

## THE FAMILY CASCADE SCREENING PROGRAMME FOR CYSTIC FIBROSIS

*Published by the Cystic Fibrosis Trust with assistance originally from Doctor Maurice Super (deceased), Dept of Clinical Genetics & CF Clinic, Royal Manchester Children's Hospital and updated by members of the Regional Genetics Service in Manchester.*

### What is Cascade Screening?

Carrier status screening can be offered to relatives (and their partners) of a person diagnosed with Cystic Fibrosis. Whenever a carrier is detected, carrier status tests are then made available and “cascade” out to their relatives.

### What is Cystic Fibrosis?

Cystic Fibrosis (CF) is an inherited disease which affects vital organs in the body, especially the lungs and pancreas, by clogging them with thick, sticky mucus. It is one of the UK's most common life-threatening inherited diseases affecting around one in 2,500 live births.

The condition is present from before birth and symptoms often appear immediately or soon after birth. Persistent infections can lead to chronic lung problems, and there is poor digestion of fat and protein. Serious symptoms and complications of CF include infection and inflammation of the lungs, malnutrition, diabetes, liver failure and osteoporosis. The lungs can be treated by physiotherapy and drugs. Poor digestion is controlled with the help of specially developed enzymes and particular attention to diet.

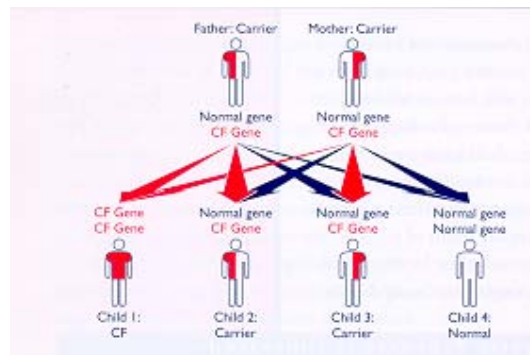
Men with Cystic Fibrosis generally find it difficult to father children due to absence of, or blockages in, the ducts which carry sperm. This means their sexual function is entirely normal but they can seldom father children naturally. However, recent medical advances have allowed some men with CF to father children, using a new technique called intra-cytoplasmic sperm injection (ICSI).

[www.cftrust.org.uk](http://www.cftrust.org.uk)

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New treatments are being developed which have improved the quality and length of life for people with CF but the condition still remains serious and burdensome. There is no cure at present, but gene therapy to cure the lung disease is a realistic possibility within the foreseeable future.

## Why is a baby born with Cystic Fibrosis?



For a baby to be born with Cystic Fibrosis, *both* parents must be carriers of the faulty CF gene. The child will have inherited the faulty gene from each parent.

The carrier parents, who are not personally affected by CF, have a normal gene and a faulty CF gene. If both parents are carriers, a child has:

- A one in four chance of being born with CF
- A two in four chance of being a carrier (like their parents) but not having the disease
- A one in four chance of being completely free of the condition – neither having CF nor being a carrier of the faulty CF gene

**The odds are the same for each successive pregnancy.**

## What is the risk for relatives?

In the general population in the UK 1 in 25 people *without a family history of CF* carry a faulty CF gene. **Relatives of someone with CF have a much higher chance of being carriers.** The chart

below gives the statistical chances of relatives (who have not been tested) of being carriers and their risk of having a child with Cystic Fibrosis.

### BEFORE TESTING

Relationship to person with CF	Chance of being a carrier	Risk of having a child with CF with an <u>untested</u> partner
Parents	100%	1 in 4
Person with CF	100%	1 in 50
Parent remarries	100%	1 in 100
Child of woman with CF	100%	1 in 100
Brother or sister	2 in 3	1 in 150
Aunt or uncle	1 in 2	1 in 200
Grandparent	1 in 2	1 in 200
First cousin	1 in 4	1 in 400
Second cousin	1 in 8	1 in 800

### Are carriers healthy?

Carriers are normally healthy and have no symptoms; in fact, they probably have a health advantage over non-carriers which would explain the fact that as many as 1 in 25 of us are carriers. There is some suggestion that this advantage might come from protection against some types of intestinal infection, like typhoid and possibly even cholera. There are some indications though that being a carrier is occasionally correlated with having some symptoms in common with Cystic Fibrosis.

### The Cystic Fibrosis Gene

The gene responsible for CF was discovered in 1989. More than 1400 mutations (alterations) have been discovered worldwide, but only a few are common. In the UK, one mutation (or alteration) accounts for the majority of CF cases. For example, 81% of CF carriers in the North West of England have the most common mutation in the UK. This mutation plus a further 29 mutations

account for more than 93% of the total mutations in the UK in native British people. The ethnic origin of the person can influence which mutations are most common. Thus people of Ashkenazi Jewish origin have a different spectrum of common mutations in amongst the 30 mutations alluded to above.

## Can I find out if my partner and I are carriers?

It is now possible to test both of you using a simple mouthwash test (in most testing laboratories in the UK, **no** blood sample is needed). Cells in the mouthwash are collected by gently rubbing the inside of the cheek with a little brush or cotton bud and are then analysed. In relatives of people diagnosed with CF, the exact gene alterations found in their affected family member are established wherever possible, no matter how rare the alteration. A test for the more common gene alterations is performed on the partner who does not have a family history of the condition.

Because the test only detects about 90% of alterations or mutations, a negative result does not entirely rule out the possibility of the person being a CF carrier, but the statistical likelihood is reduced to less than 1 in 250. (Depending on the number of genetic CF alterations tested for in your health region this figure may differ slightly.) *A positive result shows that the person is a definite carrier, even if there is no family history.*

Very occasionally both CF gene alterations – and remember, there have to be two or the person will just be a carrier – are not identified in the person with CF, because the mutation is one of the very rare ones that has not yet been identified. In these cases testing for carriers in a relative becomes a little more complicated but is generally still possible by testing for common mutations (alterations) and then identifying where possible, the CF carrying gene inherited from each parent and testing for that pattern in the relative. Except in the case of a full brother or sister of someone with CF, a negative result **does not** allow us to confirm with 100% certainty that you are not a carrier but it does mean that you have a much lower risk. The chart on the next page shows how the level of risk of having a child with CF can be estimated once testing has taken place and suggests possible course of action.

## AFTER TESTS WHICH DETECT 90% OF CF GENES

Results	Risk of having a child with CF	Action
Both partners are carriers	1 in 4	Genetic counselling. Options are discussed including tests and support available in current or future pregnancy. Pre-implantation diagnosis is also explained.
Relative carrier, partner negative	Less than 1 in 1,000	Reassurance. Low Risk. Tests not routinely offered in pregnancy. Check offspring for CF if sickly
Relative negative, partner carrier *	Less than 1 in 2,000 <b>Unless</b> the relative is a full brother or sister of the person with CF, when a negative test means non-carrier (risk zero).	Re-test to ensure no sample mix-up. Reassure – low risk. No routine tests in pregnancy. Check offspring for CF if sickly.
Both partners negative	Less than 1 in 250,000	Strong reassurance.

- *\*The reason the chances are different if the relative of someone with CF is a negative rather than someone not related to anyone with CF, is that the relative will be known to be free of the CF gene known to be in the family. In the case of someone whose full brother or sister has CF, the known mutations in that family will have been tested for and the brother/sister found to be free of any CF genes.*
- *NB In Lothian, routine ante-natal screening for CF carriers is offered to pregnant women and their partners, i.e. even in the absence of a family history. This test is not routinely offered in other parts of the UK.*

## Do I have to pay to have a carrier test?

No, not if you are a relative of someone with CF. The cascade scheme is offered as a NHS service to people with a family history of Cystic Fibrosis and their partners.

If you are not a relative of someone with CF, and wish to have the carrier status test it may be difficult to obtain on the NHS. Details of where private testing is available are included at the end of this leaflet.

## Who can have a carrier test?

Testing is offered to the close relatives (and their partners) of people with CF. Also, the relatives of anyone found to be a carrier will be offered testing. Anyone who has a family history of CF can ask for a test, ideally through his or her General Practitioner. The name “cascade” arises because whenever a carrier is detected, tests cascade out to their relatives.

## How will I receive test results?

This may differ from region to region within the NHS. The contact person in your local genetics department will be able to explain their procedures to you. In many health regions results are given in writing, stating whether the person has been discovered to be a carrier or is negative on testing. *It must be remembered that a negative result does not absolutely rule out the possibility of being a carrier, although it does reduce the likelihood at least 10 fold.* Details of the chances of still being a carrier are given to people whose test is negative and a statistical level of risk of having a child affected by CF is given to couples. Results are generally available within ten working days of the sample arriving in the laboratory.

For those couples or individuals found to be carriers, an invitation to make contact with genetic counsellors by telephone and in person is offered to explain and discuss the situation and future options. The genetic field worker will also provide further explanation and discussion. Carriers are informed that there are generally no major health risks to them from being a carrier and that the large majority of carriers probably enjoy a health advantage, explaining why as many as 1 in 25 of

us are carriers. *Specialist genetic counselling is offered in all cases where both partners are carriers.*

### Is urgent testing available?

In case of queries or anxieties arising in pregnancy, testing of couples with a result in a few days can be organised. However, we strongly recommend that where possible, testing be undertaken **before** a pregnancy.

### What are the options if my partner and I are both carriers of the CF gene?

All available options will be explained during your counselling session, so that you can decide what is right for you. All decisions are for you to make, and there will be trained staff available in the genetics department to clarify the situation and to discuss the implications of all possible courses of action. Ante-natal tests with the options of ending or continuing the pregnancy are discussed, including any dangers that may be associated with the tests. Pre-implantation tests that use IVF techniques to ensure that only an embryo free of CF is implanted into the womb are also explained. This last option is not easy to obtain on the NHS. Some Health Authorities are more willing to fund it than others, but it is becoming more widely available.

### The future

As our ability to detect more CF genes improves, it will be possible to test for the rarer mutations that currently make the carrier status test less than 100% accurate and occasionally leads to someone being told they are not a carrier when in fact they carry one of the rare and as yet unidentified mutations. This is called a false negative result. Those people with a positive test have been proved to be carriers and that will not change. Soon tests will become available that are capable of detecting CF cells from the embryo by just taking a sample of the mother's blood. This would avoid the need for chorionic biopsy (where a little piece of the developing placenta is taken at 10-12 weeks) or amniocentesis, the current test available for ante-natal diagnosis.

It must also be borne in mind that new treatments may well succeed in making Cystic Fibrosis a much less serious disease than it is at present. So going ahead with a pregnancy where it is known that the baby has, or is at high risk of having CF, may not be such a worrying prospect as some would see it now.

## Who can I contact about this service?

**A list of genetics centres in the UK offering CF carrier tests to people with a family history is attached. Your GP will be able to refer you to your local genetics centre.**

Individuals or couples without a family history of CF can also have tests. However, since this is not yet an NHS service there is a charge. Centres to contact are:

National Genetics Reference Laboratory	Leeds Antenatal Screening Service,
Dept of Medical Genetics	28 Clarendon Road,
St Mary's Hospital,	Leeds LS2 9NZ.
Hathersage Road,	Co-ordinator Mrs I.K. Sehmi.
Manchester	Telephone 0113 234 4013
M13 0JH.	
Contact: Ms Theresa Roberts	
Telephone 0161 727 2327.	

## ENGLAND

### **Clinical Genetics Service for Devon and Cornwall**

Royal Devon & Exeter Hospital  
Barrack Road, EXETER. EX2 5DW  
T: 01392 402946  
Offer mouthwash testing: Yes

### **East Anglian Medical Genetics Service**

Department of Medical Genetics  
Addenbrooke's NHS Trust  
Box 134, Hills Road  
CAMBRIDGE. CB2 2QQ  
T: 01223 217971  
Offer mouthwash testing: Yes, but prefer blood sample.

### **Great Ormond Street Children's Hospital NHS Trust**

Institute of Child Health  
30 Guilford Street  
LONDON. WC1N 1EH

### **Merseyside Regional Clinical Genetics Service**

Liverpool Women's Hospital  
Crown Street  
LIVERPOOL L8 7SS  
T: 0151 702 4219  
Offer mouthwash testing: Yes

### **Northern Genetics Service**

Institute of Human Genetics  
Central Parkway  
Newcastle upon Tyne NE1 3BZ  
Offer mouthwash testing: Yes  
Blood sample preferred for cascade testing

### **North Thames (West) Regional Genetics Centre**

The Kennedy Galton Centre  
Northwick Park Hospital and St Mark's NHS Trust, Watford Road,  
HARROW HA1 3UJ

### **Oxford Regional Genetics Service**

The Churchill  
Old Road,  
OXFORD OX3 7LJ

### **North Trent Clinical Genetics Service**

Sheffield Children's Hospital  
Western Bank  
SHEFFIELD S10 2TH  
T: 0114 271 7025  
Offer mouthwash testing: Yes

### **Nottingham Centre for Medical Genetics**

H Block, City Hospital NHS Trust  
Hucknall Road  
NOTTINGHAM NG5 1PB  
T: 0115 9627728  
Offer mouthwash test: Not routinely (ie blood sample needed)

**South Thames (East)****Regional Genetics Centre**

Genetics Centre,  
8<sup>th</sup> Floor Guy's Tower  
Guy's Hospital  
LONDON SE1 9RT  
T: 020 7188 1364

Offer mouthwash testing: No

**South Thames (West)****Regional Genetics Centre**

Medical Genetics Unit  
St George's Medical School  
Cranmer Terrace  
LONDON SW17 0RE  
T: 020 8725 5335

Contact: Genetic Department

Offer mouthwash testing: No. Blood sample required.

**South Western Regional Genetics Service**

Department of Clinical Genetics  
Bristol Royal Hospital for Children  
St Michael's Hill  
BRISTOL BS2 8BJ  
T: 0117 928 5652

**University Department of Medical Genetics and Regional Genetic Service**

St Mary's Hospital, Hathersage Road  
MANCHESTER M13 0JH  
T: 0161 276 6506  
Offer mouthwash testing: Yes

**Wessex Clinical Genetics Service**

Princess Anne Hospital  
SOUTHAMPTON SO16 5YA  
T: 02380 796166

Offer mouthwash testing: Mouthbrush testing offered

**Yorkshire Regional Genetics Service**

Department of Clinical Genetics  
Ashley Wing  
St James's University Hospital  
LEEDS LS9 7TF

**SCOTLAND****Dundee – Human Genetics**

Ninewells Hospital, Pathology Department  
DUNDEE DD1 9SY  
T: 01382 632614

(Genetics Nurse Specialist)

Offer mouthwash testing: Yes

**North of Scotland****Regional Genetics Service**

Medical School, Foresterhill  
ABERDEEN AB25 2ZD  
T: 01224 552120

Offer mouthwash testing: Yes

**South East Scotland Clinical Genetics Service**

Western General Hospital  
Crewe Road  
EDINBURGH EH9 1LF

**For further help and advice you can contact:**

**West of Scotland Regional**

**Genetics Service**

Yorkhill Hospitals

Institute of Medical Genetics

GLASGOW G3 8SJ

T: 0141 201 0365

Offer mouthwash testing: Yes

**Cystic Fibrosis Trust,**

**11 London Road**

**Bromley**

**Kent BR1 1BY.**

**Tel: 020 8464 7211**

**Fax: 020 8313 0472**

[enquiries@cftrust.org.uk](mailto:enquiries@cftrust.org.uk)

[www.cftrust.org.uk](http://www.cftrust.org.uk)

**WALES**

**Medical Genetics Services for Wales**

Institute of Medical Genetics

University Hospital of Wales

Heath Park

CARDIFF CF4 4XW

T: 02920 744035

Offer mouthwash testing: In special  
circumstances, normally blood sample.

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**NORTHERN IRELAND**

**Northern Ireland Regional Genetic  
Service**

Floor A, Belfast City Hospital Trust

Lisburn Road

BELFAST BT9 7AB

T: 028 9026 3873

Offer mouthwash testing.

**CENTRES LISTED WITHOUT  
DETAILS HAVE NOT PROVIDED  
THEM TO US.**