The basic problem

The Leeds Method of Management. April, 2008. Cystic fibrosis and the basic problem [online]. Leeds Regional Adult and Paediatric Cystic Fibrosis Units, St James's University Hospital, Leeds, UK. Available from http://www.cysticfibrosismedicine.com

Introduction

Cystic Fibrosis is an inherited disease caused by a genetic mutation (defect) on chromosome 7. The defective gene results in abnormalities in the production and function of a protein called the cystic fibrosis transmembrane conductance regulator (CFTR). In healthy cells CFTR acts as a chloride channel and a regulator of sodium, chloride and bicarbonate transport.

The widespread presence of CFTR throughout the body (lungs, salivary glands, pancreas, liver, kidneys, sweat ducts and reproductive tract) helps to explain why CF is a multisystem condition affecting many organs (figure 1). The two major systems affected are the lungs and the gastrointestinal tract.
Figure 1. Cystic fibrosis is a multisystem condition affecting many organs. This figure illustrates some of the complications frequently seen in CF.

How does CFTR affect the lungs?

In the lungs, inactive or inefficient functioning CFTR results in impaired chloride transport and enhanced sodium absorption across airway epithelial cells (Boucher, 2007; Donaldson & Boucher, 2007). This leads to a net increase in water absorption (Boucher, 2007). The volume of the liquid that sits on the airway surface is reduced and the mucus in the airways becomes more viscid (sticky). In healthy lungs the cilia (small hairs on the surface of the airways) beat in a coordinated fashion so that they continually move mucus up and out of the lungs. This cleansing action of the cilia is impaired in CF because of the presence of very sticky mucus and dry airways (figures 2 & 3) which provide a favourable environment for bacterial infection.
Structural changes in the CFTR protein have also been linked to defective phagocytosis (ingestion and destruction of bacteria by the white blood cells) of bacteria such as *Pseudomonas aeruginosa* and to reduced clearance of infection (Di *et al.*, 2006; Painter *et al.*, 2006).

Overall these changes in lung physiology lead to dry airways, sticky secretions, a predisposition to chronic chest infections and bronchiectasis (scarring).

Figure 2a and 2b. In CF, impairment of CFTR function causes reduced fluid production. Enhanced sodium absorption through epithelial Na+ channels (ENaC) and basolateral Na/K ATPase pumps results in increased fluid absorption leading to drier airways and impaired ciliary clearance.
Figure 3a. Normal ciliary clearance of bacteria and foreign particles. Cilia are fine hair like structures which cover the lining of the airways like a carpet. They beat continuously and act like a conveyor belt to remove bacteria and particles stuck to the mucus layer, driving them from the lungs to the mouth.

Figure 3b. In CF, the production of abnormal secretions and increased fluid absorption across the airway cells leads to drier, stickier secretions. This reduces the normal ciliary clearance of bacteria and
foreign particles. Cilia are fine hair like structures which cover the lining of the airways like a carpet. They beat continuously and act like a conveyor belt to remove bacteria and particles stuck to the mucus layer, driving them from the lungs to the mouth.

So why do I need treatment if I feel well?

Treatment of CF is aimed at protecting the lungs from pulmonary infections, airway inflammation and permanent lung damage. Individuals with CF may remain relatively asymptomatic despite significant decline in lung function and only develop breathlessness when a critical point is reached and lung reserve is lost. Symptoms are often a poor marker of disease severity, and other factors such as lung function, pseudomonas status and chest radiology should be taken into account (figure 4).

It is important that patients understand this because adherence to medication may be reduced if treatments are perceived as having no immediate impact on clinical status. In some cases drug therapy may transiently increase symptoms in the short term but significantly reduce long term lung damage. For example inhaled antibiotics may initially provoke coughing or some chest tightness and wheezing which settles after a few doses. It is essential that individuals are aware of the natural history of CF and the potential benefits which can result from good adherence and effective prophylactic treatments.

Key points

• The CF gene causes an abnormality in the production and function of a protein called the cystic fibrosis transmembrane conductance regulator (CFTR)

• The widespread presence of CFTR throughout the body helps to explain why CF is a multisystem condition affecting many organs

• In the lungs, inactive or inefficient functioning of CFTR lead to drier airways, sticky secretions and a predisposition to chronic chest infections and bronchiectasis (scarring)

• Treatment of CF is aimed at protecting the lungs from pulmonary infections, airway inflammation and permanent lung damage
• Symptoms are often a poor marker of disease severity, and other factors such as lung function, pseudomonas status and chest radiology should be taken into account

References


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