobramycin, aztreonam, or colistin is used for several weeks.

Eradication of chronic *P. aeruginosa* colonization is not usually possible. However, early antibiotic treatment around the time the airways are initially infected with *P. aeruginosa* may be effective in eradicating the organism for a time period.

For severe respiratory tract infection, IV antibiotics may be needed. For this treatment, the aminoglycoside tobramycin (or sometimes amikacin) is combined with another antibiotic to specifically target *Pseudomonas*. These other antibiotics include cephalosporins, penicillins, fluoroquinolones, and monobactams. This treatment often requires hospitalization, but part of the treatment may be given at home.

Long-term use of the inhaled form of tobramycin or aztreonam every other month, while also continuously taking an oral form of azithromycin three times a week may help control *Pseudomonas* infection and slow lung function decline.

Individuals who have a clinically significant NTM infection may require long-term therapy with a combination of oral, inhaled, and IV antibiotics. [3]

Antibiotic therapy [45]

Bacteria	Antibiotic class	Type(s)	Administration route*
Staphylococcus aureus	Penicillins	Amoxicillin and clavulanic acid	Oral
		Dicloxacillin	Oral
		Nafcillin and oxacillin	IV
		Piperacillin/tazobactam	IV
	Cephalosporins	Cephalexin, cefdinir	Oral
		Cefuroxime	Oral
		Cefazolin	IV
	Carbapenems	Meropenem, imipenem/cilastatin, doripenem, meropenem-vaborbactam, ertapenem	IV
	Sulpha	Sulfamethoxazole and Trimethoprim	Oral
	Tetracyclines	Tetracycline, doxycycline, minocycline, and tigecycline	Oral, IV, IM

Bacteria	Antibiotic class	Type(s)	Administration route*
	Vancomycin	Vancomycin	IV
	Lincosamides	Clindamycin	Oral, IV
	Oxazolidinone	Linezolid	Oral, IV
Pseudomonas (*P. aeruginosa*)	Penicillins	Piperacillin and tazobactam	IV
	Cephalosporins	Ceftazidime, Ceftazidime-avibactam	IV
		Cefepime	IV
		Ceftolozane-tazobactam	IV
	Aminoglycosides	Tobramycin, amikacin, gentamicin	IV, inhaled
	Macrolides	Azithromycin (may help reduce inflammation from *P. aeruginosa*)	Oral, IV
	Quinolones	Ciprofloxacin, levofloxacin	Oral, IV
	Carbapenems	Meropenem, meropenem-vaborbactam, imipenem/cilastatin, doripenem	IV
	Aztreonam	Aztreonam	IV, inhaled
	Colistimethate	Colistimethate	Inhaled, IV
Methicillin-resistant *Staphylococcus aureus* (MRSA)	Sulfa	Sulfamethoxazole/Trimethoprim	Oral
	Vancomycin	Vancomycin	IV
	Oxazolidionone	Linezolid	Oral, IV
	Cephalosporins	Ceftaroline	IV
	Tetracyclines	Doxycycline, minocycline	Oral
		Doxycycline, tigecycline	IV
	Quinolone	Ciprofloxacin, levofloxacin	Oral, IV
	Rifamycin	Rifampin (must be used in combination with another active agent)	Oral, IV
	Lincosamide	Clindamycin	Oral, IV
	Topical	Mupirocin	Topical
Nontuberculous mycobacteria (NTM)			
Mycobacterium abscessus (*M. abscessus*) Intensive phase	Macrolide	Azithromycin	Oral, IV
	Aminoglycoside	Amikacin	IV
	Cephalosporin	Cefoxitin	IV
	Tetracycline	Tigecycline	IV
	Carbapenem	Imipenem/cilastatin	IV
Consolidation phase	Macrolide	Azithromycin	Oral, IV
	Aminoglycoside	Amikacin	Inhaled
	Tetracycline	Minocycline	Oral
	Clofazimine	Clofazimine	Oral
	Quinolone	Moxifloxacin	Oral
	Oxazolidinone	Linezolid	Oral, IV
	Sulfa	Sulfamethoxazole and trimethoprim	Oral, IV
Mycobacterium avium complex (MAC)	Macrolide	Azithromycin	Oral, IV
	Aminoglycoside	Amikacin	Inhaled, IV
	Ethambutol	Ethambutol	Oral

Bacteria	Antibiotic class	Type(s)	Administration route*
	Rifamycin	Rifampin	Oral
Burkholderia cepacia (*B. cepacia*)	Tetracyclines	Tetracycline, doxycycline, minocycline, and tigecycline (treats some strains)	Oral, IV, IM
	Carbapenems	Meropenem, imipenem/cilastatin, doripenem, meropenem-vaborbactam	IV
	Cephalosporins	Ceftazidime, ceftazidime/avibactam, ceftolozane/tazobactam	IV
	Sulfa	Sulfamethoxazole and trimethoprim	Oral, IV
Stenotrophomonas maltophilia	Quinolone	Piperacillin/tazobactam	IV
	Cephalosporins	Ceftazidime, ceftazidime/avibactam	IV
	Sulfa	Sulfamethoxazole and trimethoprim	Oral, IV
Haemophilus influenzae	Penicillins	Amoxicillin/clavulanate	Oral
	Cephalosporins	Cefdinir	Oral
Achromobacter xylosoxidans	Quinolone	Ciprofloxacin, levofloxacin	Oral, IV
	Carbapenems	Meropenem, imipenem/cilastatin, doripenem, meropenem-vaborbactam	IV
	Tetracycline	Minocycline	Oral

*Intravenous (IV); intramuscular (IM)

Antifungals: Individuals with ABPA or lower airways aspergillus infection may require prolonged oral or IV therapy with an antifungal (e.g., itraconazole) and/or systemic corticosteroids. [3] [12]

CFTR modulators target the cause of CF by correcting the defective CFTR protein, whereas other CF treatments and therapies manage the symptoms of CF. CFTR modulators are taken orally long term. They help to improve lung function, pancreas function, and quality of life, increase weight, and decrease the salt concentration in sweat and the frequency of lung infections and hospitalizations. There are four CFTR modulators available: Kalydeco, Orkambi, Symdeko, and Trikafta. Indications for the different types of medications are based on the individuals' *CFTR* variants and age. Although all these drugs can be helpful, only ivacaftor and Trikafta are considered highly effective modulator therapy. [3] [12]

Kalydeco (ivacaftor) is the first-generation modulator, approved by Health Canada for treatment of a specific mutation in 2012 and for additional mutations in 2014. It is approved by Health Canada for ages one year and older with certain *CFTR* variants. Ivacaftor, a CFTR potentiator, makes the CFTR protein at the cell surface work better by allowing more chloride to pass through. [46] [47] [48]

Orkambi (lumacaftor / ivacaftor), a second-generation modulator, was approved by Health Canada in 2016 for individuals 1 year of age and older who have two copies of the *F508del* mutation on the *CFTR* gene (most common mutation of cystic fibrosis).

Lumacaftor, a CFTR corrector, increases the amount of the CFTR protein on the surface of the cell. Ivacaftor, a CFTR potentiator. makes the CFTR protein at the cell surface work better by allowing more chloride ions to pass through. [49] [50]

Symdeko (tezacaftor / ivacaftor), a second-generation modulator, was approved by Health Canada in 2018 for individuals 12 years and older who carry two copies of the *F508del* variant or one copy of *F508del* plus another specified variant.
Tezacaftor, a CFTR corrector, increases the amount of the CFTR protein at the surface of the cell. Ivacaftor, a CFTR potentiator, makes the CFTR protein at the cell surface work better by allowing more chloride ions to pass through. [46] [51] [52]

Trikafta (elexacaftor / tezacaftor / ivacaftor), a third-generation modulator, was approved by Health Canada in June 2021 for individuals aged 12 years and up with one copy of the *F508del* variant, regardless of the second mutation, and in April 2022 for those six years and up. Trikafta is a transformational drug with the potential to treat up to 90% of Canadians with CF. Elexacaftor and tezacaftor, a CFTR correctors, increase the amount of CFTR protein on the surface of the cell. Ivacaftor, CFTR potentiator, makes CFTR protein at the cell surface work better by allowing chloride ions to pass through. [46] [53] [54]

Canadian research by Stanojevic et al. 2020 estimated the potential impact of Trikafta on morbidity and mortality. By 2030, Trikafta could reduce the number of individuals living with severe lung disease by 60% and reduce the number of deaths by 15%. The findings show a significantly slower disease progression with an 18% increase in individuals with mild lung disease and 19% fewer hospitalizations or home intravenous antibiotics for pulmonary exacerbations. The estimated median age of survival for a child born with CF would increase by 9.2 years. Also, a reduction in the number of transplants required for severe lung disease. [55]

In the future, Trikafta may also be indicated for younger children if the necessary clinical trials prove it safe and effective in this age group, which means it could one day potentially benefit 90% of Canadians living with CF. [53]

Management
Regular medical check-ups are needed to monitor and control symptoms, and prevent complications. Various tests are often needed because CF can affect several organs.

Common tests include:
- Blood tests to monitor glucose and insulin production, help determine liver function, and measure fat-soluble vitamin levels.
- Bone mineral density tests.
- Pancreas functionality tests, usually by measuring the concentration of elastase in stool. Elastase is a digestive enzyme secreted by the pancreas. In a healthy pancreas, elastase will be passed in the stool. Little or no elastase in the stool demonstrates pancreatic insufficiency. Pancreatic insufficiency can cause several health problems, including malabsorption and malnutrition.

- Pulmonary function tests may be done several times a year and whenever there is a decline in health. They are the best indicators of clinical status and response to therapy.
- Respiratory cultures (oropharyngeal or sputum) are often done several times a year, especially in individuals not yet colonized with *P. aeruginosa*.
- Chest computed tomography (CT) or chest x-rays to document lung infection and extent of lung damage. Lung biopsy may be needed in some situations.
- CT or x-ray of the sinuses for those with serious sinus symptoms or nasal polyps if sinus surgery is being considered.
- Colonoscopy may be required.

Other management strategies include:
- Practising good hand hygiene and receiving all recommended vaccines (particularly for infections that can cause respiratory problems) to help prevent infection that could lead to more severe complications.
- Following a healthy, high-calorie, high-sodium diet to maintain a healthy weight. Individuals with CF lose a lot of salt in their sweat, so they must eat more salty foods, especially during hot, humid weather.
- Participating in physical activity to help improve and maintain lung function and to help with airway clearance.
- Continuing treatments, including medications, supplements, and daily ACTs as directed by attending medical practitioners. [3] [12] [39] [41] [56]

Cross-infection

Research shows individuals with CF are at particular risk for spreading certain pathogens among others with CF. These pathogens are difficult to treat and can lead to worsening symptoms and faster decline in lung function.

The Cystic Fibrosis Foundation recommends all individuals with CF, regardless of their respiratory tract culture results, be separated by at least 2 meters (6 feet) from others with CF in all settings, to reduce the risk of droplet transmission of CF pathogens. This does not apply to members of the same household. [57] [58]

Individuals with CF who have undergone a lung transplant can still get and spread pathogens among others with CF because the pathogens can remain in their upper respiratory system, including the sinuses. Because of the risk of cross-infection, it is recommended individuals with CF take the same precautions they took before lung transplantation. [40]

CF pathogens include *Pseudomonas aeruginosa*, Methicillin-resistant *Staphylococcus aureus*, *Burkholderia cepacia* complex, *Aspergillus*, and nontuberculous mycobacteria.

Pseudomonas aeruginosa (*P. aeruginosa*): *Pseudomonas* are common bacteria found in many different environments and are a major cause of lung infections in individuals with CF. These bacteria thrive in moist environments and equipment (e.g., kitchens, bathrooms, sinks, humidifiers). *Pseudomonas* are opportunistic causing infection when an individual has CF or another condition compromising the immune system.

Pseudomonas are among the most common bacteria found in individuals with CF. About half of all individuals with CF have *Pseudomonas*. Some strains have become resistant to multiple antibiotics and are very hard to treat. Research shows individuals with CF may transmit these more resistant strains to each other. [59] [60]

Methicillin-resistant *Staphylococcus aureus* (MRSA): MRSA can cause an infection on the skin and in the lungs and can be spread through contact (e.g., shaking hands, touching contaminated objects) or respiratory droplets. A study by Dasenbrook et al. (2010) showed MRSA in the respiratory tract of individuals with CF was associated with worse survival. [59] [61] [62]

Burkholderia cepacia complex (*B. cepacia*): This group of bacteria live in damp or wet places and is often difficult to treat once it infects the lungs. There are almost 20 different *B. cepacia* complex species. *Burkholderia* bacteria are often resistant to many antibiotics, which makes them difficult to treat once they infect the lungs. [59] [63]

Aspergillus: *Aspergillus* is a common fungus found indoors and outside so most individuals breathe in fungal spores every day. It is impossible to completely avoid breathing in some *Aspergillus* spores, but for most individuals breathing in these spores is not harmful. However, it can cause aspergillosis in individuals with lung disease or compromised immune systems. Some can also develop ABPA. [59] [64] [65]

Nontuberculous mycobacteria (NTM): NTM are mycobacteria other than *M. tuberculosis* (causes tuberculosis) and *M. leprae* (causes leprosy). NTM are environmental organisms found in soil, dust, and water (e.g., lakes, rivers, streams, municipal water sources). NTM can form difficult-to-eliminate biofilms, such as in plumbing and dental waterlines. NTM can survive many disinfectants and severe environmental conditions. Environmental exposure to many of these organisms is common, but most exposures do not cause infection and many infections do not cause disease.

However, NTM are opportunistic pathogens placing some groups at increased risk, including those with underlying lung disease or compromised immune systems. These pathogens are typically not transmitted person-to-person. However, person-to-person transmission of *Mycobacterium abscessus* has been reported in individuals with CF. *M. abscessus* and *Mycobacterium avium* (*M. avium* Complex or MAC) are the most common types of NTM found in individuals with CF. In general, MAC is seen in older individuals who have more mild disease and *M. abscessus* is associated with more advanced disease and a more rapid decline in lung function. Individuals with CF are at high risk of NTM infection and disease. NTM have been found in increasing numbers of individuals with CF. [59] [66] [67] [68]

Other respiratory illnesses

It is also important for individuals with CF to stay at least 2 meters away from anyone with a cold, influenza, or other respiratory illness. [40]

Influenza (i.e., the flu) is highly contagious, even among individuals without CF. For individuals with CF, the flu can lead to a severe lung infection, including pneumonia.

The flu vaccine can reduce the risk of getting the flu and when more individuals receive the flu shot every year, there is a better chance of reducing its spread.

It is best to get the flu shot early because it can take about two weeks after vaccination for the body to build immunity against the flu virus. The best time to get the flu shot is in September through October, but getting vaccinated in December or January is still helpful as flu season can last until spring. [59] [69]

COVID-19: Health Canada notes individuals of any age with chronic medical conditions, including lung diseases like CF, or who are immunocompromised, or have undergone transplantation are at an increased risk of severe illness from COVID-19. Anyone who is not fully vaccinated is also at increased risk of severe illness from COVID-19. The main way to reduce the spread of COVID-19 is for the entire community to get fully vaccinated, including booster doses. Individuals with CF should check with their medical provider on staying up to date with COVID-19 vaccinations. [70] [71]

Oral health

Studies have suggested the oral cavity could be a reservoir for *P. aeruginosa* to colonize the lungs. Cystic fibrosis and its treatment may also affect various aspects of oral health, including the dentition, periodontium, and biofilm accumulation. [72]

Enamel defects

Enamel defects, often present on the maxillary incisors, include demarcated opacities, diffuse opacities, and enamel hypoplasia. The prevalence of enamel defects ranges from 28% to 56%. Research suggests abnormal expression of the *CFTR* gene in cells that produce enamel is likely the cause of enamel defects. The *CFTR* gene appears to play a role in the enamel mineralization process. CFTR is turned on as enamel-producing cells mature and is vital for completion of enamel mineralization. It has also been hypothesized enamel defects may be due to nutritional disturbances, long-term antibiotic use, and pancreatic enzyme use. [20] [73] [74]

Dental caries

Children and adolescents with CF are thought to be at increased risk for dental caries due to factors related to CF, such as:

- Enamel defects
- Increase in intraoral *Streptococcus mutans* levels
- GERD
- High calorie diets, sugar containing oral nutritional supplements, and increased eating frequency to maintain weight.
- Oral antibiotics used to treat CF-related infections are often dosed in sugary suspensions to mask the bitter taste. The sugary suspension may coat teeth for hours between toothbrushing. [73] [75]

Despite these risk factors, reports of caries rates in individuals with CF conflict. Several studies have reported individuals with CF present with a low caries prevalence.

Several theories have been proposed as to why individuals with CF may be at reduced risk of caries, such as:

- pH buffering effects from high dairy product consumption protects the dentition from decay.
- Long-term antibiotic regimens can change the oral microbial flora, lessening caries risk.
- Individuals with CF have altered salivary content with higher calcium and phosphate concentrations, which may increase saliva's buffer capacity.
- Children and adults with CF may engage in more meticulous oral self-care behaviours to avoid oral infections that can spread to the lungs.

However, a systematic review by Chi (2013) of caries prevalence in children and adolescents with CF reported a reduced risk for caries among children with CF, but an increased caries risk for among adolescents with CF.

A possible explanation for the potential increase in caries among adolescents is the use of antibiotics, including inhaled tobramycin, to target *P. aeruginosa*, which do not affect *S. mutans*. Early in adolescence, there is a respiratory microbial shift resulting in *P. aeruginosa* becoming the predominant chronic lung pathogen. Tobramycin is a main antibiotic prescribed to adolescents with CF. Because tobramycin does not affect *S. mutans*, adolescents with CF may lose the caries protective benefits experienced in childhood. [20] [75]

Further, growing independence during adolescence in nutrition and healthcare decision making, could lead to behaviours like increased carbonated drink intake. Individuals with CF often consume large volumes of sugary drinks to promote weight gain. [76]

Biofilm accumulation

Although early studies reported individuals with CF had less plaque than those without CF, more recent studies have shown plaque levels tend to be the same among both groups. [20]

A systematic review by Coffey et al. (2020) revealed the majority of studies analyzed showed better oral hygiene, with lower levels of plaque and gingivitis among individuals with CF than controls. Also, a few studies showed increased gingivitis and higher levels of plaque, and many studies showed higher levels of calculus. It has been hypothesized the increase in dental calculus is due to increased calcium and phosphate levels in the saliva of these individuals. Calculus formation is a potential risk factor for the progression of periodontal disease. [77]

Periodontal disease

Studies have shown those with CF experience fewer gingival bleeding sites than those without CF. Long-term antibiotic therapy may change oral microbiota leading to less gingival bleeding. Individuals with CF may be at reduced risk of periodontal disease. It is thought long-term use of broad-spectrum antibiotics may have a preventative effect against the development of periodontal disease.

Azithromycin is frequently prescribed for individuals with CF, and it is particularly effective against Gram-negative bacteria. Azithromycin is able to penetrate dental biofilm, has good periodontal tissue penetration, and is retained in the periodontal pocket for up to 14 days. [20] [78]

Candidiasis

Individuals with CF are at an increased risk of oral candidiasis, due to the use of inhaled corticosteroids and long-term antibiotic regimens, and from the effects of CF-related diabetes. [20]

Enamel erosion

GERD can force stomach acid into the oral cavity, which, depending on frequency and severity of the acid reflux, can cause enamel erosion.[17] Frequent consumption of acidic drinks (e.g., soft drinks consumed for calories, sport drinks when exercising) also contribute to enamel erosion. [39] [73]

Salivary glands

CF affects all exocrine glands, including the salivary glands. Parotid glands are mainly serous producing glands (rather than mucus-secreting), and thus their saliva is only minimally affected. Submandibular, sublingual, and minor salivary glands show greater changes in gland architecture and saliva composition. As well, the submandibular glands may be enlarged and easily palpable. [78] [79]

Dry mouth

Some medications used to manage CF, such as bronchodilators and corticosteroids, can contribute to oral disease. β2 (beta2) agonist inhalers (i.e., bronchodilators such as salbutamol) reduce salivary flow, resulting in xerostomia. [78]

Mouth breathing

Mouth breathing and anterior open bite are often seen in individuals with CF, given the association with chronic nasal and sinus obstruction. Mouth breathing can also contribute to dry mouth. [78]

Perceived barriers to oral healthcare

Research has shown individuals with special medical needs may be less likely to access oral healthcare, and a 2022 report has shown individuals with CF may attend oral healthcare practices less frequently than is recommended. [80] [81]

A recent study by Coffey et al. (2023) found over one third of adults with CF reported anxiety about attending the dental office. Reasons for the anxiety included fear, embarrassment, cross-infection concerns, and difficulty with treatment, especially being in a supine position. A third of the participants did not make the office aware of their CF status.

[17] Refer to Episode 82 for discussion on erosion and Episode 60 for more information on GERD.

Feeling anxious regarding oral healthcare may result in irregular attendance and higher risk of oral disease. Therefore, it is important for oral health practitioners to be aware of the impact CF can have upon oral healthcare visits. [74]

Strategies to rectify client concerns may include:

- Allocating extra time to clients with CF for an in-depth discussion regarding their medical and oral health history, and any concerns they may have regarding their oral health and oral healthcare treatment.
- Being aware the impact CF medications and diet can have on oral health, and the impact CF can have on mental health.

Good communication skills on part of the provider, and the client experiencing a feeling of being listened to, can result in a marked improvement in client satisfaction and healthcare outcomes. Therefore, spending extra time to fully understand the client's medical condition, explaining infection prevention and control (IPAC) precautions, and making any needed accommodations (e.g., upright sitting position for treatment, taking breaks) can help to alleviate client anxiety. [74]

Caring for clients with CF

Individuals with CF typically have medical evaluations every three months. Therefore, it is important to update health history each appointment to determine health status, lung function, medication use (prescribed and over the counter), history of hospitalizations, contraindications to care, and need for medical consultation and referral.

Clients with CF experience excessive coughing, dyspnea, and tiredness, which may make it difficult to sit through an oral healthcare appointment. It may be necessary to keep appointments short and allow for breaks as needed (e.g., to rest, cough, expectorate). [82]

Appointment scheduling should be flexible since clients with CF often spend several hours per day receiving or performing breathing treatments and attending other medical appointments. [20]

Chair position should be semi-supine or upright to help improve the client's breathing. An upright sitting position helps to clear secretions from the bronchi and trachea via coughing. [20] [78]

Limiting aerosols helps prevent aspiration of oral microbes into the lungs. This includes avoiding the use of ultrasonic scalers. [78] [82]

Medical consultation is advisable if nitrous oxide sedation is contemplated. [78]

Possible strategies for oral health complications [20] [77] [83] [84]

Condition	Risk factors	Treatment	Prevention
Potential for dental caries	Frequent snacking High carbohydrate diet	Topical fluoride (e.g., fluoride varnish)	Home fluoride therapy (e.g., high fluoride toothpaste, fluoride mouthrinse) Oral self-care instruction

Condition	Risk factors	Treatment	Prevention
	Nutritional supplements with high sugar content Enamel defects Oral antibiotics are often dosed in sugary suspensions	Sealants	Mouth rinsing with water after receiving oral medications. Referral to registered dietician to manage dietary choices to support oral health
Periodontal disease	Biofilm accumulation Calculus formation Uncontrolled diabetes Osteoporosis	Periodontal debridement Referral to periodontist as required	Oral self-care instruction Regular periodontal maintenance appointments
Candidiasis	Long-term antibiotic use Inhaled and systemic corticosteroids	Antifungal medication	Mouth rinsing with water after using steroid inhaler Using a "spacer" (aerosol-holding chamber) attached to the metered-dose inhaler.
Enamel erosion	GERD Frequent consumption of acidic foods, beverages, and candies Sports drinks to balance electrolytes	Topical fluoride (e.g., fluoride varnish) Dietary assessment and advice Careful monitoring	Home fluoride therapy (e.g., high fluoride toothpaste, fluoride mouthrinse) Reduce intake of acidic beverages and avoid swishing beverages Avoid sour candies Utilizing a straw for acidic beverages Mouth rinsing after consuming acidic foods and beverages Wait for 30 minutes before brushing teeth after acid exposure to avoid brushing softened enamel[18]
Xerostomia	Certain medications reduce saliva flow (e.g., bronchodilators) Mouth breathing	Referral for treatment of nasal congestion related to mouth breathing Increasing water consumption[19]	Chewing sugar-free gum to stimulate saliva Moisturizing agents Increasing water consumption

IPAC in oral healthcare practices

Following IPAC procedures in oral healthcare settings is important for everyone, particularly those with CF. Infection can be spread between individuals with CF, especially if different bacteria or different strains of the same bacteria colonize their lungs.

In 2013, the US Cystic Fibrosis Foundation updated the infection prevention and control guidelines for individuals with CF to help reduce the spread of pathogens in healthcare

[18] Refer to Episode 82 for more information on erosion and prevention strategies.
[19] Refer to Episode 55 for dry mouth management strategies.

clinics, hospital settings, and everyday life.[20] Cystic Fibrosis Canada endorses this policy to reduce the risk of individuals with CF from acquiring and transmitting pathogens that can lead to serious lung infections. [85] [86]

The policy states to separate all individuals with CF from other individuals with CF, regardless of their respiratory tract culture results, at least 2 meters (6 feet) in all settings, to reduce the risk of droplet transmission of CF pathogens. This would include oral healthcare practices.

All individuals with CF, regardless of respiratory tract culture results, should wear a surgical mask when in a healthcare setting to reduce the risk of transmission or acquisition of CF pathogens. The document stresses the importance of hand hygiene, and wearing appropriate PPE when caring for individuals with CF. [57]

Also, exposure to others who have contagious respiratory illnesses, such as influenza or the common cold, should be avoided. Keeping clients with CF separate from others with CF or respiratory illnesses can be accomplished by careful client scheduling and escorting the client immediately into an operatory upon arrival. [40] [78]

Although many individuals with CF have a chronic cough and may appear to be ill, they are likely not contagious to individuals without CF, including oral healthcare providers, clients, or office staff, unless they have signs and symptoms of acute respiratory tract infection (e.g., fever, sore throat, runny nose, etc.). [78]

Dental waterline quality

Healthcare-associated nontuberculous mycobacteria (NTM) infections and outbreaks can occur when environmental and infection control factors permit exposure of susceptible hosts to NTM from a healthcare facility's water system, including dental waterlines. [87]

NTM can chronically colonize airways of individuals with CF and cause significant lung damage. Individuals with NTM infection often require long-term therapy (12 months or longer) with a combination of oral, inhaled, and IV antibiotics. [68]

Biofilms grow in dental unit waterlines due to the long, small-diameter tubing; low flow rates used in procedures; and frequent periods of stagnation. As a result, high numbers of common waterborne bacteria can be found in untreated dental unit water systems. Disease-causing microorganisms found in untreated dental unit water can include *Legionella, P. aeruginosa*,[21] and NTM.

Generally, high numbers of these opportunistic microorganisms are not dangerous to the general population, unless individuals are immunocompromised or have compromised respiratory function, including those with CF. [88]

[20] Infection Prevention and Control Guideline for Cystic Fibrosis: 2013 Update https://www.jstor.org/stable/10.1086/676882

[21] *P. aeruginosa* is one of the most prevalent pulmonary pathogens among individuals with CF.

Nonetheless, oral healthcare providers and clients could be placed at risk of adverse health effects if dental unit water is not appropriately treated. For example, although rare, outbreaks of NTM infections have been reported in children treated at dental offices.

In 2015, 24 cases of odontogenic NTM infections were reported in children receiving pulpotomy treatment from a pediatric dental clinic in Georgia in the U.S. Municipal water was used during dental procedures, the clinic was not using a disinfectant in their dental unit waterlines, and the clinic was not regularly monitoring the water quality. Microbial testing of the water samples taken from the dental units showed very high microbial counts of *M. abscessus*.

In 2016, an outbreak occurred at a pediatric dental clinic in California, with 71 children identified as having odontogenic NTM infections following pulpotomy treatment. Municipal water stored in a pressurized bladder holding tank was used to fill the dental unit water bottles. The clinic was not using disinfectants on their dental unit waterlines or regularly monitoring water quality.

The outbreaks in California and Georgia involved young children, ages ranging from 4 to 8 years. Many of the children developed severe infections and required hospitalization, treatments such as intravenous antibiotics, and surgical procedures. Complications from their infections included permanent tooth loss, hearing loss, facial nerve palsy, and incision fibrosis.

The US Centers for Disease Control and Prevention (CDC) is investigating a third cluster identified at a pediatric dental clinic in March of 2022. [89]

It is important to follow appropriate IPAC guidelines for dental unit waterline maintenance to reduce risk of infection, especially in clients with compromised immune and lung function. Refer to CDHO's *Infection Prevention and Control (IPAC) Guidelines*[22] and RCDSO's *Infection Prevention and Control in the Dental Office Standard of Practice*[23] for more information. Refer to Public Health Ontario IPAC *Checklist for Dental Practice Core Elements*[24] to examine, evaluate, and compare current office IPAC practices using provincial recommendations. [88] [90]

Take home messages

- Research has improved the longevity and quality of life of individuals with CF over the eighty years since the disease was first described. Advancements in specialized CF care have added years and improve the quality of the lives of individuals with CF.

[22] CDHO Infection Prevention and Control (IPAC) Guidelines https://www.cdho.org/docs/default-source/pdfs/reference/guidelines/cdho-ipac-guidelines.pdf
[23] RCDSO Infection Prevention and Control in the Dental Office https://az184419.vo.msecnd.net/rcdso/pdf/standards-of-practice/RCDSO_Standard_of_Practice_IPAC.pdf
[24] PHO IPAC Checklist for Dental Practice Core Elements https://www.publichealthontario.ca/-/media/Documents/C/2019/checklist-ipac-dental-core.pdf

- CF treatment involves a multidisciplinary team to provide optimal healthcare. Oral health professionals are valuable members of the team providing and promoting oral and overall health.
- Prognosis for CF has greatly improved in recent decades resulting in a steady increase in prevalence of CF as more adults are living with this disease. Oral health professionals will need to be prepared to provide services specifically tailored to this population.
- Factors that may impact oral healthcare and treatment decisions include the long-term use of antibiotics, bisphosphonates for osteoporosis, corticosteroids for CF-related conditions, immunosuppressive drugs for organ transplants, presence of CF-related diabetes, gastroesophageal reflux disorder, obstructive sleep apnea and sleep bruxism, and malnutrition which may be treated with high sugar nutritional supplements.

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Client Resources

Cystic Fibrosis Canada has a helpline to answer questions, information requests, referrals, and to help connect people to available community and government resources. Contact information: Email: helpline@cysticfibrosis.ca
Phone: 1-800-378-2233

Find a local CF clinic
https://www.cysticfibrosis.ca/our-programs/healthcare/how-cf-care-is-delivered/cf-clinics-in-canada

Resources for individuals with CF and their families and caregivers
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