Cystic fibrosis (CF) is the most common fatal genetic disorder among Caucasians. In the UK, CF affects over 8,500 people, with current data suggesting that five babies are born with CF and two people die from the disease each week.1

The prognosis for patients with CF has been steadily improving over the past 40–50 years. In the 1930s babies with CF were expected to live only for a few months. By the 1960s life expectancy had reached the early teenage years.2 Now, the median predicted survival in the UK has increased to 38.8 years, and it is predicted that children born with CF today will live into their 50s or beyond.3 The improved prognosis is attributed to the introduction of new therapies and strategies for disease management, in particular the care of patients in specialist CF centres.

In the UK the Cystic Fibrosis Trust collects demographic and clinical outcome data for all patients with CF via a web-based database called Port CF.1 These data are used to help design better treatment standards, develop new clinical trials and, generally, improve the delivery of care.

Genetics

CF is an autosomal recessive genetic disorder caused by the mutation of a single gene — the CF transmembrane conductance regulator (CFTR) gene on chromosome 7. Heterozygous individuals carry one mutated and one normal allele, and are called carriers. For a child to be born with CF both parents need to carry the defective gene (see Figure 1, p240). Carriers are usually asymptomatic, although there have been a few cases described where carriers developed CF-related symptoms later in life.4 Although CF should affect both sexes equally, figures show that more males than females are affected.3

The CFTR gene codes for a membrane protein called CF transmembrane conductance regulating protein (CFTRP); production of abnormal CFTRP, or a complete absence of the protein, helps to explain most of the signs and symptoms of CF (described below).3,4

### SUMMARY

Cystic fibrosis (CF) is common genetic disease and is caused by mutation of a single gene. CF affects respiratory function — sufferers produce thick mucus that is difficult to expectorate which, among other factors, leads to increased bacterial colonisation and infection.

Thick secretions can also cause gastrointestinal obstruction and blockage of bile ducts (causing liver disease) and pancreatic ducts (reducing the amount of pancreatic enzymes in the gut leading to malabsorption). The prognosis for patients with CF is improving as a result of new treatments and multidisciplinary management co-ordinated through specialist centres.

Hundreds of different CFTR-gene mutations have been identified. The most common mutation in the UK Caucasian population is a deletion of the amino acid phenylalanine in position 508, which is found in about 92% of cases. However, some ethnic groups show different mutations, which affects neonatal screening for CF.

Efforts have been made to classify CF according to the effects of a particular genotype on the function of CFTRP. Some mutations show excellent correlation with clinical features such as pancreatic function or sweat chloride concentrations.6 However, CFTR mutations do not correlate well with lung function, which is the most important factor affecting survival.
Pathophysiology

The role of CFTRP is not fully understood, but in healthy individuals it acts as a chloride channel and also helps to regulate the transport of sodium and other ions. CFTRP is found in the epithelial cells of the lungs, pancreas, intestine, gall-bladder, salivary and sweat glands, testes and uterus. Consequently, CF is a multisystem disorder with a range of clinical manifestations (see Box 1, p243).

Respiratory System

A vicious cycle of infection, inflammation and damage occurs in lungs affected by CF. In a healthy person, respiratory tract infections trigger increased production and expectoration of sputum, and initiate an inflammatory process that attracts neutrophils and phagocytes to the infection site. In CF, the absence or dysfunction of CFTRP leads to excessive absorption of water, sodium and chloride ions, causing dehydration of the epithelial surface of the respiratory tract and production of thick mucus, which is difficult to expectorate. In addition, the release of white cell and bacterial DNA after cell death increases mucus viscosity, further aggravating the problem. These events result in chronic, obstructive airway inflammation and an increased incidence of respiratory tract infections (because bacteria will easily colonise and proliferate in such an environment). In CF, the damaged lung then becomes more prone to infections caused by Pseudomonas aeruginosa, a ubiquitous, Gram-negative rod, which is difficult to eradicate. Some strains of P. aeruginosa produce a thick alginate, which helps the bacteria to attract neutrophils and phagocytes to the infection site. In CF, the absence or dysfunction of CFTRP leads to excessive absorption of water, sodium and chloride ions, causing dehydration of the epithelial surface of the respiratory tract and production of thick mucus, which is difficult to expectorate.

Bacteria that colonise the lungs in CF commonly include Staphylococcus aureus, Haemophilus influenzae and Pseudomonas aeruginosa. The first two tend to colonise the lungs of younger patients, causing cumulative damage with each acute exacerbation and reduced respiratory function. The damaged lung then becomes more prone to infections caused by P. aeruginosa, a ubiquitous, Gram-negative rod, which is difficult to eradicate. Some strains of P. aeruginosa produce a thick alginate, which helps the bacteria to cluster together in “biofilms”. Biofilms protect the organism from antibiotics and white cells. Certain strains, termed “mucoid strains”, form uneven, lumpy biofilms by over-producing alginate. These strains are more virulent and difficult to eradicate.

Colonisation with P. aeruginosa worsens the prognosis of CF by causing further lung damage and decline in lung function. Peak colonisation with P. aeruginosa occurs at 12–19 years of age. P. aeruginosa infection usually spreads to patients with CF through environmental sources rather than person-to-person contact. However, in the past 15 years it was recognised that the number of P. aeruginosa-colonised CF patients was rising more than the expected rate and that certain geographical areas had particular “epidemic” strains and patient-to-patient infection there was commonplace.

Now, to avoid the spread of these epidemic strains, patients are segregated within healthcare institutions according to the micro-organism with which they are colonised — groups with different strains attend clinics on different days of the week, are admitted to different wards in the hospital and remain in cubicles throughout their stay. These strategies have resulted in a reduction in the rates of colonisation with these strains.

Segregation of patients has also helped to tackle infections caused by Burkholderia cepacia complex organisms. This family of opportunistic micro-organisms is associated with a very rapid decline in lung function and clinical condition, and death, this is known as the “Cepacia syndrome”.

Gastrointestinal tract

The production of thick mucus secretions can cause blockage of the gastrointestinal tract.

Meconium is the material ( bile salts, bile acids and debris) found in the intestine of newborns. It is normally passed in utero or soon after birth. About 15% of newborns with CF present with meconium ileus, a condition in which babies fail to pass the meconium. Depending on the severity of the obstruction, it might resolve easily but sometimes surgery, including bowel resection, and parental nutrition are needed.

In older patients, recurrent gastrointestinal obstructions can lead to distal intestinal obstruction syndrome (also known as meconium ileus equivalent).

Pancreas

Both the exocrine and endocrine functions of the pancreas can be affected in CF. Blocked pancreatic ducts cause a lack of pancreatic enzymes (lipase, amylase and protease) in the duodenum. These enzymes are responsible for digesting dietary proteins, complex sugars and fat and, if they are not replaced, patients can suffer from malabsorption of nutrients (in particular fat-soluble vitamins) and impaired growth and development. This increases the risk of osteoporosis, osteopenia and various other arthropathies. Steatorrhoea (fatty stools) is a common symptom of CF patients who are untreated or non-compliant with enzyme replacement.

Endocrine dysfunction, characterised by a reduction in insulin production, occurs with increasing frequency after 10 years of age. Symptoms tend to be mild and diabetes is usually controlled with small doses of insulin. CF patients require a hypercaloric diet to meet their energy requirements making the treatment of diabetes difficult.

Liver

Liver disease is the second most frequent cause of death among CF patients. Bile ducts can become blocked by thick secretions leading to accumulation and overflow of bile acids in the liver and gall-bladder. Bile acids have a direct toxic effect on hepatocytes and, if left untreated, liver dysfunction may progress to cirrhosis and end-stage liver disease.
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Date of preparation: June 2011 C2005042a-B0

Reference:
Reproductive system
Most males with CF are infertile as a result of absent or blocked vas deferentia; however, sexual function and sperm production are not affected. Females with CF can also have fertility problems caused by thick cervical secretions, which can impede fertilisation by acting as a barrier to sperm.

Sweat glands
CF patients do not sweat more than people without the condition, but they lose more salt in their sweat. This clinical feature is used to diagnose the disease (see below).

Diagnosis
In the UK, most patients with CF are diagnosed through routine neonatal screening, which is conducted according to the UK screening algorithm (see Box 2, p244). Meta-analyses have shown that early detection of CF by neonatal screening:9, 13

- Limits lung damage in childhood
- Reduces the burden of care for families
- Reduces the cost for healthcare systems
- Has a beneficial effect on nutritional status, with improved growth, height and weight
- May prevent deficiency in fat-soluble vitamins and protein malnutrition
- Is less stressful for parents than delayed diagnosis

Despite this, introducing a national neonatal screening programme also has disadvantages, for example, the tests can yield equivocal or inconclusive results and false positive results may lead to unnecessary treatments for patients and emotional distress for parents.

Multidisciplinary care
CF is a multisystem disease and evidence supports the provision of care by an experienced multidisciplinary team of specialist healthcare professionals including consultants, clinical nurse specialists, physiotherapists, dietitians, social workers, psychologists and pharmacists. Patients should be cared for at specialist CF centres (either directly or via shared-care arrangements).

Nutrition
Achieving optimal nutritional status, with normal growth and development, is one of the treatment goals in CF. Regular assessments of nutrition, including height and weight measurements are carried out by specialist CF dietitians.

Energy intake from food should be maximised through a varied diet and encouraging intake of food with high caloric content (lipids and carbohydrates) and snacks. There is controversy regarding the efficacy of oral calorie supplements in CF. Authors of a recent Cochrane review concluded that such supplements do not confer any additional benefit in the nutritional management of moderately malnourished children with CF compared with the use of dietary advice and monitoring alone.

Supplementation might be indicated for acute or severe malnutrition states. There is also some debate around whether or not omega-3 (fish oil) supplements are beneficial for people with CF, further studies are needed before a formal recommendation can be made.

Physiotherapy
Chest physiotherapy is important for all CF patients because it helps to prevent thick, sticky lung secretions from blocking the respiratory tract. This reduces infection rates and prevents lung damage. Meta-analyses have shown that chest physiotherapy improves sputum expectoration and pulmonary function compared with no physiotherapy.

There is a variety of physiotherapy techniques and, since a Cochrane review has shown that there is little difference in outcomes depending on the method used, the technique chosen should be tailored to patients’ preferences whenever possible. Physiotherapy frequency and duration will depend on an individual's clinical status, assessed by a specialist CF physiotherapist. Physiotherapy techniques include:

- Active cycle of breathing techniques (ACBT) — a combination of breathing control, thoracic expansion exercises and forced inspiration exercises
- Postural drainage and percussion — gravity assisted positioning helps drainage of secretions from some areas of the lungs; percussion or “chest clapping” helps to loosen secretions for expectoration
- Positive expiratory pressure (PEP) — a machine produces positive pressure in the airways to open the airways and help move secretions higher up the respiratory tract
- Oscillating PEP — combines PEP with airway vibration (via a machine) to loosen mucus

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**Social aspects of care**

CF patients and their families have to face several challenges that can negatively affect their social, professional and developmental routines, some of which are outlined below.\(^1\)\(^2\)

**Treatment adherence**

Drug treatments for CF are numerous and can become unmanageable for some patients and their families as the disease progresses. Nebulised therapies and physiotherapy are unpopular with patients because they are time-consuming. Pancreatic enzyme replacements have to be taken with every meal, exposing the child as "different" in front of his or her peers.\(^3\)\(^4\)

Pharmacists, psychologists and specialist nurses can help to improve adherence to treatment by tailoring the treatment as much as possible to the lifestyle preferences of the patient and family.\(^5\)\(^6\)

**Education**

Children and adults with CF are as academically able as their peers. However, frequent ill-periods and hospital admissions may affect their performance. Furthermore, embarrassment due to the fact that they have to take medicines throughout the day can lead to isolation.

It is important that schools and workplaces are aware if one of their students or employees has CF, so they can offer adequate support.\(^7\)\(^8\)

In terms of quality of life, there are both advantages and disadvantages, so the decision to offer home IV therapy, and train a family to administer it, should be reached based on patients' preferences and care centre resources. Home IV therapy would not be possible without long-term venous access, which is usually in the form of a port — a device that is fully implanted under the skin.

**Transition to adult care**

Transition to adult care involves a change in the responsibility of care both for the patient and the care centre. Patients need to start taking medicines throughout the day can lead to isolation. It is important that schools and workplaces are aware if one of their students or employees has CF, so they can offer adequate support.\(^9\)

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**Home intravenous therapy**

Home intravenous (IV) therapy is an excellent way of reducing hospital admissions (therefore reducing the impact of the disease on the daily lives of patients and their families). Research has shown that home IV therapy is not harmful and that it entails fewer investigations, reduces social disruptions and may be cost-effective.\(^1\)\(^2\)

**References**