BijnierNET

Information for patients and their families and friends about

Pheochromocytoma

Appendix to the 'Quality of Care Standard for Adrenal disorders'

Introduction

This brochure is intended for people who have a pheochromocytoma and their families and friends. Although we use the pronoun 'you' and 'our' throughout this brochure, it is also intended for people in the immediate circle of a person with a pheochromocytoma; for the sake of readability, 'the patient' is taken to be a man. Healthcare practitioners can also use this brochure as a source of useful information.

This information is not intended to replace the advice of a competent physician. If you have any queries or need advice, get in touch with your GP or your specialist.

The medical information in this brochure is based on the Quality of Care Standard for Adrenal Disorders (in Dutch only), the Guidelines published by the American Association of Clinical Endocrinology (in 2014) and the Guidelines of the European Society of Endocrinology (2016) - see icons.

Journal of Clinical Endocrinology & Metabolism, June 2014

European Journal of Endocrinology, May 2016

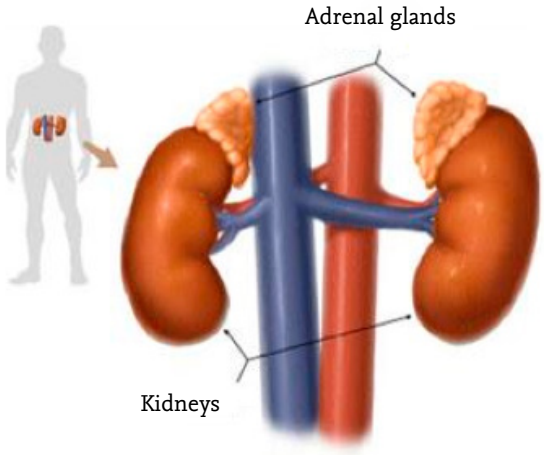
Say hello to ...
Hans-Joris aged 48

He's been feeling under the weather for quite a while. Fortunately, his garage business is doing well. But he's becoming more worried about his health. Sometimes it feels as if an elephant is dancing on his chest. He undergoes tests. There are no negative results for his heart or his lungs, except that his blood pressure is so high.

What is a pheochromocytoma?

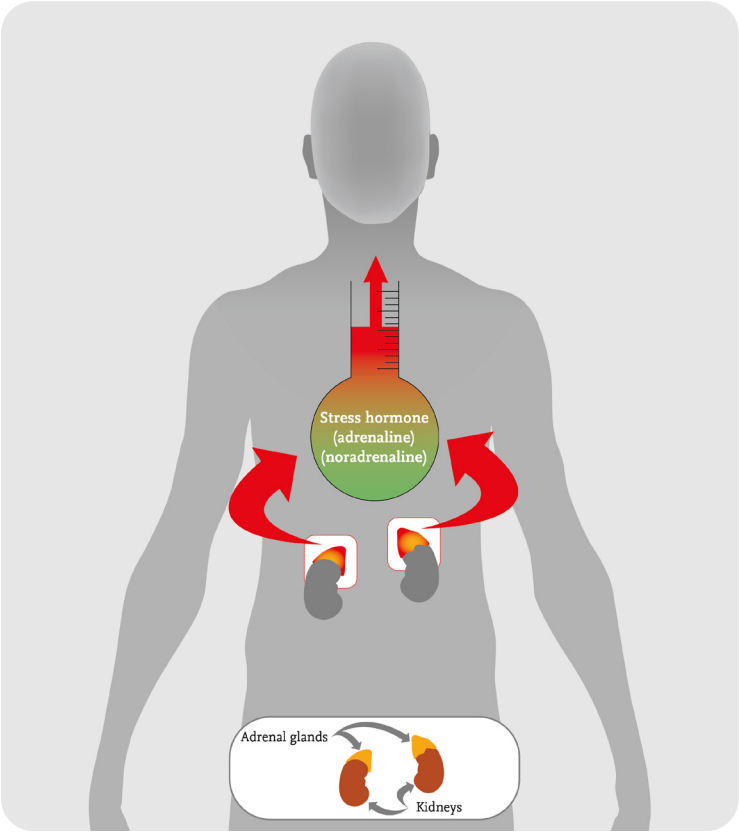
Everyone has two adrenal glands, one on each kidney, right and left. The adrenal glands consist of two parts: the outside (known as the cortex) and the inside (known as the medulla). Further information about the adrenal glands and the hormones that they produce can be found at adrenals.eu

adrenals.eu/brochure.



Pheochromocytoma

A pheochromocytoma is a tumour of the medulla of the adrenal glands that causes overproduction of stress hormones (adrenaline, noradrenaline).



Paraganglioma

A tumour of this kind can also occur outside the adrenal glands: in the chest cavity, the stomach cavity and in the pelvic area. Doctors also call this type of pheochromocytoma a paraganglioma. Paragangliomas can also occur in the head and neck area. But this type of head/neck paraganglioma, previously known as 'glomus tumours', are quite different from pheochromocytomas. They do not produce adrenaline or noradrenaline, but they do sometimes produce dopamine. The process of diagnosis and treatment is also quite different from pheochromocytomas.

Pheochromocytomas and paragangliomas are rare disorders. In the Netherlands, there are approximately 100 new patients a year with a pheochromocytoma and around 20 with a paraganglioma. Quite often these patients are in the 30 to 60 age group, but all ages can be affected. 20 to 50% of paraganglioma tumours are malignant.

What are the symptoms of a pheochromocytoma?

A pheochromocytoma causes a number of health-related symptoms. There are two reasons for this:

1. the 'overdose' of stress hormones, namely adrenaline and noradrenaline (catecholamines)
2. pressure of the tumour against surrounding tissue.

The excess stress hormones make you feel unwell, and you may develop symptoms that persuade you to consult your family doctor.

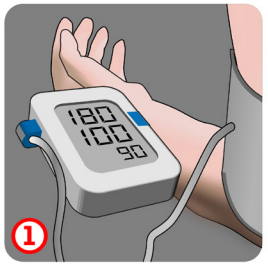
Patients say that they experience a range of different symptoms. You can find a diagram with the most common symptoms on page 7.

You won't necessarily experience all these symptoms. That partly depends on the size of the tumour. The list might help you to identify symptoms you have already noticed. The symptoms can come on suddenly, sometimes described as attacks or spells, without any cause you can pinpoint. In this situation, you are getting a sudden and severe increase of the stress hormones adrenaline and noradrenaline in your blood.

A pheochromocytoma attack can result in dangerous situations with a strong rise in blood pressure and heart rhythm disorders. This can, in turn, lead to a heart attack (myocardial infarction), a stroke (CVA + TIA), reduced consciousness and - sometimes - to death. A pheochromocytoma attack can occur without any obvious cause, but it can also be triggered by an operation or by the use of certain medicines for example. Even without attack-related symptoms, people with a pheochromocytoma or paraganglioma have a greater chance of developing cardiovascular disorders and diabetes mellitus.

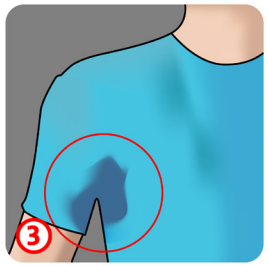
Patients who have a paraganglioma in the neck (a glomus tumour) say they experience other symptoms, including: reduced hearing, tinnitus, hoarseness, pain and coughing.

The disorder can also be diagnosed by coincidence - during a scan of the abdomen, for example - without the patient noticing any of the symptoms.



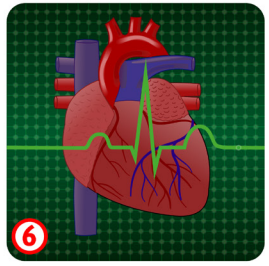
High blood pressure.

Headache.


Excessive sweating.


Hot flushes.


Shaking.


Heart palpitations.

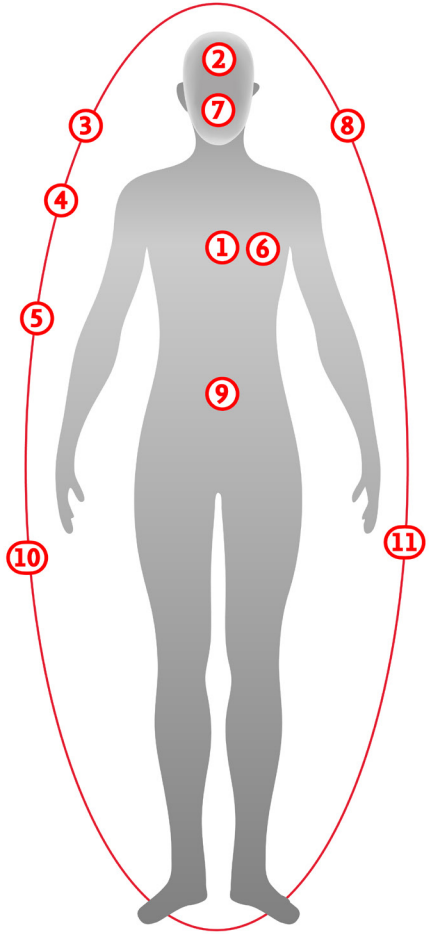

Paleness.


Anxiety/panic.


Nausea, vomiting, abdominal pain.


Weight loss.


Tiredness.



What causes a pheochromocytoma?

In about one-third of cases, there is a hereditary tendency to develop a pheochromocytoma. The tumour is caused by an error (mutation) in the genetic makeup or DNA. This tumour is called a pheochromocytoma or a paraganglioma. Various mutations have been identified, and each has its own specific characteristics. Genetic testing is always carried out nowadays, especially in patients who are still young.

Examples of hereditary forms of pheochromocytoma and paraganglioma are:

- multiple endocrine neoplasia (MEN) type 2 syndrome
- neurofibromatosis type 1 (Von Recklinghausen's disease, VRD)
- Von Hippel-Lindau disease (VHL) or
- a hereditary paraganglioma syndrome caused by an error in a gene (SDH mutation)

The animated clip 'What is a Pheochromocytoma? provides a more detailed explanation (unfortunately only in Dutch).

How is the diagnosis pheochromocytoma established?

Delayed diagnosis

Generally speaking, the search for an explanation for the symptoms starts with a visit to the family doctor. He will refer you to the hospital.

Unfortunately, pheochromocytomas are not usually identified quickly, sometimes only several years after the symptoms started. A pheochromocytoma is a rare disorder. During their career, only a few medical specialists and even fewer family doctors will come into contact with a patient who has a pheochromocytoma. Moreover, the symptoms that the patient experiences are often non-specific. This means that the symptoms have no direct link to the diagnosis of pheochromocytoma. These are two reasons why people speak of a 'search' for the diagnosis.
Studies have shown that the average time that elapses between the beginning of symptoms and the diagnosis is around three years. For the patient, his family and friends this leads to a difficult period, full of doubt and uncertainty.

Ultimately, the diagnosis is usually given by an endocrinologist or other internal specialist.

Blood and urine tests

If the internal medical specialist or endocrinologist considers the possibility that a pheochromocytoma or paraganglioma might be present, he will first check whether the patient has a raised level of stress hormones in his blood. This can be tested in the blood or from a 24-hour collection of urine. This test checks the levels of metanephrine, normetanephrine and 3-methoxtyramine . These are substances (called metabolites) that occur when the hormones adrenaline and noradrenaline are broken down. They constantly leak from the tumour and get into the bloodstream.

Before the blood sample is taken, you will be asked to lie down quietly for 20 minutes, because taking blood in the usual sitting position can lead to raised levels of metanephrine and normetanephrine - even in healthy people.

For the 24-hour urine test, you will be asked to collect all your urine over a 24 hour period. The laboratory will provide a special jar.

Before the tests can be carried out, your medical specialist will need to know what medication you are taking. Some medicines affect the results of the test, so it might be necessary to stop taking them temporarily.

The diagnosis of pheochromocytoma can be made on the basis of the results of the blood and urine tests. The next step is to determine where the tumour is located.

Imaging test

Medical imaging technology such as a CT scan, an MRI scan, an MIBG scan or a PET CT scan will be used to determine the exact location of the tumour or tumours.

MRI scan

An MRI machine takes photos with the aid of a strong magnet. The MRI machine is shaped like a tunnel, which you lie in. An example of an MRI can be found here (Dutch only).

CT scan

CT scanners take photographs using the same technology as for X-rays. The CT machine is shaped like a short tunnel. Examples of how CT scans are carried out can be found here (Dutch only).

MIBG scan (a.k.a. Scintigraphy)

MIBG is a radio-active 'tracer' substance that makes a tumour visible under a scanner. The small amount of this substance that is used is not harmful; it will be eliminated from your body with your urine.

PET scan

The PET scanner takes photos of your body in order to detect tumours and infections. A small amount of radio-active 'tracer' will be injected into a blood vessel in your arm. The tracer allows a pheochromocytoma or paraganglioma to be detected.

These imaging techniques make it possible to establish the exact location of the tumour. This is an important factor in the further treatment regime.

The website of the Dutch Association for Clinical Chemistry & Laboratory Testing (NVKC) provides an overview of the tests that are carried out in the laboratory. Unfortunately, the website is only in Dutch. If you type in the substance that is being tested for in your blood or urine, the site provides you with a summary of what the test entails, when it is carried out and what the results mean.

If you have any further questions you can contact a clinical chemist via the same website (Dutch only).

How is a pheochromocytoma treated?

A pheochromocytoma is treated with a surgical operation. Specialists prefer to carry out the operation using the laparoscopy technique (keyhole surgery). Keyhole surgery should, by preference, be carried out in a centre of expertise with the aid of a surgical robot. During the operation, the entire adrenal gland - including the tumour - will be removed.

a. Preparing for the operation

During the operation, the tumour might produce stress hormones and this could lead to very high blood pressure or heart rhythm disorders. That would be very risky.

To prevent that happening, you will be asked to take medicines to reduce your blood pressure (alpha blockers) for at least two weeks before the operation. These medicines block the receptors that are activated by adrenaline or noradrenaline. They counteract the effect these hormones have on your blood pressure. Because these medicines cause the blood vessels to expand and become wider, it is necessary to eat a salt-rich diet to prevent the effects of falling blood pressure.

Usually, patients are given a salt solution by IV (in the arm) a few days before the operation. It is also important that you drink enough fluids, approximately 3 litres (about 100 fluid ounces) each day.

These preventive measures reduce the risks of an operation to a minimum. Doctors will give special attention to patients who also have diabetes mellitus, kidney failure or cardiovascular disorders. After consultation with the patient's specialist, the treatment can be adapted so that the patient is in a stable condition and the operation can be carried out as safely as possible.

b. During the operation

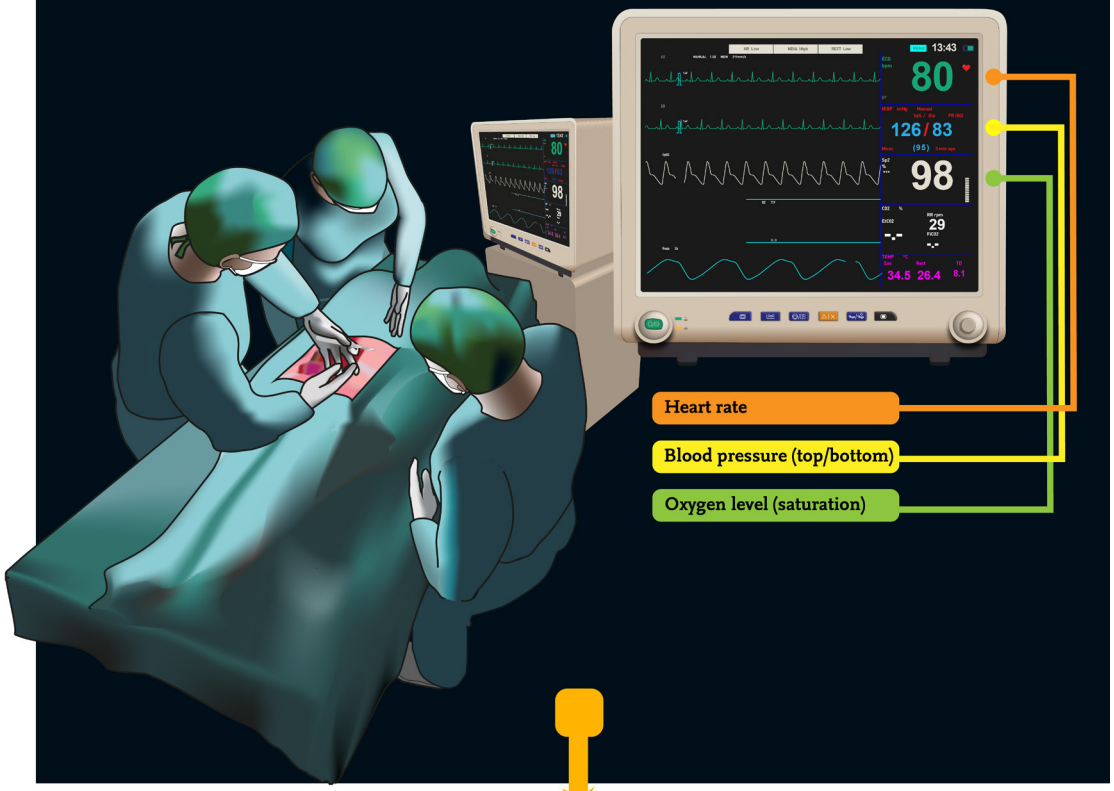
There are various reasons why you will lie on the operating table on your side, on your stomach or on your back. This can depend, for example, on your posture, whether you have had previous operations, or the extent of the tumour. For example: whether it is a malignant pheochromocytoma/paraganglioma.

An impression of the procedure

Preparation for the operation with blood pressure lowering medication. Extra salt intake. Shortly before the operation, saline solution via a drip in the arm.

Prevention of high blood pressure or blood pressure fluctuations during the operation.

Operation



Check stress hormones
- *plasma metanephrines*
- *24 hour urine (nor)metanephrines*

Annual check-up in outpatients' clinic

During the operation, the surgeon and the anaesthetist will cooperate closely. The anaesthesiologist will be particularly alert to possible changes in the blood pressure and the heart rhythm during the operation.

If there is any disruption, the anaesthesiologist can intervene immediately.

In the first 24 to 48 hours after the operation, the patient will be closely monitored on the intensive care unit or a medium-care ward. Staff will watch closely for changes in blood pressure, heart rhythm, kidney function and will monitor the level of sugar (glucose) in the blood.

If you have already had an adrenal gland removed, the so-called 'stress medication schedule' will be followed. In the period around the operation, you will be given extra high doses of hydrocortisone. This is important, because after the second adrenal gland is removed you will have primary adrenal insufficiency (AI).

For more information on this subject, you can refer to the information brochure entitled 'Adrenal Insufficiency'.

After the operation, it will be necessary to gradually reduce the higher doses of hydrocortisone that you were given around the operation until you get down to the 'normal' cortisone substitution level for AI.

The folder with the stress medication schedule provides further information about reducing the hydrocortisone medication.

When only one adrenal gland is removed, the remaining adrenal gland will usually take over the task of its counterpart.

c. Treatment and monitoring after the operation

After the operation, tests will be carried to check whether the level of stress hormones in your blood is still too high. This can again be tested in the blood itself or from a 24-hour urine collection.

You will not normally stay in hospital very long. In the Netherlands, the stay ranges from 3 to 5 days as long as no complications arise. Complications such as internal bleeding or infections are rare. After a laparoscopic operation, you will only have a couple of small cuts in the skin of your abdomen or your back.

In some cases, the tumour can recur after removal; secondary tumours (metastases) can also occur outside the adrenal gland. For this reason, you will continue to have regular check-ups for at least 10 years.

You will have an appointment at the outpatient clinic once a year when the blood test or 24-hour urine test will be repeated. You will be given information about when you should provide your blood sample or start collecting your urine.

If doctors consider you have a high risk of developing a new pheochromocytoma, you will remain under medical supervision for the rest of your life. That might be the case if it is discovered that you have a hereditary form of the disease. Large tumours always mean that you remain under medical supervision for the rest of your life. If the pheochromocytoma is discovered before you are 20 years of age, you will also remain under life-long medical supervision.

A pheochromocytoma during pregnancy

The occurrence of a pheochromocytoma during pregnancy is very rare, but it is important because this is a very serious situation. Given the rarity of a pheochromocytoma during pregnancy and the subsequent birth, treatment in the Netherlands is only provided in a small number of expert centres. Ask your endocrinologist or internal medical specialist to refer you to one of these centres if you are not already consulting a doctor there. This also applies if genetic testing is to be carried out.

How is patient care organised?

Care for patients with pheochromocytoma is complex. It is a rare disorder and testing and treatment demand specific medical expertise, knowledge and skills.

The care for patients with a pheochromocytoma in the period before and during the operation is highly specialised and - in the Netherlands - is only provided in a hospital which can call on a team that has experience of the disorder. This hospital is then designated a centre of expertise.

Various healthcare practitioners are involved in patient care, including an endocrinologist, surgeon, urologist, anaesthesiologist, cardiologist, radiologist, a specialist in nuclear medicine, clinical geneticist, pathologist and specialised nurses. It is essential that this multi-disciplinary team is well organised.

Are you looking for a hospital with the necessary experience? Then check out the website of the Dutch Federation of University Medical Centers via the TRF portal. The website is in Dutch, but you can select the tab 'Zoek TRF' and type in "Feochromocytoom". A list of the relevant Dutch centres will be presented.

The team includes various disciplines

Your medical specialist will inform your family doctor about the diagnosis of pheochromocytoma. The specialist will also get in touch with other healthcare practitioners if necessary.

Before you agree to have an operation, it is advisable to ask your medical specialist the following questions:

1. How many adrenal operations do you carry out each year, Doctor? (More than 10, preferably more than 20)
2. Will you operate via the abdomen or from the back (RPA)?
3. Does the hospital have a multi-disciplinary adrenal team in house?

Check-ups at the outpatient clinic

When you are released from the hospital, an appointment will be made for a check-up.

Every year, the medical specialist will talk to you about your health situation after the pheochromocytoma was removed. The medical specialist will continue to have contact with the other disciplines after the operation.

The medical specialist will estimate the risk that you will develop a pheochromocytoma once again. You will also be offered genetic testing for that purpose.

You should prepare yourself for the appointments with your medical specialist so that you go on receiving the best possible medical assistance. You can also discuss any other subjects that you run up against or have doubts about.

Here are some suggestions for subjects that you might talk about:

- results of the blood test or urine test
- the medicines and possible side-effects
- the consequences of long-term high blood pressure
- the consequences of the operation
- new symptoms
- the social consequences, such as effects on your work or hobbies
- the psychosocial consequences, in connection with your relationships for example
- day-to-day support, via home help for example or informal care.

Any questions you have will be welcome. Never be afraid to ask your specialist or the nurse-specialist questions!

Life after a pheochromocytoma

The symptoms caused by a pheochromocytoma usually disappear completely after the cause has successfully been removed. You can expect that you will soon feel much better. Some patients do however have residual symptoms. The symptoms that affected you physically and mentally during the illness can go on having an impact on your work and your relationships for quite some time.

The raised blood pressure, for example, may have caused damage to the heart, the blood vessels, the brain or the kidneys. These are, however, exceptions.

Even after the operation, some patients will still have high blood pressure which has to be treated. In addition, it is important that checks are made for risk factors for cardiovascular diseases, so that these risk factors can be adequately treated.

Other patients report that they feel tired for some time after the operation. Tiredness or fatigue can interfere with day-to-day tasks or might mean that you are no longer able to enjoy a particular hobby.

Patients who have had an abdominal operation can experience pain for some time, and this extends the recovery period.

It is advisable to watch the mini documentary on pheochromocytomas. In the documentary, a patient tells about the journey up to the diagnosis, the treatment and the period afterwards. (unfortunately both films only in Dutch)

Recovery from a pheochromocytoma, Suzan - 1
Recovery from a pheochromocytoma, Suzan - 2

Do you want to know more about a pheochromocytoma?

Your healthcare professional can put you in touch with patient associations that you could join, so that you can have access to and benefit from the experience and information of other patients.

Membership of a patient association brings a lot of benefits, so membership is a serious option for you to consider. In addition, the patient organisations in the Netherlands also promote the interests of their members by entering into discussions about the care to be provided and the availability and supply of medicines. They also provide reliable information about the various clinical aspects of the disorders. They also organise meetings so that patients can meet each other and/or learn about the latest developments.

Some Dutch healthcare insurers will pay part or all of the membership fee.

- adrenals.eu
- www.bijniernet.nl
- www.nvacp.nl
- www.paragangliomen.nl
- www.nve.nl
- www.nvkc.nl

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