Adrenocortical Carcinoma (ACC)

NET Patient Foundation
Adrenocortical Carcinoma - ACC

Cancer of the adrenal cortex affects between 50-100 people per year.

There are different types of adrenal tumours. These tumours can develop in either the cortex or the medulla of the adrenal gland. The benign tumours of the cortex are called adrenocortical adenomas, and the malignant tumours are called adrenocortical carcinomas. Adrenocortical carcinoma is the most accurate term used to describe cancer arising in the part of the adrenal gland that makes steroid hormones (the cortex). Doctors and other medical staff involved in the management of adrenocortical carcinoma frequently use the term ‘adrenal cancer’. In this booklet we have used the term adrenocortical carcinoma as well as its abbreviation ACC.

Being diagnosed with a rare cancer can be an extremely isolating and frustrating situation. It might be hard to find a specialist that can help or anyone who has been through the same as you. You might not be able to find information to help inform you of what to do or where to go. We hope that in some way this booklet will answer some of the questions that you may have about your condition.

If you require further information or support please do not hesitate to call or email the NET Patient Foundation www.netpatientfoundation.com. Further details can be found at the end of this booklet.
What is Cancer?

The body is made up of hundreds of millions of living cells. Normal body cells grow, divide, and die in an orderly way. During the early years of a person’s life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out, damaged, or dying cells.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of this out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells keep on growing and form new cancer cells. These cancer cells can grow into (invade) other tissues, something that normal cells cannot do. Being able to grow out of control and invade other tissues is what makes a cell a cancer cell. Carcinoma is a term used to describe tumours that are cancerous and malignant (having the ability to spread and invade other tissue).

In most cases the cancer cells form a tumour. But some cancers, like leukaemia, rarely form tumours. Instead, these cancer cells are in the blood and bone marrow. Tumours can be benign or malignant. In this booklet ‘tumour’ refers to a malignant ACC.

When cancer cells get into the bloodstream or lymph vessels, they can travel to other parts of the body. There they begin to grow and form new tumours that replace normal tissue. This process is called metastasis.

No matter where a cancer may spread, it is always named for the place where it started. For instance, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is called metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their own kind of cancer.

This booklet is looking at Adrenocortical Carcinoma (ACC): what it is, and how it is diagnosed and treated.

ACC is a rare form of cancer with an incidence worldwide of about 1-2 new cases per million per year.

Most ACC’s occur sporadically (meaning that they do not have a genetic link), but they may also be part of a congenital (present at birth) and/or familial (have a genetic family connection) condition.
What are the Adrenal Glands?

The adrenals are small glands that sit above each of the kidneys, as shown in the picture below. The kidneys are found deep inside the upper part of the belly (abdomen).

The adrenal gland has 2 parts. The outer part, called the cortex, is where adrenocortical carcinomas start. The cortex makes certain hormones for the body. These hormones are called steroids. The inner part of the adrenal gland, called the medulla, is really part of the nervous system. Nervous system hormones are made in the medulla, an example is adrenaline.
Adrenocortical carcinomas are usually found because of the symptoms they cause. They may make hormones as mentioned above that cause body changes. Some adrenal cancers get very large and cause symptoms by pressing on other organs. There are 2 types of ACC:

1- Hormone Secreting - This means that a substance that is normally secreted by non cancerous cells, are secreted too much by the abnormal cells. In this type of ACC, two major steroids are over secreted. These are called androgen and glucocorticoid.

Glucocorticoid over secretion is responsible for Cushing's Syndrome which can lead to diabetes, high blood pressure, dysfunction in sexual organs in men and women, muscle weakness and wasting, weight gain, early puberty in children, osteoporosis, a reduction in the immune system function and psychological changes.

Androgen over secretion can cause many abnormalities in women. Menstrual abnormalities, infertility, excess facial or body hair in women, baldness and deepening of the voice.

2- Non-functioning - These tumours are likely to present with symptoms due to the tumour burden, such as pain or swelling, weight loss or metastatic disease. They do not have clinical features of hormone excess, although sometimes hormones that do not cause any effects are found in the blood or urine. Sometimes tumours are found by chance, during an imaging procedure unrelated to any suspicion of adrenal disease. These tumours are described as ‘incidental’, and if an incidental tumour is larger than about 5 or 6 centimetres (2-2.5 inches), it may well be cancerous and surgery will be recommended.

Most cancers found in the adrenal gland did not start there and are not adrenal cortical cancers. These cancers started in other organs and then spread to the adrenal glands. For example, lung and breast cancers often spread to the adrenal glands. But these cancers are named after the place where they started. They are not called ACCs, and they are treated like the cancers where they started.
What Causes ACC?

Scientists do not know exactly what causes most adrenocortical carcinomas. Over the past few years, they have made great progress in learning how certain changes in a person’s DNA can cause cells in the adrenal gland to become cancer. DNA carries the instructions for nearly all the things our cells do. We often look like our parents because they are the source of our DNA. But DNA affects more than the way we look. DNA changes play a part in our risk for getting certain diseases including some types of cancer. Adrenal tumours are common, but ACCs are not. Most DNA changes that are seen in cancers happen during life rather than having been inherited. These changes may be caused by exposure to radiation, lifestyle or cancer-causing chemicals. But many of these changes happen for no known reason.

A risk factor is anything that increases a person’s chance of getting a disease. Different cancers have different risk factors. Some risk factors, such as smoking, can be controlled. Others, like a person’s age or race, can’t be changed. But scientists have found a few risk factors that make a person more likely to get adrenal cancer. Even if a person does have one or more risk factors for adrenal gland tumours, we can’t know for sure how large a part they played in causing the cancer.

Family history: Most ACCs are not linked to heredity. But certain clusters of symptoms called syndromes can cause a higher risk of several types of cancer, including ACC. Some of these syndromes are:

- Li-Fraumeni Syndrome
- Beckwith-Wiedemann Syndrome
- Familial adenomatous polyposis (FAP)

ACCs due to these syndromes are very rare indeed.
How is ACC Found?

It is hard to find ACCs early. In most cases the tumour has grown quite large before it is found. It is often found earlier in children than in adults because children react more to the hormones these tumours make. In adults, these tumours may be found early by accident, for example when a CT scan is done for some other health problem. Mostly, ACC is found due to the symptoms caused by either the hormones they make or because the tumour has grown large.

What tests are needed?
These days, the first imaging test to be used is likely to be a CT scan, and other tests may be used both to find out more about the size and spread of the tumour to local structures or distant areas such as liver and lungs. This enables the doctors to determine the ‘stage’ of the disease, i.e. how advanced it is, and to select the right treatment or combination of treatments. Not all the tests described need to be performed in every patient. Biochemical tests of urine and blood are also essential to look for hormones that the tumour may be making.

Imaging tests are ways to take pictures of the inside of your body. One or more of these tests may be done if the doctor thinks you may have an ACC.

CT scans (computed tomography): A CT scan uses x-rays to make detailed pictures of your insides. Instead of taking just one x-ray, a CT scanner takes many pictures as it moves around you. A computer then combines these into a picture of a slice of your body. CT scans can show the adrenal glands and can often confirm whether a tumour is present, how large it is, and whether it has spread to nearby sites. CT scans also show the organs near the adrenal glands, as well as lymph nodes and distant organs. This test can help show if the cancer has spread to the liver or other organs.

Before any pictures are taken, or after the first scan, you may also get an IV (intravenous) line through which you get a contrast dye. This helps the outline structures in your body look clearer. The contrast dye can cause some redness and a warm feeling that may last hours to days. A few people are allergic to the dye. Rarely, more serious reactions like trouble breathing and low blood pressure can happen. Medicine can be given to prevent and treat these problems. Be sure to tell the doctor if you have ever had a reaction to any contrast substance used for CT scans.

CT scans take longer than regular x-rays and you need to lie still on a table while they are being done. Also, you might feel a bit confined by the large ring the table slides through while the scan is being done.

PET scan (positron emission tomography): For a PET scan, a type of radioactive sugar is put into your vein. The sugar collects in cancer cells. A scanner can spot these areas. This test is useful for finding cancer that has spread beyond the adrenal glands. It is also helpful in finding adrenocortical carcinoma that has spread outside of the adrenal glands. The type of PET scan is called an F-FDF PET.
MRI (magnetic resonance imaging): MRI scans use radio waves and strong magnets instead of x-rays to take pictures. MRI pictures look a lot like those of a CT scan. An MRI scan can also show views from different angles. The MRI sometimes gives similar information to a CT scan but may be of extra value. In long term follow-up MRI may be used to avoid repeated irradiation from a CT scan. An MRI is especially helpful in looking at the brain and spinal cord.

MRIs are a little more uncomfortable than CT scans. First, they often take up to an hour. Also, you must lie still inside a narrow tube, which may be upsetting to some people. If you have problems with tight spaces, tell the doctor before your MRI is set up; you may be able to have the test done using an open MRI scanner. The machine makes thumping and clicking noises as the magnet switches on and off. Some places have earplugs or headphones with music to block this out.

Chest x-ray: This can show if the cancer has spread to the lungs. This might be performed to check on your health status before an operation.

Ultrasound: This test uses sound waves to make pictures of your insides. A computer shows the picture on a screen. This test can show if there is a tumour in the adrenal gland. It can also show if there is a tumour in the liver. This would not be the first choice of test as a CT scan would be preferable.

Blood and urine tests: If there is a suspicion that the tumour is making too much of a hormone, then it can be measured in the bloodstream or in a urine collection. In some patients hormone tests are done after a dose or a few doses of a synthetic steroid called dexamethasone given as a tablet. It may also be possible to detect hormones that do not cause any effect on the body. These can be useful after surgery to see if there is any evidence of recurrence of the tumour, and these are called ‘tumour markers’. In addition, it may be necessary to do more common blood tests to assess your general level of health.

Other tests:

Biopsy: With current imaging tests and biochemical tests it is unusual for a biopsy to be performed to make a diagnosis of ACC. In a biopsy a sample of tissue is removed to see whether cancer cells are in it. This test may be done before surgery by using a needle that takes out small pieces of tissue. A CT scan or ultrasound might be used to help guide the needle. If it looks as if the cancer has spread to another part of the body, such as the liver, then a biopsy may be done in those places, too.
**Staging of ACC**

Doctors use the term ‘staging’ to determine the extent of disease, and this guides the treatment and also gives information on the long term survival. The staging is done both by imaging tests and with further information obtained after surgery. It is vital that the staging tests are carried out, so that the right treatment option can be offered to you.

The stage of ACC is determined by the size of the primary cancer, the degree of local invasion, and whether it has spread to lymph nodes or other organs. If you want to know more about how your cancer is staged, please talk to your nurse or doctor.

**Treating ACC**

For ACC the only ‘curative’ option is surgery. This can be achieved if the tumour is localised (just in one place) and if stage 1 or 2 or 3. Follow-up is essential however even if ‘curative surgery’ has been achieved. Even after complete removal the tumour can recur, and your doctor would want to ensure that he/she caught any recurrence in good time. Unfortunately, ACCs can be quite a fast growing type of cancer. They are often diagnosed in the later stages (when they are quite advanced) and this means it can be difficult to cure them. Nevertheless, even if surgery cannot remove all the tumour, it may be helpful to reduce the volume to allow other treatments to be used.

ACCs are rare and treatment should be carried out by specialist teams. Specialist centres that offer surgery and other therapies for adrenal cancer will have a ‘multidisciplinary team’ that meet regularly to discuss ACCs. Nowadays, all decisions about surgery and other treatments should be taken by a team including a number of doctors of different specialities rather than one individual. You should make sure that you have been referred to a multidisciplinary team interested in ACC and other adrenal tumours.

Your doctor may suggest:

- Surgery
- Radiotherapy
- Chemotherapy
- Mitotane
- Combination treatments
- Clinical Trials
**Surgery**

If your cancer is diagnosed early enough, surgery to remove the cancer and the adrenal gland is the first choice of treatment and can cure the cancer. This operation is called an adrenalectomy. If your surgeon thinks the cancer may have spread locally, they will remove the tissues immediately surrounding the adrenal gland and nearby lymph nodes. When tumours are large it may be that they grow into surrounding structures such as the liver or kidney, in these cases surgery may still be possible but needs to be more extensive. Even when there is evidence that the tumour has spread (metastasised) to other organs it may still be appropriate to remove the initial tumour with other metastases removed later or treated by other means.

If you need to have one of your adrenal glands removed, your other one will carry on making all the hormones you need. If you have both adrenal glands removed, you will have to take hormone replacement tablets every day for the rest of your life.

**Surgical approaches**

The procedure your doctor will use will depend on the type and size of the tumour and also your individual needs. There are different surgical approaches that can be performed to remove malignant ACCs. Most frequently, surgeons will make either a horizontal, diagonal or vertical cut to open the abdomen, to remove the tumour. Since the tumours are often large, the incisions need to be large too. Sometimes surgeons use an incision in the side just below the ribs.

*Laparoscopic Adrenalectomy* - in this procedure, a number of small incisions are made in the abdomen for operating instruments and a fibre optic scope is inserted through a small incision to see inside the abdominal cavity. This is the preferred approach for small benign (non-cancerous) tumours since it is a less invasive procedure and generally causes less pain than other approaches. However, for ACC this is not usually either possible or appropriate and mostly the cancers are better treated by a conventional open operation. It may sometimes be used in cases where the tumour is fairly small and it is not clear if it is a cancer or not.
Mitotane (Lysodren)

Your doctor may suggest a drug called Mitotane (Lysodren). It works by damaging both normal and cancerous adrenal cells. Mitotane can be used in four different situations:

1 - Treatment of persistent or recurrent disease
If the initial surgery is unable to remove all the tumour or the tumour returns later, Mitotane has been proven to reverse the disease and can sometimes lead to complete remission for years. Most doctors would be cautious about claiming that it can ‘cure’ the condition in this situation. Mostly, Mitotane will be continued for life.

2 - Adjuvant therapy
There is evidence that Mitotane may be useful in preventing cancer returning when the surgical team think it has all been removed. In this setting, Mitotane is used for perhaps a few years although this is an uncertain area.

3 - Primary therapy
In some patients the disease is advanced and no surgical treatment can be performed. In this situation, Mitotane may shrink the tumour(s) and this can be monitored by a scan.

4 - Controlling hormone secretion
Sometimes hormones that cause problems remain high after surgery or when surgery cannot be undertaken. Mitotane may be helpful to control the hormone levels and prevent distressing symptoms.

Mitotane may be used alongside chemotherapy, although this is mostly in clinical trials. Mitotane can also treat the symptoms of advanced adrenocortical carcinoma. You take Mitotane each day as a number of tablets (often 6-12). Side effects are common and include nausea, and most often anti-sickness pills are used as well at the same time. Mitotane also causes tiredness and dizziness. Other side effects can occur but generally can be controlled by using a lower dose. Mitotane kills normal adrenal cells and the normal hormones need to be replaced with tablets caed hydrocortisone and fludrocortisone.

Mitotane is effective if the level in the body is controlled to a particular level (14-20mg/L). This requires blood samples to be taken every 1-2 months to keep the level high enough to kill the cancer cells, but not to cause side effects.

Radiotherapy

Radiotherapy is most often used for ACC that has spread. It can be very useful for shrinking cancer that has spread to the bones. You may have radiotherapy for earlier stage ACC, but this is still an experimental treatment and you are most likely to have this as part of a clinical trial.
Chemotherapy

Chemotherapy uses anti cancer (cytotoxic) drugs to destroy cancer cells. You may have just one drug or a combination of more than one drug. Chemotherapy is usually only used to treat adrenocortical carcinomas that have spread to other parts of the body.

**Primary chemotherapy** (treatment with chemotherapy only) is given when chemotherapy, on its own, is expected to control or cure the cancer; it can be given for acute treatment or long-term control.

**Adjuvant Chemotherapy** (chemotherapy given after surgery) is used in this manner to decrease the risk of the cancer coming back. This is done even when no clear evidence of cancer can be found, but certain factors (e.g. metastasis to the lymph nodes, large tumour size) predict an increased risk of cancer recurrence.

**Neoadjuvant Chemotherapy** (chemotherapy given before surgery) is used in this manner to shrink a tumour before surgery, which may allow the surgeon to perform a smaller surgery and/or remove all visible tumour.

**Combined Modality Chemotherapy** is the practice of using chemotherapy in combination with other treatment modalities, such as radiation or surgery. Therapies are combined to obtain a greater response rate than could be achieved with a single treatment modality. Today, using more than one treatment modality is common for most cancers.

Your doctor will discuss which options are suitable for you.

Some of the chemotherapy drugs used to treat ACC are:

- Cisplatin
- Doxorubicin (Adriamycin)
- Paclitaxel (Taxol)
- Fluorouracil (5FU)
- Vincristine
- Etoposide (VP16)

**Combination Therapy**

In some cases the use of one single medical intervention as a treatment is not as effective as combining two different treatments together.

Examples of combination treatments are:

- Etoposide + Doxycycline + Cisplatin + Lysodren
- Streptozotocin + Lysodren
- Etoposide + Cisplatin + Lysodren
Multidisciplinary teams

ACC care can be complex, and for the patient the journey can encompass not only a whole host of emotions, but also a whole range of investigations, treatments and healthcare professionals. The very fact that there is often not just one treatment option at diagnosis and throughout the patient journey, means that there has to be a collaboration among all key healthcare professional groups, who are making clinical decisions for individual patients.

This collaboration has been termed an MDT (multidisciplinary team). This is a formula that is now being used across the world in the care of cancer patients.

An MDT will usually be formed by a particular specialist with expertise and interest in ACCs and other adrenal tumours. This specialist is commonly an endocrinologist or oncologist.

A patient may see some or all of the following people:

- Oncologist
- Surgeon
- Endocrinologist
- Radiology staff
- Dietitian
- Nurse Specialist
- Palliative Care Team
- Pain Team
- General Practitioner/Practice Nurse
- Counselling Staff
- Various Technicians
- Clinic Staff
- Hospital Staff
- Hospice Team

Patients can feel more confident in the knowledge that all aspects of their care have been discussed and that the best possible treatment plan will be formulated. A well coordinated and disciplined MDT is a very important aspect for care when striving to achieve the best quality of life and the best outcome for ACC patients.
Clinical Research

Research is a step-by-step process that involves collecting and examining information. Research into adrenocortical carcinomas is vital to improve our understanding of the disease and how it can be treated.

Research goals include:

- Understanding what causes ACCs
- Understanding how ACCs form
- Formulating more effective diagnostic scans and tests
- Discovering new treatment options, and ensuring that current treatments are being implemented to provide the best therapeutic benefit

ACCs are a rare form of cancer, and there are small teams of dedicated medical professionals around the world who treat patients every day. It is important that these specialists are allocated the resources to carry out research within their units, so that our understanding of this disease and how to treat it continues to grow.

In clinical trials, patients agree to try new therapies (under careful supervision) in order to help doctors identify the best treatments with the fewest side effects.

If patients want to take part in a clinical trial, they should discuss this with their specialist, who will know whether they are eligible.

All studies are run on strict inclusion and exclusion criteria for the safety of the patients. It can be frustrating for patients to discover that they are ineligible, but no medical professional is able to influence any decisions based on these criteria.

No one should ever include a patient in a clinical trial without his or her knowledge. A doctor, nurse or other researcher will ask for permission, and they cannot enter a patient into the trial unless that patient has given his or her consent.

To help patients decide whether they want to take part, the researchers should tell them all about the study:

- what it is trying to find out
- how they will be treated
- what they will have to do.

Even after consent has been given, a patient may leave the trial without giving a reason at any time. If a patient is having a new treatment as part of a trial and then leaves the trial, he or she may not be able to continue having the new treatment. In this situation, patients would be given the appropriate standard treatment for their type of cancer.
You can find out more about current trials at:

**Current Controlled Trials**
This website allows users to search, register and share information about randomised controlled trials. Covers multiple registers, including England, Scotland and the US.
http://www.controlled-trials.com/

**ClinicalTrials.gov**
This is a register of federally and privately supported clinical trials conducted in the United States and around the world.
clinicaltrials.gov

You can also search for research trials available to patients in the UK and Europe on these websites:
www.macmillan.org.uk
www.cancerhelp.org.uk
www.ctu.mrc.ac.uk (The Medical Research Council Clinical Trials Unit)
www.ncrn.org.uk (National Cancer Research Network)
www.eortc.be/ (European Organisation for Research and Treatment of Cancer)

**Useful Organisations**

**NET Patient Foundation**
Patient support and advice
0800 434 6476
www.netpatientfoundation.com

or

**Rarer Cancers Foundation**
www.rarercancersfoundation.org
0800 434 6476

The **British Society for Endocrinology** was set up in 1946 to promote the advance of endocrinology. The Society currently has about 1900 members and is increasing its size and range of activities rapidly. Membership is open to anyone anywhere in the world working in an endocrine-related field, at any stage of their career.

The **European Society of Endocrinology** has been created to promote for the public benefit research, education and clinical practice in endocrinology by the organisation of conferences, training courses and publications, by raising public awareness, liaison with national and international legislators, and by any other appropriate means.