IMPORTANCE FOR FAMILY MEMBERS

Until recently, there was no treatment for pulmonary fibrosis, other than lung transplantation. Now there are medicines available that can slow the worsening of the pulmonary fibrosis. Because symptoms of pulmonary fibrosis only occur once the disease has advanced considerably, it is assumed that starting medication earlier would be sensible. If someone is known to have a hereditary predisposition for pulmonary fibrosis, regular check-ups are recommended to discover and treat the pulmonary fibrosis at an earlier stage.
The check-ups consist of:

- annual lung function and blood testing (liver values and complete blood panel)
- HRCT once every 5 years

EXAMINATION OF FAMILY MEMBERS

Families in which a hereditary predisposition is found:
In some patients DNA testing reveals that the pulmonary fibrosis is caused by one specific DNA mutation. This can be examined in family members through DNA testing of a blood sample to see if they have inherited that mutation. Family members who turn out to be carriers of the mutation have an increased risk of developing pulmonary fibrosis. Carriers are advised to have regular check-ups by a pulmonologist specialised in pulmonary fibrosis once they become adults.

Families in which no hereditary predisposition is found:
In families that are found not to have a DNA mutation that causes pulmonary fibrosis (as far as can currently be determined), the disease can still be hereditary. Family members cannot be examined for their carrier status with DNA testing. But family members are recommended to have regular check-ups.

CONSIDERATIONS

If pulmonary fibrosis can be detected early on, the disease can be treated earlier. There can be disadvantages, however, with examining someone who does not (yet) have symptoms. For example, they can feel less healthy if a lung disease (or a genetic predisposition for it) is diagnosed. Or it can raise questions when arranging a life or disability insurance policy. An insurer in the Netherlands is only allowed to ask about hereditary diseases when a life or disability insurance policy that exceeds a certain legally set limit is being arranged.

DO I NEED A REFERRAL FOR GENETIC TESTING

In the Netherlands a referral from a pulmonologist or GP is needed for genetic testing.
There it is best to get a referral to a Genetics Department that works with and consults an expertise centre for pulmonary fibrosis.

COST

You can ask your own insurer for details.

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Familial pulmonary fibrosis

This folder contains information about familial pulmonary fibrosis. Pulmonary fibrosis can be a hereditary condition.

What this is, how it can be diagnosed, and what it means for family members of familial pulmonary fibrosis patients are detailed in this folder.

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Familial pulmonary fibrosis

EXPLANATION OF CLINICAL PICTURE AND DIFFERENT TYPES

Pulmonary fibrosis is a rare and severe lung disease in which fibrosis (scar tissue) develops around the alveoli. The fibrosis restricts more and more the amount of oxygen that can be absorbed by the lungs. A pulmonologist diagnoses pulmonary fibrosis through a combination of physical examination, lung function tests and a CT scan of the lungs.
There are many different types of pulmonary fibrosis. Pulmonary fibrosis can develop after exposure to radiation, breathing in certain substances, specific infections and the use of certain medicines. There can also be an underlying auto-immune disease, for example scleroderma or rheumatism. There is also a hereditary form of pulmonary fibrosis.

WHAT ARE THE SYMPTOMS OF FAMILIAL PULMONARY FIBROSIS

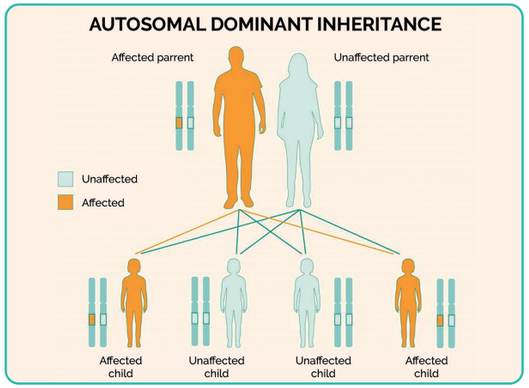
Symptoms can vary widely from person to person. In most cases the symptoms start developing at a later age (50-70 years), but pulmonary fibrosis can also occur earlier. The symptoms can consist of a worsening cough that does not abate, shortness of breath upon exertion (get out of breath faster) and fatigue. External factors like smoking, infection, metal dust, stone dust and wood dust can worsen and accelerate the scar formation.

HOW OFTEN DOES IT OCCUR AND IN WHOM

In the Netherlands between 2000 and 3500 people have pulmonary fibrosis, the precise number is unknown. Pulmonary fibrosis occurs in both men and women. Most people with pulmonary fibrosis are the only one in their family with the disease. In about 20% (1 in 5) there are also affected family members. If two or more family members have pulmonary fibrosis, familial pulmonary fibrosis is diagnosed, and there is a need for genetic testing.

HEREDITARY ASPECT OF PULMONARY FIBROSIS

If someone has familial pulmonary fibrosis, then there is usually a 50% (1 in 2) chance of transmitting the predisposition for pulmonary fibrosis to their children. This applies to their sons and daughters. Not everyone who has the predisposition for familial pulmonary fibrosis will develop the symptoms. The severity of fibrosis formation and the age at which symptoms manifest can vary widely.



INDICATION FOR GENETIC TESTING

There is an indication for genetic testing if:

- Pulmonary fibrosis is diagnosed in 2 or more family members
- Combination of pulmonary fibrosis / bone marrow failure / liver cirrhosis / squamous cell carcinoma in one family or one patient
- Patient with pulmonary fibrosis who is younger than 50 years old.

WHAT DOES THE GENETIC TESTING INVOLVE?

If there is an indication for genetic testing, the patient or family member can referred to a clinical geneticist. The pulmonologist or GP can do this. The patient or family member will first talk with a clinical geneticist. This can be done by telephone, video calling or in the outpatient clinic.

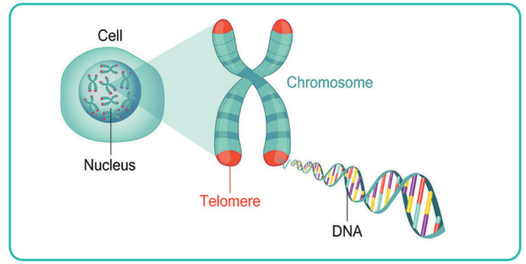
- The family history will be discussed and a family tree created.
- You will be given information about familial pulmonary fibrosis, how the disease is inherited and the consequences of DNA testing.
- The medical details of affected family members will be requested.
- DNA testing of the blood of a family member who has pulmonary fibrosis will be initiated.
- If all affected family members have died, then, in the Netherlands, a search will be made for any DNA stored in the biobank.
- Once the outcome of the DNA testing is known, it will be discussed along with its meaning for family members.

WHAT DOES THE DNA TESTING INVOLVE?

DNA testing is done on a blood sample. The genetic material – DNA – is isolated from the blood. The genes that could cause pulmonary fibrosis can be examined in DNA. Of course, this is done in compliance with the privacy legislation rules, and the data are not shared with third parties without your permission.
The genes for familial pulmonary fibrosis can be classified into two groups:

- **Surfactant genes**
  These genes play a role in producing a fluid. The fluid ensures that the alveoli remain open when someone breathes. Due to a mutation in one of these genes, this fluid cannot be properly produced. Then the alveoli can be damaged, leading to scar tissue.

- **Telomere-related genes**
  These genes play a role in cellular division. Due to a mutation in one of these genes, this division does not proceed properly. As cells continue to divide our entire lives, such a mutation can lead to damage of bodily tissues, including the lungs.



OTHER SYMPTOMS

Changes in telomere-related genes can also produce problems outside the lungs. Possible problems arising are: bone marrow problems (bone marrow failure and leukaemia), liver disease (cirrhosis), mucosal cancer (in the mouth/throat area and around the anus/genitalia) and congenital skin, hair and teeth aberrations.
The symptoms can also arise earlier in the next (or later) generation.

It is likely that we have not yet found all of the genes for familial pulmonary fibrosis. If the DNA testing does not find any disease-causing mutation, the pulmonary fibrosis can still be familial.

Pulmonary fibrosis is a shared disorder

From left to right: Bram, Harry and Marc de Wit.
The three brothers have pulmonary fibrosis.