
بسم الله الرحمن الرحيم

Cystic Fibrosis 2

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TREATMENT

- General Approach to Care Initial efforts after diagnosis should be intensive and should include baseline assessment, initiation of treatment to prevent pulmonary involvement in young infants or reverse it in those diagnosed later, nutritional maintenance or remediation, and education of the patient and parents.
- Follow-up evaluations are scheduled every 1-3 mo, depending on the age at diagnosis, because many aspects of the condition require careful monitoring.

- An interval history and physical examination should be obtained at each visit.
- A sputum sample or, if that is not available, a lower pharyngeal swab taken during or after a forced cough is obtained for culture and antibiotic susceptibility studies.
- Because irreversible loss of pulmonary function from low-grade infection can occur gradually and without acute symptoms, emphasis is placed on a thorough pulmonary history and physical exam and routine pulmonary function testing.

- Protection against exposure to methicillin-resistant S. aureus, P. aeruginosa, B. cepacia, and other resistant Gram-negative organisms is essential, including contact isolation procedures and careful attention to cleaning of inhalation therapy equipment.
- A nurse, physical therapist, respiratory therapist, social worker, and dietitian, as members of the multidisciplinary care team, should evaluate children regularly and contribute to the development of a comprehensive daily care plan.

- Because secretions of CF patients are not adequately hydrated, attention in early childhood to oral hydration, especially during warm weather or with acute gastroenteritis, may minimize complications associated with impaired mucous clearance.
- Intravenous therapy for dehydration should be initiated early.
- The goal of therapy is to maintain a stable condition for prolonged periods.

- Intravenous antibiotics may be required infrequently or as often as every 2-3 mo.
- The goal of treatment is to return patients to their previous pulmonary and functional status.

- Pulmonary Therapy The object of pulmonary therapy is to clear secretions from airways and to control infection.
- When a child is not doing well, every potentially useful aspect of therapy should be reconsidered.

Inhalation Therapy Human recombinant DNase

- Inhalation Therapy Human recombinant DNase (2.5 mg) enzymatically dissolves extracellular DNA released by neutrophils, a major contributor to the characteristically sticky and viscous CF airway secretions.
- It is usually given as a single daily aerosol dose, improves pulmonary function, decreases the number of pulmonary exacerbations, and promotes a sense of well-being.
- Benefit for those with mild, moderate, and severe lung disease has been documented.
- Improvement is sustained for 12 mo or longer with continuous therapy.

Nebulized hypertonic saline

- Nebulized hypertonic saline, acting as a hyperosmolar agent, is believed to draw water into the airway and rehydrate mucus and the periciliary fluid layer, resulting in improved mucociliary clearance.
- Seven percent hypertonic saline nebulized 2-4 times daily increases mucous clearance and reduces pulmonary exacerbation, with only a slight short-term improvement in pulmonary function.

Airway Clearance Therapy

- Airway clearance treatment begins in infancy with chest percussion (with or without postural drainage) and derives its rationale from the idea that cough clears mucus from large airways, but chest vibrations are required to shear secretions for the airway wall and move secretions from small airways, where expiratory flow rates are low.
- Chest PT can be particularly useful for patients with CF because they accumulate secretions in small airways first, even before the onset of symptoms.
- Airway clearance therapy is recommended 2-4 times a day, depending on the severity of lung dysfunction, and usually increased during acute exacerbations.

- Vest-type mechanical percussors (high-frequency chest wall oscillation) are commonly used past infancy due to their convenience, as are a variety of oscillatory positive expiratory pressure devices (such as Acapella and Aerobika) and other controlled breathing techniques (e.g., autogenic drainage).
- Routine aerobic exercise appears to slow the rate of decline of pulmonary function, and benefit has also been documented with weight training.

Antibiotic Therapy

- Antibiotics are the mainstay of therapy designed to control progression of lung infection.
- The goal is to reduce the intensity of endobronchial infection and to delay progressive lung damage.
- Antibiotic treatment varies from intermittent short courses of 1 antibiotic to nearly continuous treatment with 1 or more antibiotics.
- Dosages for some antibiotics are often 2-3 times the amount recommended for minor infections because patients with CF have proportionately more lean body mass and higher clearance rates for many antibiotics than other individuals.

Oral Antibiotic Therapy

- Oral Antibiotic Therapy Indications for oral antibiotic therapy in a patient with CF include the presence of respiratory tract symptoms, physical signs, or changes in pulmonary function testing or chest x-ray.
- Common organisms, including S. aureus (MRSA or MSSA), nontypeable H. influenzae, P. aeruginosa; B. cepacia and other Gram-negative rods, are encountered with increasing frequency.
- The usual course of therapy is 2 wk, and maximal doses are recommended.

- The quinolones are the only broadly effective oral antibiotics for Pseudomonas infection, but resistance against these agents may emerge.
- Macrolides may reduce the virulence properties of P. aeruginosa, such as biofilm production, and contribute antiinflammatory effects.
- Long-term therapy with azithromycin 3 times a week improves lung function in patients with chronic P. aeruginosa infection.

Aerosolized Antibiotic Therapy

- Aerosolized antibiotics are often used as part of daily therapy when the airways are infected with P. aeruginosa.
- Aerosolized tobramycin inhalation solution or powder, or aztreonam inhalation solution used as a suppressive therapy (on 1 mo, off 1 mo), may reduce symptoms, improve pulmonary function, and decrease the occurrence of pulmonary exacerbations.

- Other antibiotics have been used via inhalation, including liposomal amikacin and levofloxacin for P. aeruginosa, and there was no inferiority of efficacy compared with inhaled tobramycin.

Intravenous Antibiotic Therapy

- For the patient who has not responded to oral antibiotics and intensive home measures with return of signs, symptoms, and FEV1 to baseline, intravenous antibiotic therapy is indicated.
- The ideal duration of treatment is unknown; although many patients show improvement within 7 days, many CF physicians believe that it is usually advisable to extend the period of treatment to at least 14 days.

- In general, treatment of Pseudomonas infection is thought to require 2-drug therapy.
- A 3rd agent may be given for optimal coverage of S. aureus or other organisms.
- Aminoglycosides are usually effective when given every 24 hr to minimize toxicity and optimize convenience.

- If patients do not show improvement, complications such as right heart failure, asthma, or infection with viruses, A. fumigatus (especially ABPA) , nontuberculous mycobacteria , or other unusual organisms should be considered.
- B. cepacia complex and acinetobacter are Gram-negative rods that may be particularly refractory to antimicrobial therapy.

Bronchodilator Therapy

- Reversible airway obstruction occurs in many children with CF, sometimes in conjunction with frank asthma or allergic bronchopulmonary aspergillosis.
- Reversible obstruction is conventionally defined as improvement of ≥12% in FEV1 or FVC after inhalation of a bronchodilator.
- In many patients with CF, these may improve by only 5–10% (physiologic response), but subjects may report subjective benefit.

Table 432.6 Antimicrobial Agents for Cystic Fibrosis Lung Infection

ROUTE	ORGANISMS	AGENTS	DOSAGE (mg/kg/24 hr)	NO. DOSES/24 hr
Oral	*Staphylococcus aureus*	Dicloxacillin	25-50	4
		Linezolid	20	2
		Cephalexin	50	4
		Clindamycin	10-30	3-4
		Amoxicillin-clavulanate	25-45	2-3
	Haemophilus influenzae	Amoxicillin	50-100	2-3
	Pseudomonas aeruginosa	Ciprofloxacin	20-30	2-3
	Burkholderia cepacia	Trimethoprim-sulfamethoxazole	8-10*	2-4
	Empirical	Azithromycin	10, day 1; 5, days 2-5	1
		Erythromycin	30-50	3-4
Intravenous	*S. aureus*	Nafcillin	100-200	4-6
		Vancomycin	40	3-4
	P. aeruginosa	Tobramycin	8-12	1-3
		Amikacin	15-30	2-3
		Ticarcillin	400	4
		Piperacillin	300-400	4
		Ticarcillin-clavulanate	400†	4
		Piperacillin-tazobactam	240-400†	3
		Meropenem	60-120	3
		Imipenem-cilastatin	45-100	3-4
		Ceftazidime	150	3
		Aztreonam	150-200	4
	B. cepacia	Chloramphenicol	50-100	4
		Meropenem	60-120	3
Aerosol		Tobramycin (inhaled)	300§	2
		Aztreonam (inhaled)	75	3

Antiinflammatory Agents

- Corticosteroids are useful for the treatment of allergic bronchopulmonary aspergillosis and severe asthma occasionally encountered in children with CF.
- Prolonged systemic corticosteroid treatment of CF lung disease reduces the decline in lung function modestly but causes predictably prohibitive side effects.
- Inhaled corticosteroids have theoretical appeal, but there are contradictory and weak data regarding efficacy unless the patient has clinically diagnosable asthma.

- Ibuprofen, given chronically in high doses adjusted to achieve a peak serum concentration of 50-100 μg/mL, is associated with a slowing of disease progression, particularly in younger patients with mild lung disease.
- Macrolide antibiotics have an antiinflammatory effect, and 3 days/wk azithromycin has been shown to reduce the likelihood of development of pulmonary exacerbations, especially in patients with chronic Pseudomonas airway infection, so this is a commonly used therapy.

Cystic Fibrosis Transmembrane Conductance Regulator Modulator Therapies

- A major breakthrough in CF therapy is ivacaftor, a small molecule potentiator of the CFTR mutation, G551D (present in ~5% of patients).
- Ivacaftor therapy resulted in improvement in FEV1 by an average of 10.6%, decreased the frequency of pulmonary exacerbations by 55%, decreased sweat chloride by an average of 48 mEq/L, and increased weight gain by an average of 2.7 kg.
- Ivacaftor is approved for patients older than 2 yr of age with class III and class IV mutations.

- The combination of ivacaftor with lumacaftor, a corrector that stabilizes misfolded F508del and enables trafficking of the mutant molecule to the apical cell membrane where it is potentiated by ivacaftor, is available for patients older than 6 yr of age who are homozygous for the F508del mutation.
- Tezacaftor and ivacaftor is another combination indicated for patients ≥ 12 yr with 1 or 2 Phe508del alleles.
- This combination improves predicted FEV1 and overall well-being .

Table 432.7 Cystic Fibrosis Transmembrane Regulator Modulators for Cystic Fibrosis

DRUG	FDA-APPROVED INDICATION	FORMULATIONS	USUAL DOSAGE
Ivacaftor	≥ 12 mo with a responsive mutation[1]	150 mg tabs; 50, 75 mg granule packets[2]	≥ 6 years: 150 mg q12 hr[3]
Lumacaftor/ivacaftor	≥ 2 yr, F508del-homozygous	100/125, 200/125 mg tabs; 100/125, 150/188 mg granule packets[2]	6-11 yr: 200/250 mg q12 hr ≥ 12 yr: 400/250 mg q12 hr[4]
Tezacaftor/ivacaftor	≥ 12 yr, F508del-homozygous or F508del-heterozygous with another responsive mutation[1]	100/150 mg tabs co-packaged with ivacaftor 150 mg tabs	≥ 12 yr: 100/150 mg tab qAM, then 150 mg ivacaftor qPM

Other Therapies

- Expectorants such as iodides and guaifenesin do not effectively assist with the removal of secretions from the respiratory tract.

- Inspiratory muscle training can enhance maximum oxygen consumption during exercise, as well as FEV1.

TREATMENT OF PULMONARY COMPLICATIONS

Atelectasis

- Lobar atelectasis occurs relatively infrequently; it may be asymptomatic and noted only at the time of a routine chest radiograph.
- Aggressive intravenous therapy with antibiotics and increased chest PT directed at the affected lobe may be effective.
- If there is no improvement in 5-7 days, bronchoscopic examination of the airways may be indicated.
- If the atelectasis does not resolve, continued intensive home therapy is indicated because atelectasis may resolve during a period of wk or mo.

Hemoptysis

- Endobronchial bleeding usually reflects airway wall erosion into hypertrophied bronchial vessels secondary to infection.
- Although more common in patients with advanced disease, it is sometimes seen in adolescents with relatively mild lung disease.
- Blood streaking of sputum is particularly common.
- Small-volume hemoptysis (<20 mL) is usually viewed as a need for intensified antimicrobial therapy and chest PT.

- Massive hemoptysis, defined as total blood loss of ≥250 mL in a 24-hr period, is rare in the 1st decade and occurs in <1% of adolescents, but it requires close monitoring and the capability to replace blood losses rapidly.
- Bronchoscopy rarely reveals the site of bleeding.
- Bronchial artery embolization can be useful to control persistent, significant hemoptysis.

Pneumothorax

- Pneumothorax is encountered uncommonly in children and teenagers with CF, although it may lead to significant compromise in lung function and occasionally may be life threatening.
- The episode may be asymptomatic but is often attended by chest and shoulder pain, shortness of breath, or hemoptysis.
- A small air collection that does not grow can be observed closely.
- Chest tube placement with or without pleurodesis is often the initial therapy.
- Intravenous antibiotics are also begun on admission.

- Video-assisted thoracoscopic surgery (VATS) with plication of blebs, apical pleural stripping, and basal pleural abrasion should be considered if the air leak persists.
- Surgical intervention is usually well tolerated even in cases of advanced lung disease.
- The thoracotomy tube is removed as soon as possible.
- Previous pneumothorax with or without pleurodesis is not a contraindication to subsequent lung transplantation

Allergic Bronchopulmonary Aspergillosis

- Allergic bronchopulmonary aspergillosis occurs in 5–10% of patients with CF and may manifest as wheezing, increased cough, shortness of breath, and marked hyperinflation, or most commonly, a decrease in FEV1 that does not respond to antibiotic therapy.
- In some patients, a chest radiograph shows new, focal infiltrates.
- A very elevated total serum immunoglobulin E (IgE) level (>1,000) is usually the initial indication of the diagnosis.
- The presence of rust-colored sputum, the recovery of Aspergillus organisms from the sputum, a positive skin test for A. fumigatus, the demonstration of specific IgE and IgG antibodies against A. fumigatus, or the presence of eosinophils in a fresh sputum sample supports the diagnosis.

- Treatment is directed at controlling the inflammatory reaction with oral corticosteroids.
- Oral antifungals are usually reserved for patients who relapse after initial steroid treatment.
- For refractory cases, omalizumab, humanized monoclonal anti-IgE, has been effective.

Nontuberculous Mycobacteria Infection

- Injured airways with poor clearance may be colonized by Mycobacterium avium-complex but also Mycobacterium abscessus, Mycobacterium chelonae, and Mycobacterium kansasii.
- Persistent fevers and new infiltrates or cystic lesions coupled with the finding of acid-fast organisms on sputum smear suggest infection.
- Treatment is prolonged and requires multiple antimicrobial agents.
- Symptoms may improve, but the nontuberculous mycobacteria are not usually cleared from the lungs.

Bone and Joint Complications

- Hypertrophic osteoarthropathy causes elevation of the periosteum over the distal portions of long bones and bone pain, overlying edema, and joint effusions.
- Acetaminophen or ibuprofen may provide relief.
- Control of lung infection usually reduces symptoms.
- Intermittent arthropathy unrelated to other rheumatologic disorders occurs occasionally, has no recognized pathogenesis, and usually responds to nonsteroidal antiinflammatory agents.

- Back pain or rib fractures from vigorous coughing may require pain management to permit adequate airway clearance.
- These and other fractures may stem from diminished bone mineralization, the result of reduced vitamin D absorption, corticosteroid therapy, diminished weight-bearing exercises, and perhaps other factors.

Sleep-Disordered Breathing

- Particularly with advanced pulmonary disease and during chest exacerbations, individuals with CF may experience more sleep arousals, less time in rapid eye movement sleep, nocturnal hypoxemia, hypercapnia, and associated neurobehavioral impairment.
- Nocturnal hypoxemia may hasten the onset of pulmonary hypertension and right-sided heart failure.
- Prompt treatment of airway symptoms and nocturnal oxygen supplementation or bilevel positive airway pressure support should be considered in selected cases, especially in patients with advanced lung disease.

Acute Respiratory Failure

- Acute respiratory failure rarely occurs in patients with mild to moderate lung disease and is usually the result of a severe viral or other infectious illness.
- In addition to aerosol, postural drainage, and intravenous antibiotic treatment, oxygen is required to raise the arterial PaO2.
- An increasing PCO2 may require ventilatory assistance.
- Endotracheal or bronchoscopic suction may be necessary to clear airway inspissated secretions and can be repeated daily.

- Right-sided heart failure should be treated vigorously.
- High-dose steroids have been anecdotally reported to be of benefit in this setting.
- Recovery is often slow.
- Intensive intravenous antibiotic therapy and postural drainage should be continued for 1-2 wk after the patient has regained baseline status.

Chronic Respiratory Failure

- Patients with CF acquire chronic respiratory failure after prolonged deterioration of lung function.
- Although this complication can occur at any age, it is seen most frequently in adult patients.
- Because a long standing PaO2 <50 mm Hg promotes the development of right-sided heart failure, patients usually benefit from low-flow oxygen to raise arterial PO2 to ≥55 mm Hg.
- Increasing hypercapnia may prevent the use of optimal fraction of inspired oxygen.
- Most patients improve somewhat with intensive antibiotic and pulmonary therapy measures and can be discharged from the hospital.
- Low-flow oxygen therapy is needed at home, especially with sleep.

- Noninvasive ventilatory support can improve gas exchange and has been documented to enhance quality of life.
- Ventilatory support may be particularly useful for patients awaiting lung transplantation.
- These patients usually display pulmonary hypertension and cor pulmonale, and this complication should be treated.
- Caution should be exercised to avoid ventilation-suppressing metabolic alkalosis that results from CF-related chloride depletion and, in many cases, from diuretic-induced bicarbonate retention.
- Chronic pain (headache, chest pain, abdominal pain, and limb pain) is frequent at the end of life and responds to judicious use of analgesics, including opioids.
- Dyspnea has been ameliorated with nebulized fentanyl

Lung transplantation

- Lung transplantation is an option for end-stage lung disease that is increasingly offered .
- Survival and quality of life after lung transplantation is better in patients with CF than other chronic lung diseases, probably due to the relatively younger age of recipients with CF, but the current estimated 5-yr survival is about 50%, somewhat reduced compared with that of other solid organ transplants.
- Because of bronchiolitis obliterans and other complications, transplanted lungs cannot be expected to function for the lifetime of a recipient, and repeat transplantation is increasingly common.

Pulmonary Hypertension and Cor Pulmonale

- Pulmonary Hypertension and Cor Pulmonale Individuals with long-standing, advanced pulmonary disease, especially those with severe hypoxemia (PaO2 < 50 mm Hg), often acquire pulmonary hypertension and chronic right-sided heart failure.
- Evidence for concomitant left ventricular dysfunction is often found.
- The arterial PO2 should be maintained at >50 mm Hg, if possible, and hypercarbia corrected with noninvasive ventilation or intubation if necessary.

- Intensive pulmonary therapy, including intravenous antibiotics, is most important.
- Adjunctive therapy with salt restriction, diuretics, and pulmonary vasodilators may be indicated.
- The prognosis for heart failure is poor, but a number of patients survive for ≥5 yr after the appearance of heart failure.
- Heart-lung transplantation may be an option.

Nutritional Therapy

- Nutritional Therapy Up to 90% of patients with CF have loss of exocrine pancreatic function leading to inadequate digestion and absorption of fats and proteins.
- They require dietary adjustment and augmentation, pancreatic enzyme replacement, and supplementary vitamins.
- In general, children with CF need to exceed the usual required daily caloric intake to grow.
- Daily supplements of the fat-soluble vitamins are required.

- Most children with CF have a higher-than-normal caloric need because of malabsorption despite the use of pancreatic enzyme supplementation.
- Encouragement to eat high-calorie foods is important and often begins with more concentrated, high-calorie formulas in the 1st yr.
- Even so, most mothers can breastfeed successfully.

- It is vitally important to promote adequate weight gain in the early years, both because of a clear relationship to later lung function and also because early deficiencies make later catch up growth more difficult.
- The liberal use of appetite stimulants, especially cyproheptadine, in early childhood, makes the struggle a bit easier.
- Poorly controlled lung disease increases metabolism and decreases appetite and needs to be considered when efforts to improve weight gain are unsuccessful

- Maintenance of good weight gain and body mass index in the 1st yr of life leads to better long-term preservation of lung function, but there is a strong correlation between body mass index and FEV1 that persists through all ages in people with CF.
- Better nutrition also leads to improved quality of life and psychologic well-being and provides better reserves when weight loss occurs in association with intermittent acute pulmonary exacerbations.
- Malabsorption is an important contributor to nutritional deficiencies, and it is important to ensure that pancreatic enzyme dosing is adequate and consistently being taken correctly with all meals and feedings.

- Appetite stimulants when cyproheptadine is not successful may include megestrol, oxandrolone, dronabinol, antidepressants such as mirtazaoine, and even growth hormone.
- CF-related diabetes needs to be ruled out.
- When all these therapies fail, weight stabilization or gain can be achieved with nocturnal feeding via nasogastric tube or gastrostomy tube.

Pancreatic Enzyme Replacement

- Pancreatic exocrine replacement therapy given with ingested food reduces but does not fully correct stool fat and nitrogen losses.
- Current products are enteric-coated, pH-sensitive enzyme microspheres that come in capsules and given to children before they can swallow by opening the capsule and mixing the beads in small amounts of acidic foods such as applesauce.

- Administration of excessive doses has been linked to fibrosing colonopathy and colonic strictures, so recommendations are for enzyme dosing to stay below 2,500 lipase units/kg/meal in most circumstances.
- Snacks should also be covered.
- Some individuals require proton pump inhibitor therapy to correct acid pH in the duodenum which is due to lack of exocrine pancreatic secretions; neutralization of duodenal pH permits activation of enteric-coated pancreatic exocrine replacement therapy granules.

Vitamin and Mineral Supplements

- Because pancreatic insufficiency results in malabsorption of fat-soluble vitamins (A, D, E, K), vitamin supplementation is recommended.
- Despite this supplementation, vitamin D deficiency is common and should be treated with doses of cholecalciferol (vitamin D3) rather than ergocalciferol (vitamin D2) in the range of 1,000 units/kg/wk.
- Salt supplementation is also needed during infancy and is started at the time of diagnosis.

TREATMENT OF INTESTINAL COMPLICATIONS

- Meconium Ileus When meconium ileus is suspected, diatrizoate (Gastrografin) enemas with reflux of contrast material into the ileum not only confirm the diagnosis but may also result in the passage of meconium and clearing of the obstruction.
- Children in whom this procedure fails require operative intervention.
- Children who have had meconium ileus are at greater risk for nutritional deficiency and more likely to develop problems with DIOS when older.
- Infants with meconium ileus should be assumed to have CF unless proven otherwise.

Distal Intestinal Obstruction Syndrome

- Distal Intestinal Obstruction Syndrome and Other Causes of Abdominal Symptoms Despite appropriate pancreatic enzyme replacement, a number of patients accumulate fecal material in the terminal portion of the ileum and in the cecum, which may result in partial or complete obstruction.
- For intermittent symptoms, pancreatic enzyme replacement should be continued or even increased, and stool hydrators such as polyethylene glycol (MiraLAX) should be given.
- If this fails or symptoms are more severe, large-volume bowel lavage with a balanced salt solution containing polyethylene glycol may be taken by mouth or by nasogastric tube.
- When there is complete obstruction, a diatrizoate enema, accompanied by large amounts of intravenous fluids, can be therapeutic.

Rectal Prolapse

- Although uncommon, rectal prolapse occurs most often in infants with CF and less frequently in older children with the disease.
- It was much more frequently seen in the past among undiagnosed young children with steatorrhea, malnutrition, and repetitive cough.
- The prolapsed rectum can usually be replaced manually by continuous gentle pressure with the patient in the knee-chest position.

- Sedation may be helpful.
- Adequate pancreatic enzymes, stool softener, and control of pulmonary infection result in improvement.
- Occasionally, a patient may continue to have rectal prolapse and may require sclerotherapy or surgery.

Hepatobiliary Disease

- Liver function abnormalities associated with biliary cirrhosis can be improved by treatment with ursodeoxycholic acid.
- The ability of bile acids to prevent progression of cirrhosis has not been clearly documented.
- Portal hypertension with esophageal varices, hypersplenism, or ascites occurs in ≤8% of children with CF .
- Obstructive jaundice in newborns with CF needs no specific therapy once the etiology has been established.
- End-stage liver disease is an indication for liver transplantation in children with CF .

Pancreatitis

- Recurrent pancreatitis is seen primarily in patients with pancreatic sufficiency, and it can lead to the development of pancreatic insufficiency.
- Patients can be treated with pancreatic enzyme therapy and a low-fat diet (in well-nourished patients) to rest the pancreas.

Cystic Fibrosis-Related Hyperglycemia and Diabetes

- Onset of hyperglycemia occurs most frequently after the 1st decade.
- Approximately 20% of young adults are treated for hyperglycemia, although the incidence of CF-related diabetes may be up to 50% in CF adults.
- Ketoacidosis is rarely encountered.
- The pathogenesis includes both impaired insulin secretion and insulin resistance.
- Routine screening consisting of an annual 2-hr oral glucose tolerance test is recommended in children older than 10 yr of age, although some cases may begin earlier.

- Glucose intolerance with blood sugars that remain less than 200 is usually not treated unless nutrition is compromised or lung function seems affected.
- When treatment is indicated, insulin treatment should be instituted.
- The development of significant hyperglycemia favors acquisition of P. aeruginosa and B. cepacia in the airways and may adversely affect pulmonary function, especially in women.
- Thus careful control of blood glucose level is an important goal.
- Long-term vascular complications of diabetes can occur, providing an additional rationale for good control of blood glucose levels.

OTHER COMPLICATIONS

Nasal Polyps

- Nasal polyps occur in 15–20% of patients with CF and are most prevalent in the 2nd decade of life.
- Local corticosteroidsand nasal decongestants occasionally provide some relief.
- When the polyps completely obstruct the nasal airway, rhinorrhea becomes constant or widening of the nasal bridge is noticed, surgical removal of the polyps is indicated; polyps may recur promptly or after a symptom-free interval of months to years.

Rhinosinusitis

- Opacification of paranasal sinuses is universal in CF and is not an indication for intervention.
- Acute or chronic sinus-related symptoms are treated initially with antimicrobials, with or without maxillary sinus aspiration for culture.
- Functional endoscopic sinus surgery has anecdotally provided benefit.

Salt Depletion

- Salt losses from sweat in patients with CF can be high, especially in warm arid climates.
- Children should have free access to salt, especially when thirsty in hot weather.
- Salt supplements are often prescribed to newborns and to children who live in hot weather climates.
- Hypochloremic alkalosis should be suspected in any patient who feels unwell in hot weather or who has had symptoms of gastroenteritis, and prompt fluid and electrolyte therapy should be instituted as needed.

Surgery

- Patients with good or excellent pulmonary status can tolerate general anesthesia without any intensive pulmonary measures before the procedure but should be adherent to their usual prescribed airway clearance therapy.
- Those with moderate or severe pulmonary infection usually do better with a 1- to 2-wk course of intensive antibiotic treatment and increased airway clearance before surgery.
- If this approach is impossible, prompt intravenous antibiotic therapy is indicated once it is recognized that major surgery is required.
- General anesthesia may provide an opportunity to perform bronchoscopy to evaluate the airway and obtain good cultures, and this should be considered in any child with CF who will undergo surgery for any indication.

PROGNOSIS

- CF remains a life-limiting disorder, although survival has dramatically improved .
- Outcomes are variable and related to CFTR mutation class, modifier genes, biologic and chemical exposures, disease management, and socioeconomic status.
- Children with CF should not be restricted in their activities.
- Most adults with CF find satisfactory employment, and an increasing number marry.

- With increasing life span for patients with CF, a new set of psychosocial considerations has emerged, including dependence-independence issues, self-care, peer relationships, sexuality, reproduction, substance abuse, educational and vocational planning, medical care costs and other financial burdens, and anxiety concerning health and prognosis.
- Anxiety and depression are prevalent, as in any other chronic disease, and impact quality of life and disease self-management; screening for both is now part of comprehensive care.
- With appropriate medical and psychosocial support, children and adolescents with CF generally cope well.