key points

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Dr Peter Saul
GP with an interest in respiratory medicine, Wrexham, UK

Cystic fibrosis (CF) is an autosomal recessive disorder resulting from two disease-causing mutations in the cystic fibrosis transmembrane regulator (CFTR) gene located on chromosome 7. CFTR is a chloride and bicarbonate channel found in sweat glands and the epithelial cells of the respiratory and digestive tracts. Ion transport systems in the airway epithelium control the movement of salt and water across airway epithelial cell membranes. This process regulates the airway surface liquid, which is critical for the effective mucociliary clearance of the airways. The reduced volume of airway surface liquid results in abnormal airway mucus and impaired mucociliary clearance. This creates an environment for chronic infection and inflammation.

CF is the most common life-limiting genetic disorder in the UK, diagnosed in one in every 2,500 babies. The median age of death in the UK has been rising and is 36 years. Most deaths in young people are the result of rapidly progressing lung disease. CF lung disease is characterised by acute and chronic bacterial and fungal infection. In conjunction with the resulting airway inflammation, this leads to the gradual loss of healthy lung architecture, bronchiectasis, accelerated decline in respiratory function, and ultimately respiratory failure. Infections are treated with prolonged courses of targeted oral and intravenous antibiotics and frequently prophylactic oral and inhaled antibiotics. Regular daily airway clearance with physiotherapy is a cornerstone of CF treatment.

Viscous pancreatic exocrine secretions, resulting from altered ion transport processes similar to those occurring in the airways, block the pancreatic duct leading to exocrine pancreatic failure and fat malabsorption. This results in faltering growth and is frequently the first clinical sign of the condition. Autodigestion of the pancreas leads to endocrine pancreatic failure in more than half of CF patients over time. Approximately 10% of children with CF present with meconium ileus in the neonatal period and require urgent bowel surgery.

CF outcomes depend on several factors including the class of CFTR mutations which will affect the severity of the disease, nutritional status, prompt treatment of any respiratory infection with a prolonged course of oral or intravenous antibiotics and adherence to CF treatments. Physiotherapy, mucoactive agents, antibiotics and nutrition continue to be mainstays of treatment.

The recent discovery of small molecules affecting CFTR function such as the potentiator ivacaftor and the correctors lumacaftor, tezacaftor and elexacaftor has led to a significant change in CF management by addressing the underlying protein defect. CFTR modulators have resulted in a step change in CF management, improved lung function and will help to improve survival. The CFTR modulators to treat individual patients are chosen based on the patient's CFTR mutation profile.