Cystic fibrosis

Key facts

- Cystic fibrosis (CF) is an inherited condition of the exocrine glands, most commonly presenting during early childhood.
- CF is a progressive multi-system disorder and the extent to which different systems are affected varies from person to person. Some affected individuals develop signs in infancy and others remain unaffected until adulthood.
- Early diagnosis, treatment and management improves outcome and quality of life for those affected with CF.
- CF is an autosomal recessive condition, owing to mutations in the *CFTR* (cystic fibrosis transmembrane conductance regulator) gene.
- All newborn babies in the UK are now screened for CF by the newborn bloodspot test. This means that the majority (90%-95%) of children with CF will now be diagnosed shortly after birth before symptoms develop.
- CF is one of the most common inherited conditions, affecting between 1 in 2,000 to 1 in 3,000 newborns of northern European ancestry. It is much less common in other ethnic groups.

Clinical features

The clinical features of CF are due to the production of abnormally thick mucus from the affected glands. The most common features are:

- chronic respiratory infections;
- malabsorption (failure to thrive);
- prolonged diarrhoea;
- male infertility / female reduced fertility; and
- meconium ileus (in newborns).

Diabetes and osteoporosisare also relatively common.

Diagnosis

- In the UK, cystic fibrosis is usually diagnosed at birth as part of the national screening programme. As screening will not identify all affected individuals, where there is still a clinical suspicion of CF a sweat test should be undertaken, even if the baby has had newborn screening.
- The sweat test is the standard test for confirming a diagnosis of CF; people with CF produce more salt in their sweat than unaffected individuals. This can be measured in a standardised way.
- DNA testing can be useful in helping to make the diagnosis (see below), particularly when the result of the sweat test is equivocal.

Genetic basis

- CF is an autosomal recessive condition, which means that the affected individual has two altered copies of the *CFTR* gene. The parents are healthy because although they have one altered copy of the gene, this has no adverse effect when the second copy of the gene is unaltered. They are said to be carriers for CF. Each child of two carriers has a 25%, or 1-in-4, chance of inheriting both gene alterations and developing CF.

- Between 1 in 22 and 1 in 27 people in the UK are carriers, most of whom have no known family history of CF.
- CF is due to alterations (mutations) in the *CFTR* gene. More than 1,000 different alterations in the CFTR gene have been identified worldwide. About 30 of these are relatively common, accounting for 85%-90% of all alterations, while the others are individually rare. Currently the most commonly used laboratory tests will detect these 30 common alterations. The single most common alteration is known as delta-F508 (technically now known as c.1521_1523 del CTT: p Phe 508 del) and is present in about 76% of carriers in the UK. Different genetic alterations are more common in different ethnic groups. Mutation analysis does not always provide prognostic information, but individuals affected by CF who have two copies of the delta-F508 alteration usually have pancreatic insufficiency.

Clinical management

- Children and adults with CF in the UK are usually cared for by local doctors with the help and support of specialist centres with multidisciplinary teams.
- There is currently no cure for CF. At present physiotherapy and antibiotics are used to prevent and treat chest infections, and enzyme tablets taken with food and support from a specialist dietitian help to keep the patient well nourished and control digestive symptoms.
- Patients and their parents should be offered genetic testing to look for alterations in the *CFTR* gene and may wish to be seen by a clinical geneticist. Genetic testing may also be appropriate for other family members.

Genetic testing

Indications for genetic testing and genetic counselling include:

- a child with a positive sweat test result;
- confirmation of a diagnosis in the case of a borderline sweat test;
- siblings and relatives of affected children with symptoms suggestive of the condition;
- two carriers contemplating a pregnancy who may consider prenatal or preimplantation genetic diagnosis. Prenatal diagnosis is usually possible by chorionic villus sampling (CVS) or amniocentesis. If a couple are considering prenatal diagnosis, referral should be made to the local clinical genetics service prior to a pregnancy. This ensures that appropriate advice and investigations are undertaken and confirms whether or not prenatal diagnosis is possible. All couples considering preimplantation genetic diagnosis must be referred to their local clinical genetics service. Non-invasive prenatal diagnosis may be possible for some families, but needs to be facilitated by clinical genetics departments or fetal medicine units;
- to provide information about the genetic status of other relatives of someone with CF through carrier testing; and
- presence of features suggestive of cystic fibrosis on routine antenatal ultrasound scans, even when that pregnancy is not known to be at increased risk.

Genetic testing is available in the UK and usually provided through specialist clinics or regional genetic centres.

This information is intended for educational use and was current in March 2015. For clinical management, it is recommended that local guidelines and protocols are used.