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Mini Review

Cystic Fibrosis: From Genetic Defect to Lifelong Multisystem Care

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Abstract

Cystic fibrosis (CF) is a hereditary, multisystem disorder caused by pathogenic variants in the CFTR (cystic fibrosis transmembrane conductance regulator) gene. The resulting dysfunction of epithelial ion and water transport produces abnormally thick secretions that affect the respiratory, gastrointestinal, hepatobiliary, reproductive, and other organ systems. Although chronic pulmonary disease has historically been the major cause of morbidity, advances in diagnosis, infection management, nutritional support, and CFTR modulator therapy have substantially changed the clinical course of the disease. This article reviews the underlying genetic and molecular mechanisms of cystic fibrosis, major clinical manifestations, diagnostic approaches, complications, and contemporary principles of management. Particular attention is given to the importance of individualized treatment, airway clearance, nutritional optimization, infection prevention, and mutation-specific CFTR modulator therapy. Early diagnosis and coordinated multidisciplinary care remain essential for reducing disease progression and improving quality of life. The continuing development of precision therapies offers further potential to transform CF from a predominantly progressive disorder into a condition that can be managed more effectively across the lifespan.

Introduction

Cystic fibrosis is one of the best-known inherited disorders affecting multiple organ systems. It is caused by abnormalities in the CFTR protein, which functions as an ion channel involved in regulating chloride and bicarbonate movement across epithelial surfaces. When CFTR activity is reduced or absent, the composition and hydration of secretions change. In the lungs, this promotes mucus retention, airway obstruction, persistent inflammation, and recurrent infection. In the digestive system, impaired pancreatic secretions can lead to malabsorption and nutritional deficiencies.

The clinical expression of CF varies considerably between individuals. Some patients develop severe respiratory symptoms during infancy or childhood, whereas others are diagnosed later because of milder or atypical manifestations. This variability reflects differences in CFTR variants, modifier genes, environmental factors, and access to effective treatment.

Genetic and Molecular Basis

Cystic fibrosis follows an autosomal recessive inheritance pattern. An affected individual generally inherits a disease-causing CFTR variant from each parent. Parents who carry one pathogenic variant usually do not have the characteristic clinical disease but can transmit the variant to their children.

The CFTR gene provides instructions for producing the CFTR protein. Different variants can interfere with the protein at different stages, including its production, processing, movement to the cell surface, opening, or stability. Consequently, CF is not a single uniform molecular disorder; it represents a spectrum of defects involving CFjTR functionThe consequences are particularly important in tissues where epithelial fluid regulation is essential. Thickened secretions can obstruct small airways, pancreatic ducts, and other passageways, creating a cycle of obstruction, inflammation, infection, and tissue injury

Clinical Manifestations

Respiratory System

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Pulmonary involvement is a defining feature of cystic fibrosis. Abnormally viscous airway mucus can impair normal mucus clearance and create an environment favorable to bacterial colonization.

Common respiratory manifestations include:

- Persistent cough
- Production of thick sputum
- Recurrent respiratory infections
- Wheezing and shortness of breath
- Bronchiectasis
- Progressive reduction in lung function

Repeated infection and inflammation can cause structural damage to the airways. Over time, bronchiectasis may become established, further impairing mucus clearance and increasing susceptibility to infection

Gastrointestinal and Pancreatic Disease

Many individuals with CF develop exocrine pancreatic insufficiency. Obstruction and progressive damage to pancreatic ducts reduce the delivery of digestive enzymes to the intestine. This can result in impaired absorption of fats and fat-soluble vitamins.

Possible consequences include:

- Poor weight gain
- Malnutrition
- Bulky or greasy stools
- Abdominal symptoms
- Deficiency of vitamins A, D, E, and K

Pancreatic enzyme replacement therapy is therefore an important component of care for patients with pancreatic insufficiency

Hepatobiliary Involvement

Abnormal biliary secretions can contribute to liver disease in some individuals with CF. The severity ranges from mild abnormalities in liver function to clinically significant CF-associated hepatobiliary disease.

Regular monitoring is important because liver involvement may develop gradually and can remain clinically subtle in its early stages.

Reproductive System

CF can affect reproductive health, particularly in males. Congenital bilateral absence or obstruction of the vas deferens may result in infertility despite otherwise preserved sexual function. Female fertility can also be affected by factors such as thickened cervical mucus, nutritional status, and overall disease severity

Modern CF care increasingly incorporates reproductive counselling and individualized family-planning support.

Psychosocial Considerations

Living with a chronic genetic disorder can affect education, employment, relationships, emotional well-being, and daily routines. Treatment itself may require substantial time and adherence to multiple therapies

Psychological support, social services, nutrition counseling, respiratory care, and other multidisciplinary resources can help patients and families manage the long-term demands of the disease. Care should therefore address not only lung function and laboratory measurements but also quality of life and individual goals

Future Directions

Research in cystic fibrosis is increasingly focused on precision medicine. The development of therapies directed toward specific CFTR defects demonstrates how understanding disease mechanisms at the molecular level can influence treatment decisions.

Future research may expand treatment options for people whose variants are not adequately addressed by currently available CFTR modulators. Gene-based approaches, RNA-based strategies, improved antimicrobial therapies, and regenerative or mutation-independent treatments are areas of continuing investigation.

Conclusion

Cystic fibrosis is a complex inherited disorder in which a defect in CFTR-mediated epithelial transport produces widespread effects across multiple organ systems. Its clinical course is shaped by genetic variation, infection, inflammation, nutrition, and access to effective care. Advances in newborn screening, multidisciplinary management, and CFTR modulator therapy have significantly changed the outlook for many individuals with the disease.

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