Lesson S15: PreAnesthetic Assessment of the Patient with Cystic Fibrosis – Part 2

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A COURSE OF STUDY FOR AMA/PRA CATEGORY 1 CREDIT
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TARGET AUDIENCE: Anesthesiologists

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Needs statement
Approximately 30,000 Americans are affected by cystic fibrosis (CF). Although it is mainly a disease of the young, improvements in diagnosis and treatment have increased prevalence in older adults. Research is focused on gene manipulation and gene therapy but breakthroughs are slow in coming. Knowledge of the pathophysiology of the disease and methods of early diagnosis enables physicians to anticipate problems and offer system-specific treatments.

This is a two part activity. Part 1 was presented in Supplementary Lesson 14 and covered the historical significance, genetic application, and clinical manifestations of cystic fibrosis. Part 2 is presented here and will discuss diagnostic criteria, appropriate testing and perioperative management.

Learning Objectives
At the end of this activity, the participant should be able to:

1. Describe commonly performed diagnostic tests.
2. Discuss surgical treatment for CF.
3. Understand the need for early diagnosis of CF.
4. Detail prognostic indicators for CF.
5. Identify radiological findings that are suggestive of CF.
6. Outline treatment plans for patients with specific organ involvement.
7. Order appropriate lab tests to for a surgical patient with CF.
8. Describe the sweat test and understand its significance.
10. Manage anesthesia for a pregnant patient with CF.

**Case History**

A 15 year old girl presented to the emergency room with severe abdominal pain of 36 hours duration. Her medical history reveals a diagnosis of cystic fibrosis made shortly after birth, and frequent respiratory infections treated with multiple courses of antibiotics. She was also diabetic. A CT scan of her abdomen revealed a probable intussusception and she was scheduled for laparotomy.

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**Diagnosis and Assessment of Cystic Fibrosis (CF)**

Several tests and evaluations can be used to diagnose and assess the presence and severity of CF disease including newborn screening, sweat testing, or genetic testing. As of 2006, in the United States, 10 percent of cases were diagnosed shortly after birth as part of newborn screening programs. The newborn screen initially measures for raised blood concentration of immunoreactive trypsinogen. Infants with an abnormal newborn screen require a sweat test to confirm a diagnosis of CF. In many cases, a parent will report that the infant’s skin has a salty taste. Trypsinogen levels can be increased in individuals who have a single mutated copy of the CFTR gene (carriers) or, in rare instances, in individuals with two normal copies of the CFTR gene. Due to these false positives, CF screening in newborns can be controversial. Most states and countries do not screen for CF routinely at birth. Therefore, most individuals are diagnosed after symptoms (e.g. sinopulmonary disease and GI manifestations) prompt an evaluation for cystic fibrosis.

The most commonly used form of testing is the sweat test. Sweat testing involves application of a sweat-inducing medication (pilocarpine) delivered through the skin via iontophoresis. One electrode is placed on top of the applied medication and an electric current is passed to a separate electrode on the skin. The resultant sweat is then collected on filter paper or in a capillary tube (at least 100mg is required) and analyzed for abnormal amounts of sodium and chloride. People with CF have increased amounts of sodium and chloride in their sweat. The test is inherently cumbersome and often performed twice. A consistently high level of salt is an indication of CF. Normal sweat chloride levels are below 30mEq/L. Chloride sweat concentrations exceeding 60mEq/L in children and 70mEq/L in adults are considered diagnostic for cystic fibrosis. Approximately 1%–2% of patients with clinical features compatible with cystic fibrosis have normal or borderline (40–60mEq/L) chloride results. Other conditions associated with increased sweat chloride levels include untreated adrenal insufficiency, ectodermal dysplasia, hereditary nephrogenic diabetes insipidus, glucose phosphatase deficiency, hypothyroidism, hypoparathyroidism, familial cholestasis, pancreatitis, mucopolysaccharidosis, fucosidosis, and malnutrition. The sweat test is not useful in diagnosing cystic fibrosis heterozygotes. It does not indicate the severity or prognosis of the disease and may not be useful in newborns who produce little or no sweat.

Genetic analysis of a blood sample may confirm a diagnosis of CF. About 90 percent of cases of CF can be detected through genetic analysis. Researchers have identified more than 800 changes in a gene
that when paired with another abnormal gene can result in CF. Testing is possible on approximately 30 of the most common genetic mutations. Because CF is an inherited disease, the asymptomatic siblings a child with CF may be undergo testing. First cousins can also be advised to undergo testing.

People with CF have lesser amounts of thiocyanate and hypotliocyanite in their saliva. Saliva testing is used to identify carriers of defective CFTR genes.

A multitude of tests are used to identify complications of CF and to monitor disease progression. Tests that measure lung, pancreatic and liver function aid in determining the extent and severity of CF. X-rays and CAT scans are useful for examining the lungs for signs of damage or infection. Sputum cultures are useful for identifying and treating bacteria that are colonizing or causing symptomatic infection in the lower respiratory tract so that effective antimicrobial therapy can be provided. Testing for organisms such as *Burkholderia cepacia* is required for candidates of lung transplantation as persistent bacterial colonization reduces the chance of survival.

**Radiological Studies**

Radiological findings may indicate the presence of CF but are not diagnostic for CF. Hyperinflation of the lungs is noted early in the course of the disease. Subsequent changes include bronchial thickening and plugging in the upper lobes, bronchiectasis, infiltrates, atelectasis, and hilar adenopathy. With advanced disease, segmental or lobar atelectasis, bleb formation, extensive bronchiectasis, impressive hyperinflation, and enlarged pulmonary arteries are seen.

Radiological pictures of meconium ileus include unevenly distended loops of bowel with absent or scarce air-fluid levels and collections of granular material in the lower central abdomen. Barium enema examination shows a micro colon and may demonstrate obstructing masses in the distal ileum. Again, these findings are not specific for cystic fibrosis.

**Pulmonary Function Tests**

Pulmonary function studies can be performed reliably in patients over age 6 years to document the extent of pulmonary involvement and evaluate the effects of therapy. In the initial stages of pulmonary disease, an obstructive pattern is evident. Small-airway obstruction and increased gas trapping decrease maximal mid-expiratory flow rate, increase residual volume/total lung capacity (RV/TLC) ratio, and decrease forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) ratio. The response to bronchodilators remains unpredictable and varies with the underlying pulmonary status. Airway reactivity is increased in 50% of patients with cystic fibrosis as demonstrated by bronchoprovocative challenges. With progression of the lung injury and fibrosis, the restrictive component becomes more prominent, as demonstrated by decreased total lung capacity and vital capacity.

Increased ventilation-perfusion mismatching results in increased alveolar-arterial oxygen gradient, gradual hypoxemia, and pulmonary hypertension. Significant elevation of PaCO₂ heralds end-stage disease and carries a poor prognosis.
Microbiology

The isolation of *Staphylococcus aureus* and/or *Pseudomonas aeruginosa* from a sputum culture strongly supports the diagnosis of cystic fibrosis. Mucoid strains that are culture-positive for *P. aeruginosa* are strongly suggestive of CF.\(^{37}\)

CF Therapy

Treatment of cystic fibrosis is guided by a comprehensive program administered through a nationwide network of specialized centers supported by the Cystic Fibrosis Foundation. Therapeutic goals that were formulated 40 years ago remain valid today: prevention and control of pulmonary infections, promotion of mucus drainage, and provision of adequate nutrition. The fundamental objectives of a therapeutic plan are to maintain prolonged periods of stability and to intervene early with aggressive treatment of clinical exacerbations. (See Table 2.) For most patients, therapies target the lungs, GI tract, and reproductive organs and may include assistive reproductive technology and psychological support.

Regular assessments at intervals of 1 to 3 months by the multidisciplinary team—primary physician, nurse, respiratory therapist, physical therapist, dietitian, psychologist, and social worker—allow evaluation and adjustment of the home treatment program and also provide the opportunity for nutritional, genetic, financial, educational, vocational, and premarital counseling, as well as encouragement and psychosocial support for patients and families.\(^{37,39}\) Hospital admissions are indicated for the treatment of severe deterioration of the clinical condition and management of life-threatening complications.

Pulmonary Therapy

Pulmonary disease is typically treated with antibiotic therapy, respiratory therapy and, in selected individuals, bronchodilator therapy.\(^{35}\) The goals of antibiotic therapy are to reduce the numbers of bacteria, to reduce the intensity of endobronchial infection, and to delay progressive lung damage.\(^{17,43}\) Evidence suggests that early and aggressive antibiotic intervention may deter the onset of chronic colonization.\(^{44}\)

Antibiotic regimens are usually based on sputum culture results with consideration of the most commonly encountered organisms (e.g., *P. aeruginosa*, *S. aureus*, and *Haemophilus influenzae*). Antibiotics are administered orally, intravenously, and/or by aerosol (tobramycin and aztreonam are both available in aerosol formulations that can be applied directly to the airways). A standard treatment course lasts 14 days or more, and maximal doses are used because of increased total-body clearance and volume of distribution.\(^{37}\) Traditionally, intravenous antibiotic therapy required hospitalization, but home therapy with intravenous antibiotics is possible and effective in patients with secured, permanent intravenous access.\(^{45}\) A typical intravenous antibiotic regimen used against *P.
*P. aeruginosa* consists of two agents, such as the combination of an aminoglycoside with a third-generation cephalosporin and/or anti-Pseudomonas penicillin, and/or monocyclic β-lactam.\(^{37-39}\) Macrolide antibiotics may also be effective in the treatment of *P. aeruginosa*.\(^ {46}\)

The quinolones remain the only effective oral agents against *P. aeruginosa* pulmonary infection, but clinical usefulness is limited by rapid emergence of resistant organisms.\(^ {47}\) Aerosolized antibiotics are an important adjunct in the long-term therapy of chronic, resistant *P. aeruginosa* infections.\(^ {35}\) *S. aureus* and *H. influenzae* colonizations and infections are usually controlled with oral antibiotics, but intravenous semi-synthetic penicillin may be used to treat severe *S. aureus* infections. As most CF patients are on one or more antibiotics at all times, resistance develops quickly. The most frequently used antibiotics are listed in Table 3.

### Table 3. Commonly used antibiotics

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<tr>
<th>ROUTE</th>
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<td>H. influenzae</td>
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<td>P. aeruginosa</td>
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<td>Intravenous</td>
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<td>P. aeruginosa</td>
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<td>P. cepacia</td>
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<td>Aerosol</td>
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Chest physiotherapy remains an important part of the comprehensive treatment program. Daily regimens of postural drainage, manual or mechanical percussion, vibration, and assisted coughing are designed to promote increased clearance of bronchial mucus secretions.\textsuperscript{47,48} Physical activity programs of forced expiratory exercises and positive expiratory pressure breathing are often used as an adjunct to physiotherapy.\textsuperscript{47,48}

Inhalation therapy, in conjunction with chest physiotherapy, is frequently used in cystic fibrosis patients with reactive airways.\textsuperscript{37} Bronchodilator treatment is followed by chest physiotherapy, and then an aerosolized antibiotic is administered.\textsuperscript{37} Alternatively, a \( \beta \)-agonist and/or cromolyn sodium can be nebulized with antibiotics.\textsuperscript{37} Bronchodilator treatment is cautiously initiated because some patients may respond with a paradoxical decrease in expiratory flow rates and decreased PaO\(_2\) secondary to increased airway collapse during expiration.\textsuperscript{49}

Some case reports have noted success in using non-invasive positive pressure ventilatory (NIPPV) machines as an alternative to intubation for patients with borderline respiratory failure with the only complication being skin breakdown over the nose.\textsuperscript{50} A transition to long term nighttime NIPPV with a BiPAP machine is also possible.\textsuperscript{50}

Inhalation of N-acetyl-cysteine, a known mucolytic agent, has not been shown to be clinically effective in improving mucus clearance and/or lung function.\textsuperscript{38} It is toxic to ciliated epithelium, and its administration is associated with a significant incidence of bronchospasm.\textsuperscript{48} At present the inhalation route is utilized for investigation of newer forms of treatment aimed at modification of sputum composition, reduction of mucus viscosity, anti-inflammatory effect, and reversal of the underlying genetic defect through application of gene therapy.

Cystic fibrosis respiratory secretions are extremely viscous and dehydrated because of abnormally increased sodium absorption from the airway lumen into the epithelial cells and possibly because of lack of chloride secretion from the epithelial cells into the airway lumen. Conceivably, the inhibition of airway epithelium sodium absorption and/or stimulation of airway epithelium chloride secretion would result in improvement of composition and clearance of sputum. In a pilot study, amiloride, a sodium channel blocker diuretic, has been shown to improve sputum viscosity and elasticity in aerosolized form and to reduce the rate of loss of FVC (forced vital capacity).\textsuperscript{51} Although the effects of amiloride on sputum properties have been replicated by several researchers, the beneficial effects on lung function have not been confirmed.\textsuperscript{52,53} Nebulized adenosine triphosphate and uridine triphosphate (ATP and UTP) stimulate CF epithelial cells to secrete chloride onto the airway lumen.\textsuperscript{54} These extracellular nucleotides have the potential to become a useful therapeutic modality capable of improving the physical properties of the cystic fibrosis airway secretions.

Apart from abnormal electrolyte content, viscosity of infected sputum is increased by its high concentration of deoxyribonucleic acid (DNA) derived mainly from the nuclei of polymorphonuclear neutrophils.\textsuperscript{55,56} In the late 1960s, aerosolized bovine pancreatic DNA was shown to reduce the viscosity of lung secretions was abandoned due to severe allergic reactions.\textsuperscript{57,58} Pulmozyme \(^\text{\textregistered}\) (dornase alfa), is a clear, highly purified solution of recombinant deoxyribonuclease 1 (rhDNase), an enzyme that selectively cleaves DNA. The protein is produced from genetically engineered Chinese hamster ovary cells containing DNA encoding for the native human protein, deoxyribonuclease 1. It is administered by inhalation of an aerosol mist produced by a compressed air-driven nebulizer system. The medication has been found to significantly reduce the number of respiratory infections by fragmenting DNA, thus making mucus thinner and easier to expectorate. Also slight-to-significant
improvement in pulmonary function and quality of life, as well as reduction of exacerbations of respiratory symptoms, hospital days, and use of parenteral antibiotics for lung infections was shown.\textsuperscript{59-64} Transient voice alteration was the only significant side effect noted, and anaphylactic reactions were not associated with rhDNase administration.\textsuperscript{64} Despite the high cost, the aerosolized form of rhDNase appears to be a promising addition to classic cystic fibrosis therapy.

Pulmonary inflammation, in response to chronic bacteria colonization, is a well-recognized contributing factor to lung damage in cystic fibrosis. Steroids were shown to reduce morbidity and to improve pulmonary function in one investigation,\textsuperscript{65} but a subsequent, larger study failed to replicate and validate these results.\textsuperscript{66} At present the role of steroids in the treatment of cystic fibrosis is not defined although the mode of therapy is used in Europe.\textsuperscript{67}

Other approaches to anti-inflammatory therapy include the use of nonsteroidal anti-inflammatory drugs as well as the application of aerosolized antiproteases, such as alpha 1-antitrypsin and secretory leukoprotease inhibitors.\textsuperscript{68-70} These antiproteases inhibit the inflammatory process by neutralizing the natural proteolytic enzymes released by activated neutrophils and by reducing the activity of chemotactic factors that attract neutrophils.\textsuperscript{69,70} Early results are encouraging.

Promoting bronchial airway drainage is essential for sufferers of CF. Chest physiotherapy requires manual clapping on both sides of the chest. In some cases an electric clapper or mechanical percussor is used. Inflatable vests with an attached machine that vibrates at high frequency can also help coughing. Bronchial airway drainage is recommended at least twice per day for 20-30 minutes.

Gene therapy for CF lung disease is a focus of investigation.\textsuperscript{71,72} The objective of this new form of treatment is to correct the ion transport defect by introducing the normal CFTR gene into affected cells of the airway epithelium. Localization studies and functional analysis indicate that targeted cells are situated mostly in the proximal respiratory surface epithelium as well as in significant portions of the distal respiratory surface epithelium.\textsuperscript{72} These types of cells can be reached easily by inhalation or lavage.

Vector systems capable of transferring normal CFTR gene into abnormal cells include liposomes and adenoviruses.\textsuperscript{73} The liposomes have been shown to correct the cystic fibrosis defect in transgenic mice.\textsuperscript{74} Clinical human studies of gene therapy using liposomes are under way.\textsuperscript{35} Adenoviruses are non-enveloped DNA viruses known to produce mild, self-limited respiratory illness in humans.\textsuperscript{72} Despite the fact that only one gene requires correction and the airway is easily accessible, there are problems associated with gene therapy methods involving efficiency (i.e., liposomes’ insufficient protein) and delivery (i.e., the virus prompts an immune response). The safety of the E1-deleted (and therefore replication-deficient) adenoviruses have been evaluated in nonhuman primates.\textsuperscript{75-77} These investigations showed that transferring the CFTR gene to respiratory epithelium was accompanied by local inflammatory and immune response only at higher virus doses.\textsuperscript{75-77} The E1-deleted adenoviruses are currently being tested in patients with CF in the United States.\textsuperscript{71,72}

Although the advent of gene therapy carries the promise of an ultimate cure for cystic fibrosis, this form of treatment may not generally be available for some time, after all safety and efficacy concerns have been studied and addressed. These newer modalities of treatment are likely to benefit recently diagnosed patients who are in the early stages of the disease as well as individuals with advanced pulmonary involvement.
At present the therapeutic regimen of advanced cystic fibrosis lung disease consists of antibiotics, chest physiotherapy, and the treatment of major life-threatening pulmonary complications. Lobar atelectasis is managed with aggressive intravenous antibiotic therapy and chest physiotherapy directed at the collapsed lobe. Bronchoscopy is indicated if atelectasis persists beyond 5 to 7 days of treatment. Lobectomy may be necessary in refractory cases.

Management of pneumothorax in cystic fibrosis is determined by the size of the pneumothorax and the presence or absence of symptoms. A pneumothorax may be small (<10%), stable, and asymptomatic with a recurrence rate of approximately 60%. Larger, symptomatic pneumothoraces require more aggressive management. Initial evacuation of the pneumothorax, using a chest tube, followed by chemical pleurodesis has been recommended. Recurrent pneumothorax may be an indication for upper partial pleurectomy with obliteration of pleural blebs by anterior thoracotomy or thoracoscopy.

Mild hemoptysis can be successfully managed with bed rest, intravenous antibiotics, and supplemental doses of vitamin K if the prothrombin time is prolonged. Hemoptysis exceeding 250ml in 24 hours requires bronchoscopy to localize the site of bleeding. Selective bronchial artery embolization may be necessary to control persistent, recurrent endobronchial hemorrhage.

Right-sided failure with associated cor pulmonale is treated with diuretics, salt restriction, and oxygen. Digitalis is not generally effective. Vigorous therapy is essential when cor pulmonale and respiratory failure are accompanied by pulmonary infection and obstruction. Oxygen therapy in respiratory failure is aimed at increasing PaO2 above 50mmHg to prevent pulmonary vasoconstriction and exacerbation of cor pulmonale. Increased PaCO2 may limit the use of increased FIO2. Mechanical ventilation is indicated for management of respiratory failure during acute exacerbations in patients who have good baseline pulmonary status and for management of otherwise stable patients during the perioperative period. Individuals with chronic, progressive respiratory failure do not benefit from ventilatory assistance because they are usually unable to be weaned from ventilatory support.

Heart-lung transplantation is an effective but rarely used treatment for terminal cardiorespiratory failure in cystic fibrosis. In a “domino” operation, the recipient heart is donated to another patient. The increased demand for cardiac transplants has decreased the availability of heart-lung blocks. Alternatively, double lung transplants have been successfully performed in patients. There is one report of successful transplantation of lungs and liver. Although the overall survival rate in transplantation recipients exceeds 50% and transplanted lungs do not develop cystic fibrosis pathology, the organ shortage and strict selection criteria limit wider use of this therapeutic option.

**Gastrointestinal Therapy**

Patients with CF are susceptible to malnutrition because the pancreatic enzymes needed for digestion do not reach the small intestine. As a result, CF patients require 50 percent to 100 percent more calories to maintain health. Supplemental high-calorie nutrition, vitamins and enteric-coated oral pancreatic enzymes enable most people with CF to maintain or gain weight.

Exocrine pancreatic deficiency and abnormal digestion of fat and proteins is treated with enzyme replacement, adequate nutrition, and vitamin and mineral supplementation. The objective of pancreatic enzyme replacement is to deliver an adequate concentration of digestive enzymes into the duodenum. Several hog pancreas extracts that contain between 4,000 and 24,000 units of lipase are
commercially available. Enteric-coated capsules designed to protect the enzymes from gastric acid inactivation are most effective. Although pancreatic enzyme replacement significantly reduces fat and nitrogen in stools, it does not completely correct the abnormal fat absorption.

The dose of pancreatic preparations should be adjusted empirically, based on the consistency, size and number of stools. The usual dose consists of 1 to 3 capsules per meal. Infants may be given powdered pancreatin preparations. Enteric-coated preparations need an alkaline environment to be effective. Persistent steatorrhea may signal gastric acid inactivation of the enzymes or low duodenal pH. In such cases, fat absorption may be improved by adding bicarbonate or an H2-receptor antagonist.

The importance of adequate nutrition in cystic fibrosis cannot be overemphasized. The goal of nutritional therapy is to promote normal growth. Most patients require a higher-than-normal caloric intake because of the increased work of breathing and the incomplete absorption of nutrients. A high-protein, high-calorie diet without fat restriction is currently recommended. A low-fat diet is no longer advised because normal amounts of fat in the diet are usually well tolerated with administration of improved pancreatic enzyme preparations. In addition, a low-fat diet may be associated with essential fatty acid deficiency.

Infants may be breast-fed if adequate enzyme supplements are provided. Infant formula should not contain predigested protein with medium-chain triglycerides. Nocturnal enteral feeding via a nasogastric tube or gastrostomy and parenteral hyperalimentation are reserved for patients who have poor growth in spite of adequate oral intake. Daily supplementation of fat-soluble vitamins is necessary to avoid symptoms of deficiency resulting from malabsorption. Vitamins A and D are usually provided as multivitamin products. Vitamin E is given commonly in doses of 100–200 units. Vitamin K supplementation is indicated only in the newborn period, the perioperative period, during hemoptysis, and in patients with documented extensive liver involvement and coagulation defects. Routine supplementation of vitamin K is not recommended. Iron deficiency is relatively common in cystic fibrosis, and iron therapy may be required when anemia is present. Glucose intolerance and clinically significant diabetes mellitus, that is occasionally seen in the second and third decades, are managed with dietary adjustments and small doses of insulin.

The management of intestinal obstruction due to meconium ileus includes an initial Gastrografin® enema, intravenous hydration, and ultimately surgical intervention if obstruction persists. A partial obstruction of the distal intestine (distal intestinal obstruction syndrome) is treated with increased doses of pancreatic enzymes, laxatives or stool softeners, increased fluid intake, and large-volume bowel lavage with salt solution containing polyethylene glycol. Complete obstruction due to distal intestinal obstruction syndrome or intussusception requires a Gastrografin enema. Volvulus, as well as persistent intussusception, is an indication for surgery. Rectal prolapse is usually treated with manual reduction followed by stool softeners. Surgical intervention is occasionally indicated.

Treatment of patients with hepatobiliary complications of cystic fibrosis is similar to the treatment of other individuals with liver disease. Liver transplant may be indicated when end-stage liver disease is present and pulmonary status is good.
Prognosis

There has been significant improvement in the survival of patients with cystic fibrosis. The median survival age has increased from less than 2 years in the 1940s to almost 45 years. Now, nearly half of the cystic fibrosis patients are 18 years of age or older. The clinical course and prognosis depend on the degree of pulmonary and pancreatic involvement. Patients who initially present with respiratory symptoms have a generally poorer prognosis. Individuals with established pulmonary disease who do not have severe pancreatic insufficiency have better survival rates. Finally, early diagnosis and aggressive antibiotic therapy appear to correlate with longer survival. Recent progress in the genetics of cystic fibrosis may not only produce an effective cure but may also have profound implications in prevention of the disease.

Surgery

Many patients with cystic fibrosis undergo elective and emergency surgery during their lifetimes. Surgical procedures are required for complications related to cystic fibrosis or other conditions.

Approximately 10% of newborns with cystic fibrosis initially present with meconium ileus. Although treatment with Gastrografin enema is frequently effective, surgery may be indicated to resolve the problem. Procedures range from irrigation or insertion of a T-tube to ileostomy followed in a few weeks by closure. Some patients may require bowel resection. The mortality rate has decreased dramatically from an average 55% to 15%. The decrease is attributable to frequent performance of less extensive procedures, thereby minimizing surgical time and trauma.

Other intraabdominal operations undertaken at an older age include procedures prompted by complaints of right lower quadrant pain. Differential diagnoses in these cases include, among others, appendicitis, intussusception, and distal intestinal obstruction syndrome. Frequent recurrence of rectal prolapse requires surgical correction. Procedures related to hepatobiliary complications of cystic fibrosis are also common.

By far, the most common surgery in patients with cystic fibrosis beyond the neonatal period is nasal polypectomy to relieve symptoms of nasal obstruction. The operation is safe, and surgical complications are rare. However, recurrences are common, and patients may require more than one procedure. Patients are usually admitted 1 day prior to the procedure and discharged within 24–48 hours postoperatively. Surgery performed on an outpatient basis is generally not recommended. In most patients nasal packing is left overnight to control persistent nasal bleeding.

Thoracic procedures are reserved for the treatment of persistent bronchiectasis, atelectasis, pneumothorax, and hemoptysis that do not respond to conservative medical management. Surgical resection of lung tissue is limited to the most severely affected areas. Preoperative optimization of pulmonary status and intraoperative sparing of functional lung parenchyma minimizes the incidence of perioperative complications. Careful selection of patients is crucial for favorable surgical outcome. Patients with preoperative FEV1 or FVC less than 30% of predicted values will have poor tolerance and are not likely to benefit from resection. Although pleural stripping procedures carry a significant anesthetic risk because of advanced pulmonary disease, in at least one review no intraoperative complications were seen, and the recurrence rate of pneumothorax was low.
Insertion of a permanent central vascular access cannula or device for multiple courses of antibiotics is another procedure frequently performed in patients with cystic fibrosis. Although these surgeries can often be successfully completed with sedation techniques only, general anesthesia and control of the airway may be indicated for a patient who has poor lung function or is actively coughing. Surgery may also be required for removal of a catheter that has been in place for an extended time and become incorporated into the vessel walls.

**Preanesthetic Assessment**

Patients with cystic fibrosis may present for surgery at different stages of their disease. The clinical spectrum ranges from an asymptomatic individual scheduled for a minor elective procedure to a moribund patient for emergency thoracotomy. In any case, a thorough preoperative evaluation should minimize the risk of postanesthetic morbidity.

Preanesthetic assessment of the patient with cystic fibrosis should be directed at the most commonly affected organs and systems. The severity of pulmonary and cardiac compromise and the extent of liver involvement should be assessed by history, physical examination, and additional studies as indicated. Information elicited during the preoperative interview should include the duration of pulmonary disease, the frequency and severity of exacerbations, the quality and quantity of recent sputum production, the degree of exercise intolerance, and current medical treatment. Past surgical and anesthetic history should be discussed and available medical records reviewed.

Physical examination should focus on general nutritional status, signs of respiratory distress, respiratory rate, abnormal breath sounds, and evidence of right-sided heart failure, such as peripheral edema and hepatomegaly. Cyanosis and digital clubbing should be noted. If nasal intubation is planned, the presence of nasal polyps should be excluded. Signs of liver disease should be sought.

Laboratory data should include complete blood count, electrolyte panel, blood sugar, and coagulation profile. Baseline liver function tests should document the extent of hepatic involvement. Chest x-ray should be scrutinized for evidence of active pulmonary disease and cardiomegaly. Preoperative ECG has been recommended in all patients with cystic fibrosis. Recent spirometry tests should be reviewed to quantify the degree of pulmonary dysfunction, and arterial blood gas analysis should be obtained to determine the preoperative values of pO2 and pCO2.

**Anesthetic Plan**

The anesthetic plan for patients with cystic fibrosis scheduled for elective surgical procedure depends upon the extent of surgery and the age of the patient. The patient should be in optimal medical condition consistent with the stage of pulmonary disease. Parenteral vitamin K preparations are administered to patients who are not on oral vitamin K supplements. Premedication with oral benzodiazepines is safe. Opioids are avoided because of their respiratory depressant effect. Although use of atropine has not been associated with any increase in pulmonary complications, its administration is controversial because of possible further inspissation of secretions. If used, atropine should be given during induction. Regional anesthesia is preferred when appropriate for a procedure, but general anesthesia can be safely administered. Coagulopathy should be excluded prior to regional anesthesia. One case
report documents the successful use of combined spinal epidural techniques for elective cesarean delivery in a 20 year old parturient at 32 weeks gestation. If general anesthesia is selected, intravenous induction is preferred because pronounced V/Q mismatch may prolong inhalation induction in patients with advanced pulmonary disease. Ketamine should be avoided as it may increase bronchial secretions. Endotracheal intubation and controlled ventilation are recommended. Because compliance can change rapidly during the operative period, an airway pressure monitor must be incorporated in the circuit.

Maintenance of general anesthesia with an inhalation agent is preferred because it allows the use of higher concentrations of oxygen, causes bronchodilation, and decreases the responsiveness of hyper reactive airways. The choice of inhalation anesthetic should take into consideration the possibility of silent hepatic disease. Another important consideration is that an otolaryngologist performing a polypectomy will frequently administer epinephrine which will have cardiovascular effects. All cystic fibrosis patients are at risk of sudden rupture of emphysematous bullae, but nitrous oxide has been used safely in patients undergoing nasal polypectomy. Adequate hydration and humidification of inspired gases as well as frequent tracheal suction are important in preventing intraoperative inspissation of secretions. Fully awake tracheal extubation is performed after appropriate criteria are met and thorough tracheal suction is accomplished.

Management of the Case Presented

The case presented was deemed to be semi-emergent. A nasogastric tube was passed. The patient was small for her age and therefore only 0.5 mg midazolam was used for premedication. She did not receive any atropine or glycopyrrolate. The airway was easily secured after a rapid sequence induction with propofol and succinylcholine. Anesthesia was continued with sevoflurane and oxygen and air. The intussusception was easily identified and released by a laparoscopic approach. Suctioning was performed at the end of the case. She was given mucolytic treatments in the postanesthetic care unit. Pain relief postoperatively was obtained with patient controlled analgesia. She was discharged home on the 2nd postoperative day.

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REFERENCES


Post-test

1. Which of the following is not a property of N-acetyl-cysteine?
   a. Toxic to ciliated epithelium
   b. Causes bronchospasm
   c. Mucolytic agent
   d. Bacteriocidal

2. Dornase alfa:
   a. Cleaves RNA
   b. Repairs the CFTR gene defect
   c. Contains DNA encoding for the native human protein deoxyribonuclease 1
   d. Can increase rates of pulmonary infection

3. The most commonly performed surgery in patients with CF after the neonatal period is:
   a. Appendectomy
   b. Hernia repair
   c. Pleural stripping
   d. Nasal polypectomy

4. The sweat test:
   a. Indicates CF in non symptomatic carriers
   b. Is very easy to perform
   c. Involves the iontophoresis of pilocarpine into the skin
   d. Is always reliable in confirming a diagnosis of CF in infants

5. For patients with CF, the goal of antibiotic therapy includes:
   a. Reducing the numbers of bacteria
   b. Reducing the intensity of endobronchial infection
   c. Delaying progressive lung damage
   d. All of the above.
6. **Standard medical therapy of CF complications does not include:**
   a. Nebulized steroids
   b. Antibiotics
   c. Mucolytic agents
   d. Pancreatic enzyme preparations

7. **Patients undergoing nasal polypectomy:**
   a. Are best treated as inpatients with a 1 or 2 day hospital stay
   b. Always require general anesthesia
   c. Must not be given epinephrine
   d. Are at great risk of cardiac complications when given anesthesia

8. **Regarding dietary requirements for patients with CF:**
   a. Regular diet suffices
   b. High protein, high calorie, high fat is preferable
   c. Diet should be low in fat
   d. Protein supplementation is contraindicated

9. **Radiological findings of meconium ileus:**
   a. Can confirm the diagnosis of cystic fibrosis
   b. Show evenly distended loops of bowel with multiple air fluid levels
   c. May demonstrate a distal obstruction
   d. All of the above

10. **Which of the following should not be included in the anesthetic plan for a patient with CF?**
    a. Premedication with oral benzodiazepines
    b. Administration of vitamin K supplements
    c. Administration of opioids
    d. Maintenance of general anesthesia with an inhalation agent