Table of Contents:

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Important Phone Numbers</td>
<td>5</td>
</tr>
<tr>
<td>Introduction</td>
<td>6</td>
</tr>
<tr>
<td><strong>Overview: Information to Help You Make Treatment Decisions</strong></td>
<td></td>
</tr>
<tr>
<td>About the adrenal glands</td>
<td>7</td>
</tr>
<tr>
<td>What are the adrenal glands?</td>
<td>7</td>
</tr>
<tr>
<td>What do the adrenal glands do?</td>
<td>7</td>
</tr>
<tr>
<td>What is cancer and how does it affect the adrenal glands?</td>
<td>8</td>
</tr>
<tr>
<td>Tumors of the Adrenal Medulla</td>
<td>9</td>
</tr>
<tr>
<td>Tumors of the Adrenal Cortex</td>
<td>9</td>
</tr>
<tr>
<td>Tumors that Spread to the Adrenal Glands</td>
<td>10</td>
</tr>
<tr>
<td>How common is adrenocortical cancer and who is at risk?</td>
<td>10</td>
</tr>
<tr>
<td>Is adrenocortical cancer hereditary?</td>
<td>10</td>
</tr>
<tr>
<td>What are the symptoms of adrenocortical cancer?</td>
<td>11</td>
</tr>
<tr>
<td>How is adrenocortical cancer diagnosed?</td>
<td>12</td>
</tr>
<tr>
<td>How is adrenocortical cancer staged?</td>
<td>15</td>
</tr>
<tr>
<td><strong>Treatment: Information about the Treatment of Adrenal Cancer</strong></td>
<td></td>
</tr>
<tr>
<td>Treatment of adrenal cancer</td>
<td>16</td>
</tr>
<tr>
<td>How does a patient decide on treatment?</td>
<td>16</td>
</tr>
<tr>
<td>Surgery</td>
<td>16</td>
</tr>
<tr>
<td>Adrenalectomy</td>
<td>17</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>19</td>
</tr>
<tr>
<td>How is radiation therapy used to treat adrenal cancer?</td>
<td>20</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>20</td>
</tr>
<tr>
<td>What is chemotherapy?</td>
<td>20</td>
</tr>
<tr>
<td>How does chemotherapy work?</td>
<td>20</td>
</tr>
<tr>
<td>When is chemotherapy given to treat adrenal cancer?</td>
<td>21</td>
</tr>
<tr>
<td>Clinical trials</td>
<td>24</td>
</tr>
<tr>
<td>What is the prognosis for adrenal cancer?</td>
<td>25</td>
</tr>
<tr>
<td>What care will I receive after treatment?</td>
<td>26</td>
</tr>
</tbody>
</table>
Overcoming Barriers: Information to Help Manage Physical and Emotional Challenges

Excess hormone secretion (Endocrine Syndromes) .......................... 27
Adrenal insufficiency ................................................................. 29
What can be done to treat my pain? ............................................. 31
  Why does this happen? .......................................................... 31
  What can be done? ............................................................... 31
What can I do to maintain my weight and increase my appetite? .... 34
  Why does this happen? .......................................................... 34
  What can be done? ............................................................... 34
What can be done to prevent constipation? ............................... 36
  Why does this happen? .......................................................... 36
  What can be done? ............................................................... 36
How do I cope with my feelings? .............................................. 37

Resources: Information Available at U-M and in the Community

Web Resources ........................................................................ 41
E-mail Groups (Listservs) .......................................................... 43
Pheochromocytoma Fast Facts .................................................. 44
Notes .................................................................................... 45

Illustrations:

  Figure #1: The Adrenal Glands and Surrounding Organs .......... 7
  Figure #2: Anatomy of the Adrenal Glands ............................ 8
  Figure #3: Blood Supply to the Adrenal Glands ....................... 14

Table:

  Table #1: Overview of Mitotane Therapy .................................. 23
Important Phone Numbers

Cancer Center Clinic Contact

- New Patient Coordinator .................................. 734-232-0040
- Clinic Call Center .............................................. 734-647-8906
- M-Line (doctor to doctor) ...................................... 800-962-3555

Appointments

- CT Appointments .............................................. 734-936-4500
- Endocrine Oncology Scheduling ............................. 734-647-8906
- General Surgery Scheduling .................................. 734-936-5783
- Nuclear Medicine Department ............................... 734-936-4500
- Preoperative Center at Domino Farms ..................... 734-936-3604

Resources

- Cancer Center Nutrition Clinic .............................. 877-907-0859
- Complementary Therapy Programs ......................... 877-907-0859
- Patient & Family Support Services ......................... 877-907-0859
- Patient & Visitor Lodging/Accommodations Program ... 800-544-8684
- Patient Education Program .................................. 734-647-8626
- Patient Assistance Center ................................... 877-907-0859
- PsychOncology Appointments ............................... 877-907-0859
- Social Work ...................................................... 877-907-0859

Operating Rooms

- Main OR Family Waiting Room .............................. 734-936-4000
- East Ann Arbor Surgical Center ............................ 734-232-3000
- Surgery Cancellation .......................................... 734-936-8800
Introduction

The doctors and healthcare staff at the University of Michigan Rogel Cancer Center Multidisciplinary Endocrine Oncology Program created this book to explain adrenal cancer and the treatment options available to you. This is not a comprehensive guide to treatment options – they are changing every day. Rather, we hope this guide helps you move forward with a firm understanding of adrenal cancer, how it is treated, and what the experience may include. With this information in hand, you will be prepared to make thoughtful decisions along with your medical team.

You will find blank pages at the back of the book (Page 45) to use for writing down questions, appointments, or other notes.
Overview

About the Adrenal Glands

What are adrenal glands?

Everyone has 2 adrenal glands. They are small, about the size of a walnut, and shaped like a pyramid. They sit in a position on top of each kidney. They are sometimes called "supra-renal glands" which is Latin for "above the kidney".

![Adrenal Glands and Surrounding Organs](image)

What do the adrenal glands do?

The adrenal glands may be small, but they play an important role in the way you think and feel. The adrenal glands are organs that make and secrete hormones. The hormones produced by these small powerhouses affect the way every tissue, organ and gland in your body works.

Each adrenal gland is made up of 2 parts: an inner area called the **medulla**, and an outer area called the **cortex**. The adrenal glands play an important role in how your body responds to stress.
The adrenal medulla makes a chemical called epinephrine that is also called adrenaline. Epinephrine is responsible for the regulation of blood pressure, blood flow and your body's acute response to stress.

The adrenal cortex makes a variety of hormones including:

- Mineralocorticoids (such as aldosterone) that help regulate blood pressure and the fluid and salt balance in the body.
- Glucocorticoids (such as cortisol) are released by the adrenal cortex to help the body to cope with long term stress. Glucocorticoids help regulate the amount of sugar and fat stored in the body and act as anti-inflammatory agents.
- Hormones related to sex hormones. While proper sexual development and function is regulated by "real" sex hormones secreted by the gonads (testis & ovaries), there is no definite function assigned to sex hormones secreted by the adrenal cortex.

**What is cancer and how does it affect the adrenal glands?**

Normal cells grow, divide, and die in a controlled way that is regulated in the body. Cancer is a disease that causes cells to divide and grow in an abnormal, out of control way where the balance of cell growth and death is disturbed.
Medical research has led to a better understanding of these abnormalities and continues to be a focus in the understanding of how to treat cancer.

Cells that continue to grow and divide without control become a mass or tumor. This mass will eventually affect how an organ works. The original site of the abnormal cell growth is called the cancer’s “primary site.” In adrenal cancer, the primary site is the adrenal gland.

Abnormal or uncontrolled cells can also grow and invade nearby organs and structures. This spreading is called metastasis. Tumors that invade and spread are called **malignant or cancerous**, while benign adrenal tumors never spread or invade other organs.

**Tumors of the adrenal medulla**

Tumors in the adrenal medulla are not common. There are 2 types called **pheochromocytomas** and **neuroblastomas**. The information in this booklet will not address these tumor types. Sources of further information about medullary tumors are found in the Resources section of this book. You can obtain additional information regarding adrenal medullary tumors by contacting the Rogel Cancer Education Program at 734-647-8626 or e-mail CCC-PERC@med.umich.edu.

**Tumors of the adrenal cortex**

Non-cancerous tumors of the adrenal cortex are called **adenomas**. These are small tumors that are usually seen on a CT scan or MRI of the abdomen. They are the most common type of adrenal tumors and are most often silent tumors that cause no symptoms. Some call these tumors **incidentalomas** because they are very often found incidentally when x-ray studies are done for other reasons.

Cancerous tumors that develop in the adrenal cortex are called adrenal cancer or more specifically, **adrenocortical cancer**. These are primary adrenal cancers,
meaning they haven’t started somewhere else in the body and spread to the adrenal glands. These cancers are very rare. The rest of this book will talk more in detail about this type of tumor.

**Tumors that spread to the adrenal glands**

Cancers that begin in other areas of the body commonly spread (metastasize) to the adrenal gland. This is different from primary adrenal cancer which starts in the adrenal gland. Cancer that spreads to the adrenal gland is still called cancer of the primary site. So, if lung cancer spreads to the adrenal gland, it is called and treated as "lung cancer metastasized to the adrenal gland." It is not called or treated as "adrenal cancer." Typical cancers that spread to the adrenal gland are lung cancer, breast cancer, melanoma and kidney cancer.

**How common is adrenal cancer and who is at risk?**

Primary tumors of the adrenal cortex are very rare, occurring in 1 person in every 1,000,000. In the United States, about 300-500 people are diagnosed with adrenocortical cancer every year. They usually occur in only 1 adrenal gland, but can occur in both.

There are two main age groups in which adrenocortical cancer is observed, in children under 5 years of age and in adults between the ages of 40 and 50. It is also slightly more common in females.

In general, there are no known causes of adrenocortical cancer; therefore, there are no known methods for reducing the risk of developing adrenal cancer.

**Is adrenal cancer hereditary?**

For most patients, there is no genetic link to the development of adrenocortical cancer. These are called "sporadic" adrenal cancer. However, patients with some genetic defects may be at greater risk. One such rare genetic disorder is Li-Fraumeni syndrome. These patients have a defect (called a mutation)
of a tumor suppression gene, the TP53 gene. This defect can lead to the development of several different kinds of cancers, including adrenocortical cancer.

Another genetic disorder is Lynch syndrome, which also increases the risk for colorectal and uterine cancer. The genes altered in this condition are involved in removing "spelling errors" in the DNA. Overall, about 1 in 10 (10%) of all adrenal cancer patients will have a hereditary condition. Genetic testing can help other family members identify any hereditary conditions and be screened for cancers early.

Adrenal cancer can also be found in some other rare conditions, such as Multiple Endocrine Neoplasia Type 1 or Beckwith-Weidemann syndrome. Every patient with adrenal cancer should meet with a genetic counselor to discuss the possibility of a hereditary component.

**What are the symptoms of adrenal cancer?**

Adrenal cancers act in one of two ways: they can cause symptoms related to hormone production, or they can cause symptoms from tumor size and compression of other organs.

The most common symptom reported by patients with adrenocortical cancer is pain in the back or side (called the flank). Unfortunately, this type of pain is common and does not directly suggest a disease of the adrenal cortex. In adrenocortical cancer, this symptom is usually from the tumor compressing organs, nerves, and other structures around the adrenal gland.

Some people describe feeling full with no appetite because of pressure on the stomach and other abdominal organs. Fewer than 70 out of 100 (70%) of adrenocortical cancers are only in the adrenal gland at the time of diagnosis.
The other common way adrenal cancers cause symptoms is through hormone production. Tumors secrete hormones and are called functional tumors. Some adrenal cancers, and even some benign tumors, are functional and secrete excessive amounts of hormones. These are the same hormones the adrenal cortex usually produces: most commonly cortisol or weak male sex hormones. Approximately 60 out of 100 (60%) of patients will experience symptoms because of high levels of hormones in the blood. These symptoms include:

- Weight gain and fluid retention
- Early puberty in children
- High blood pressure (more common in adenomas and pheochromocytomas)
- Excess facial and body hair growth in women
- Excess breast tissue in men
- Easy bruising
- Muscle weakness
- Diabetes
- Osteoporosis
- Mood changes

**How is adrenal cancer diagnosed?**

Adrenal cancers are often found after a person seeks treatment for the symptoms caused by the cancer. However, some tumors are found when a doctor orders imaging testing for another condition.

People with symptoms that suggest adrenal cancer will undergo tests to determine the cause of these symptoms. The first step is a thorough medical history and physical exam to determine the extent of symptoms and their possible causes.
Further evaluation may include the following:

- **Blood and urine tests** will be done to evaluate levels of adrenal hormones. Remember that adenomas (benign tumors) may produce high levels of adrenal hormones, so high hormone levels do not always indicate an adrenal cancer. Some blood and urine tests may be done after you are given a steroid such as dexamethasone.

  The blood and urine tests taken after the medication will measure your body’s response to the steroid, indicating the presence of a hormone secreting tumor or other problem with the adrenal gland.

- **Computed Tomography (CT)** The CT scan can show small tumors as well as important blood vessels that the tumor might be growing into or around. It can also look at surrounding organs for spread (metastasis) of the cancer into lymph nodes or other organs in the abdomen.

  A CT scan takes longer than a regular scan. You will lie still on a table while it is being done. Usually, you will need an IV placed for a dye injection just before the scan. You may also be asked to drink a contrast solution before the exam, this helps outline the intestine so it is not mistaken for tumors.

- **Magnetic Resonance Imaging (MRI)** The MRI scan uses magnets to make a picture of the inside of the body. MRIs produce very sharp, precise pictures of the area and can be helpful in distinguishing an adenoma from a cancer.

- **Positron Emission Tomography (PET)** A PET scan involves the injection of radioactive sugar into a vein followed by a body scan that looks for areas taking up the sugar. Cancer cells take up sugar much faster
than normal tissue, so cancerous areas can be located with this test. Research studies have shown the usefulness of PET scanning in identifying adrenal tumors. However, studies are still in progress to look at ways PET scanning can be used to tell the difference between adrenal cancers and benign adenomas and between primary adrenal cancers and metastatic tumors that started in other organs. One of these studies uses a substance called metomidate as the radioactive substance. Some studies suggest it can be helpful in distinguishing primary tumors from metastatic ones.

Figure 3: Blood Supply to the Adrenal Glands
How is adrenocortical cancer staged?
In general, patients with adrenocortical cancer are divided into 4 groups or stages of adrenal cancer.

The 4 stages of adrenal cancer are:

**Stage 1:** The cancer is smaller than 5 centimeters (2 inches) and has not spread outside of the adrenal gland.

**Stage 2:** The cancer is larger than 5 centimeters and has not spread outside of the adrenal gland.

**Stage 3:** The cancer has spread into the fat surrounding the adrenal gland or adjacent organs or has spread to lymph nodes or other organs near the adrenal gland.

**Stage 4:** The cancer has spread to other parts of the body.

Because adrenal cancer is so uncommon, there are several staging systems that may be used. The most common system is the ENSAT (European Network for the Study of Adrenal Tumors) staging system.
Treatment of Adrenal Cancer

International consensus conferences have recently agreed to standardized approaches in the treatment of adrenocortical cancer. In general, adrenal cancers confined to the gland should be surgically removed. Those with spread to nearby or distant organs may be treated with surgery along with other therapies, or may be ineligible for surgical removal. Adrenal cancer can be a very aggressive cancer. The prognosis is best when the cancer can be surgically removed.

How does a person decide on treatment?

When people are first diagnosed with adrenal cancer, they are overwhelmed. Shock and stress can make it difficult to think of everything you might want to know. It is helpful to have family or friends come with you for discussions about treatment.

Because adrenal cancer is rare and few doctors have experience treating it, most people seek evaluation at a multidisciplinary adrenal cancer or endocrine clinic. A multidisciplinary adrenal cancer clinic often involves surgeons, medical oncologists, endocrine specialists, radiologists, endocrine pathologists and radiation oncologists along with other medical specialists who will review your individual case and make treatment recommendations. Treatment generally starts within a few weeks of the first evaluation. There is time to discuss your options and to learn more about adrenal cancer, treatment approaches, and the clinical trials that are available to you.

Surgery

Adrenal cancer is an aggressive cancer. The only known cure is complete surgical removal of the cancer. In many cases, people come to their doctor after the cancer has spread to other organs in the body, or the cancer has spread to places that cannot be removed, and the cancer is considered inoperable. If the
tumor can be removed, it is very important that your surgery is performed by a surgeon experienced in the treatment of adrenal cancer (most surgeons see one adrenal cancer patient in a lifetime). The covering (capsule) of the tumor should not be broken during surgery and a wide margin of normal tissue around the tumor should be removed to make sure resection is complete and to minimize the chance of the cancer coming back. Careful preoperative evaluation and planning is very important in adrenal cancer patients to assure the best outcome.

There are two types of surgery for adrenal cancer – laparoscopic and open.

**Laparoscopic surgery:** Any mass suspected to be cancer should not be removed laparoscopically. It is thought that laparoscopic instruments rub against the tumor and spread tumor cells to other parts of the abdomen leading to early recurrence (return of the cancer). Additionally, if the entire tumor is not taken out when the procedure is performed laparoscopically, the “margins” (edges of the tissue removed) could be positive for tumor cells. This leads to recurrent tumor growth and spread in most cases.

**Open approach:** (Through a larger incision along the rib cage or up and down the midline of the abdomen.) Allows the surgeon to remove a margin of normal (benign) tissue around the tumor more easily to help decrease rates of recurrence in the abdomen.

**Adrenalectomy**

The surgical procedure to remove one or both of the adrenal glands is called an adrenalectomy. This procedure can be done in different ways. In general, each of these methods means the complete removal of the adrenal gland and the entire tumor mass. The surgeon will do a careful inspection of the surrounding organs such as the kidneys, along with all blood vessels, and remove any visible cancer.
Open Adrenalectomy

There are different approaches the surgeon may choose when performing an open adrenalectomy.

**Anterior approach:** The surgeon makes an incision in the abdominal wall (the front of your body). Usually the incision will be horizontal (side to side), just under the rib cage. The incision may carry over to the other side. Sometimes the surgeon will make a vertical (up and down) incision in the middle of the abdomen. An open anterior approach gives the surgeon the best view of the adrenal glands, surrounding organs and blood vessels. Depending on how aggressive the cancer is, other organs may also need to be removed. After surgery, patients may spend 3 to 7 days on average in the hospital. Recovery takes 4 to 6 weeks after this surgery.

This approach may be combined with an incision into the chest cavity (called the thorax) or through the breast bone (called the sternum). These approaches may be used if the tumor is very large or there is extension of the tumor into one of the blood vessels that carries blood back to the heart (called the inferior vena cava).

**Posterior approach:** The surgeon makes a curved incision in the back along the eleventh or twelfth rib. One or two ribs may need to be removed to get to the area of the cancer. This approach is rarely used, but has some advantages, especially in people who have had extensive abdominal surgery before.

**Retroperitoneal or flank approach:** The surgeon makes an incision in the person’s side (called the flank). This approach is rarely used, as it does not allow full inspection of the abdominal cavity to look for evidence of tumor spread, but may be used in people who have undergone previous extensive intra-abdominal surgery.
Laparoscopic adrenalectomy

Laparoscopic adrenalectomy is an excellent option for non-cancerous adrenal growths or for cancers that have traveled from another site (metastasized) to the adrenal gland, but is not appropriate for cancers that originate from the adrenal gland. This surgery is done using instruments that are inserted through the abdominal wall. The surgeon makes 3-4 small incisions in your abdomen, and instruments are then inserted that allow your surgeon to visualize the area and remove the adrenal gland.

Tumors that are suspicious for, or are known to be cancer, should not be removed using this approach for the reasons stated before. In some cases, your surgeon may decide to start the operation using a laparoscopic approach if the mass appears entirely benign and is being removed due to physical complaints or excess secretion of hormones. If during the operation your surgeon sees anything suspicious, the operation will be converted to an open approach; however, if the tumor is cancerous, tumor cells may already have been spread throughout the abdomen.

People generally stay in the hospital 1-2 days after laparoscopic surgery. Recovery and returning to normal every-day activities after laparoscopic adrenalectomy is usually 1-2 weeks, with heavy lifting and strenuous physical activity being limited for 4 weeks.

Radiation therapy

Radiation therapy (also called radiotherapy, x-ray therapy, or irradiation) is the use of a beam of energy (called ionizing radiation) to kill cancer cells and shrink tumors. Radiation therapy injures or destroys cells in the area being treated (the target tissue) by damaging their genetic material (DNA), making it impossible for these cells to continue to grow and divide.
Although radiation damages both cancer cells and normal cells, most normal cells can recover from the effects of radiation and function properly. The goal of radiation therapy is to damage as many cancer cells as possible, while limiting harm to nearby healthy tissue.

**How is radiation therapy used to treat adrenal cancer?**

In general, radiation therapy is used in two different settings for adrenocortical cancer. It can be used for certain circumstances including:

- Treatment after surgery to decrease the risk of local recurrence; or
- Managing or controlling areas of tumor metastasis. This is particularly useful in treating bones affected by adrenal cancer.

Local recurrence means that cancer cells have come back in the same area of the body where the tumor started and this can happen when tumor cells were left behind or were not killed.

Radiation therapy is usually delivered daily, Monday through Friday for 5 to 7 weeks. The side effects can include fatigue, skin reactions such as redness and irritation, diarrhea and nausea.

**Chemotherapy**

**What is chemotherapy?**

Chemotherapy is the treatment of cancer with drugs that can destroy cancer cells. These drugs often are called anticancer drugs.

**How does chemotherapy work?**

Normal cells grow and die in an orderly way. When cancer occurs, the abnormal tumor cells keep dividing and forming more cells without control. Anticancer (chemotherapy) drugs destroy cancer cells by stopping them from growing.
or multiplying. Healthy cells can also be harmed, especially those that divide quickly. Harm to healthy cells is what causes side effects. However, healthy cells usually repair themselves after chemotherapy.

Other types of drugs may be used to treat your cancer. These may include certain drugs that can block or increase the effect of your body’s response to the cancer or affect hormone production by the tumor.

**When is chemotherapy given to treat adrenal cancer?**

Chemotherapy is the treatment of choice for adrenal cancer that cannot be cured by surgery. This stage of adrenal cancer is usually metastatic (spread to other organs). Chemotherapy drugs can have an effect on the cancer by stopping the growth of cancer cells or their ability to multiply.

The goals of chemotherapy treatment are to control the cancer, keep it from spreading by slowing the cancer's growth and improve or reduce the symptoms of the disease.

The most common chemotherapy used to treat adrenocortical cancer is **Mitotane**. This drug has been used the longest in the treatment of adrenal cancer and works by blocking the hormones produced by the cancer, killing adrenal cancer cells.

Mitotane is a chemotherapy tablet taken by mouth in several doses throughout the day. It is important to take each dose exactly as scheduled and to have blood levels regularly monitored.

People receiving Mitotane therapy are closely followed by their doctor for common side effects. These may include somnolence (extreme drowsiness) and abnormalities in blood work. See Table 1 (Page 23) for a description of Mitotane treatment. Mitotane treatment can also lead
to adrenal insufficiency, a condition in which the adrenal glands do not produce adequate amounts of steroid hormones. Therefore, it is recommended that patients receive cortisol replacement along with Mitotane therapy.

A number of chemotherapy drugs can be combined either with each other or with Mitotane to treat adrenocortical cancer. These include a combination regimen with etoposide, doxorubicin and cisplatin or streptozocin. Two combinations have been studied in the treatment of advanced adrenal cancer: a regimen called EDP/M (etoposide, doxorubicin and cisplatin, and Mitotane) and a combination of Mitotane and streptozotocin. A large international Phase 3 clinical trial (FIRM-ACT) has established EDP/M as the superior treatment regimen.

In general, adrenocortical cancer can be aggressive and resistant to most chemotherapy. Most studies have demonstrated response rates of 30% to 50%. Studies of newer chemotherapy agents are ongoing.
### Table 1: Overview of Mitotane Therapy

<table>
<thead>
<tr>
<th>What is Mitotane?</th>
<th>A chemotherapy taken by mouth used to treat adrenocortical cancer.</th>
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<tbody>
<tr>
<td>How does it work?</td>
<td>Mitotane works by blocking hormone production from the cancer, and by killing the adrenal cancer cells.</td>
</tr>
<tr>
<td>How is it taken?</td>
<td>Mitotane is taken by mouth, usually several times a day.</td>
</tr>
<tr>
<td>What side effects may occur?</td>
<td>Nausea, drowsiness, depression, adrenal insufficiency (see page 28), and blood work abnormalities.</td>
</tr>
</tbody>
</table>
| What are the more serious side effects? | Contact your doctor if you experience:  
  • Balance difficulties and severe memory impairment.  
  • Weakness, tiredness, nausea, vomiting, and weight loss.  
  • Fever (temperature above 101 degrees Fahrenheit) or body aches that don’t go away.  
  • Light-headedness or fainting.  
  • Problems with your vision. |
| What should I do if I miss a dose? | Mitotane must be taken on a regular schedule. Call your doctor if you miss a dose. |
| Special considerations of Mitotane therapy | • Store this medicine in a closed container at room temperature. Avoid heat, moisture and direct light. Do not store this medication in a bathroom due to the humid environment.  
  • Keep this medicine away from children.  
  • Notify your doctor if you are taking blood thinners such as warfarin (Coumadin®).  
  • This medication may make you dizzy or drowsy. Avoid driving, using heavy machines or doing anything that could be dangerous if you are not alert.  
  • Patients taking Mitotane require frequent monitoring by their doctor including routine blood work.  
  • Every patient taking Mitotane needs adrenal hormone replacement with hydrocortisone. |
Clinical Trials

Your doctor may suggest that you consider participating in a clinical trial (a research study or protocol) for the treatment of adrenal cancer. Clinical trials are one very important reason that the University of Michigan Rogel Cancer Center is able to offer our patients access to the latest cancer treatments.

Clinical trials are used to test new treatments. The goal of these trials is to find ways to improve therapy or decrease side effects. While a trial or study is active or in-progress, we do not know whether any potential improvement has been found. The trial must be closed and the data analyzed before the treatment being studied is made widely available to patients.

There may be some risks associated with research. Your doctor will discuss both the potential risks and benefits in detail with you and obtain your written permission before starting you on a research protocol.

Oversight committees at Michigan Medicine conduct an extensive review of all clinical trials. These committees include an “Institutional Review Board” (IRB) composed of cancer doctors, doctors in other specialties and lay people. The IRB reviews all protocols before they are available to patients and again at different times during the research to be sure that the protocol remains appropriate and safe for patients.

All patients on a protocol receive the best care possible, and their reactions to the treatment are watched very closely. If the treatment does not seem to be helping, a doctor can take a patient out of a study. Also, the patient may choose to leave the study at any time. If a patient leaves a study for any reason, they will receive standard care and treatment.
There are 3 phases of clinical trials in which a treatment is studied before it is eligible for approval by the Food & Drug Administration (FDA). These are:

**Phase 1:** The purpose of these trials is to find the best way to give a new treatment and to determine how much of it can be given safely. Phase 1 begins after the treatment has been well tested in animals and lab studies, but the side effects in people are not completely known. The main purpose of a Phase 1 study is to test the safety of the drug, although doctors are always hoping to help patients.

**Phase 2:** These studies are designed to see if the drug or treatment works. The cancer team closely evaluates the effect of the new treatment on the cancer itself.

**Phase 3:** These studies compare the new drug or treatment to the most accepted or standard treatment currently used. This is done with large numbers of patients who are placed into 1 of 2 groups. One group receives the standard treatment; the other group receives the new treatment under study.

Clinical trials are voluntary. Your adrenocortical cancer will be treated whether you decide to join a protocol or not.

**What is the prognosis for adrenal cancer?**

The best prognosis for adrenocortical cancers is seen in patients whose cancer is in Stage 1 or 2. This means their cancer is confined to the adrenal gland and can be removed with surgery. The 5 year overall survival rate, which means the number of patients who will be alive 5 years after cancer treatment, is 40-60 out of 100 (40-60%).
Stage 3 cancers have an overall survival rate of 20 out of 100 (20%); Stage 4 cancers’ overall survival rate is 10 out of 100 (10%). Prognosis is better in younger patients, while hormone-secreting tumors are associated with worse prognosis.

**What care will I receive after treatment?**

People treated for adrenocortical tumors are usually followed every 3-6 months for several years after treatment.

If your adrenocortical tumor was functional (secreting hormones), your doctor will monitor the levels of these hormones in your blood. People treated for a non-functional or non-secreting tumor will have an MRI or CT scan periodically for the first few years.

Your cancer doctor will work closely with your primary care doctor to address any late effects that you may experience from the cancer itself or from the cancer treatment. Late effects are those seen after cancer treatment.
Overcoming Barriers

If you have cancer, you may notice every ache, pain, or sign of illness. Even little aches may make you worry. The information in this section is designed to help you become an informed partner in your care, but it is only a guide. Self-help can never take the place of professional health care.

Ask your medical team any questions you may have. Also, don’t hesitate to tell them about any side effects that you may have. They want and need to know.

Not all patients will experience the symptoms or side effects listed in this section, we include them to help you understand what may be happening to you. We know these are obstacles to your health and quality of life. Your multidisciplinary team will work with you to reduce or eliminate these problems.

Excess hormone secretion (endocrine syndromes)

The adrenal glands secrete a number of essential hormones. Functional tumors of these glands cause an overproduction of hormones in many patients. Symptoms of overproduction depend on the hormone secreted. Below is a list of syndromes that may be caused by adrenal tumors, including:

- **Cushing’s Syndrome** (too much cortisol) Cushing’s Syndrome describes a group of symptoms that are caused by high levels of the steroid hormone, cortisol, in the body. Cortisol is a form of glucocorticoid and is produced by the adrenal cortex. High levels of cortisol can be due to problems in a complex system of hormone production that includes not only the adrenal gland, but the pituitary gland and the hypothalamus as well. Symptoms associated with Cushing’s syndrome include a moon face appearance, fat buildup on the trunk of the body, muscle weakness and loss of strength, impotence, high blood
pressure, depression, and weight gain. Cushing’s syndrome involving the adrenal gland is more commonly caused by benign adenomas than by cancer. Treatment of Cushing’s syndrome is targeted at the original cause, such as surgical removal of the adrenal tumor. However, there are also several newer drugs that can reduce the cortisol production by the tumor or decrease cortisol effects. Typically drugs such as ketoconazole, metyrapone, or mifepristone are used.

- **Virilization** (male traits develop because of excess male sex-hormone). Symptoms of virilization include excess hair on the face and body (called hirsutism), baldness, acne, deepening of the voice, increased muscularity, and an increased sex drive.

It is caused by an excess of the male hormones called androgens. Tumors that cause virilization are the most common functional adrenocortical tumors in children. These children might experience "precocious puberty." Children with this syndrome will experience puberty earlier than normal due to high levels of sexual steroids.

- **Feminization** (female traits develop because of too much estrogen). Feminization is rare; virilization is a more common syndrome.

- **Conn Syndrome** (too much aldosterone) Another name for this syndrome is primary aldosteronism. Conn syndrome is characterized by high blood pressure caused by too much aldosterone. High blood pressure (hypertension) may be the only sign of Conn syndrome. However, the aldosterone may also cause the kidneys to leak potassium, so a low blood level of potassium may occur as well.

Diagnosis of Conn syndrome is done with blood tests to evaluate the level of aldosterone and rennin. Conn syndrome is more commonly seen in benign adenomas; however, there are other causes of the syndrome such as adrenal
hyperplasia. Conn syndrome is eliminated with surgical removal of the adrenal tumor, but may be chronic in patients with hyperplasia.

**Adrenal insufficiency**

Adrenal insufficiency happens when the body completely lacks adrenal hormones.

Adrenal insufficiency can be caused by several conditions. In adrenal cancer patients, it can be caused by the surgical removal of both adrenal glands such as in a bilateral (both-sided) adrenalectomy or by removal of a large cortisol producing tumor (because it needs some time to jump start cortisol production by the remaining adrenal gland). It can also be caused by some chemotherapies, such as Mitotane, that stop the gland from producing all hormones.

Symptoms of adrenal insufficiency include:

- Weakness or tiredness
- Patchy tanning of the skin or an all-over darker coloring of the skin
- A craving for salt and salty foods
- Dehydration
- Weight loss
- Nausea, vomiting and diarrhea
- Disorientation
- Light-headedness or dizziness
- Low blood pressure that falls further when standing
- Muscle aches
- Belly pain

A lack of adrenal hormones puts a person at increased risk for infections, causes a lack of general motivation and tiredness. It can also cause hypoglycemia and problems with salt and water regulation and can lead to a
serious condition called an adrenal crisis. Adrenal insufficiency is a potentially fatal disease if it is unrecognized and untreated.

Treatment of adrenal insufficiency includes managing its symptoms and replacing the adrenal hormones that are lacking. Hormones produced by the adrenal cortex include mineralocorticoids and glucocorticoids. They are replaced with tablets, often taken 2 to 3 at a time every day.

Hormones produced by the adrenal medulla (adrenalin) are also produced at other sites in your body. Thus, they do not need to be substituted.

Adrenal crisis is a condition of dangerously low blood pressure that can lead to death. This crisis happens when your body is placed in a condition of severe stress that is most commonly caused by an infection such as pneumonia or by having a surgical procedure.

It is essential that patients with adrenal insufficiency or those who are being treated with Mitotane alert their doctors of their medical history. In the case of severe stress, patients with adrenal insufficiency require extra doses of glucocorticoids that can be given as a tablet or as an intravenous injection. Your doctor can help your body deal with stressful situations with advanced planning to supplement your body’s lack of adrenal hormones.
What can be done to treat my pain?

Why does this happen?
Patients who are diagnosed with adrenal cancer commonly have pain. Pain is described differently by each patient, but many describe it as a cramping, aching, and radiating (spreading) to your flank or shoulders. The most common areas of pain experienced by patients with adrenal cancer are the upper abdominal and back areas. There are many causes of pain including the cancer itself, which may cause pressure on other organs, nerves and vessels.

What can be done?
Pain can be treated, but there are often barriers that prevent proper treatment. Some of these barriers are a lack of understanding in how to take the pain medications, fear of addiction and a concern that pain may be uncontrollable later if medicines are used at the time of initial pain. These are all issues that should be addressed with your medical team. Do not let these barriers prevent you from keeping any pain you may have under control.

Good pain control can lead to increased physical activity and well-being in people with adrenal cancer. People who have chronic pain may need to take medications regularly to obtain the best control of pain. An understanding of how to take these medications will help you get better control of your pain.

There are many different medications used to treat pain. Opioids (narcotics) are the most common. Other types of medications used to treat pain include antidepressants, anti-convulsants (anti-seizure medications), anti-inflammatory and steroid medications.

Opioid medications come in several forms: tablets, liquids, skin patches and intravenously by a pump. These medicines are available as a sustained release or long acting preparation, and as an immediate release pain medication. The long acting and immediate release pain medications are often used together.
Sustained release or long acting pain medications
These should be taken at a **regular, scheduled** time, usually morning and evening, whether you have pain or not. They are taken on a schedule and work best when that schedule is not changed.

Examples of these types of medications include:
- Fentanyl (Duragesic® patch)
- Morphine (Oramorph®, MSContin®)
- Oxycodone (Oxycontin®)

Immediate release medications or “breakthrough pain medications”
The immediate release medications should be taken when you are having pain while taking a long acting pain medication. This is called “breakthrough pain” as it occurs while you are taking regularly scheduled medication, but may need some extra medication for control and to prevent it from becoming severe. These medications work within 15-20 minutes and are usually taken on an "as needed" basis because pain can vary from day to day. These medications can be taken at any time, even if it is the same time as the sustained release or long-acting pain medications.

Examples of breakthrough pain medications:
- Oxycodone
- Hydrocodone (Vicodin®)
- Hydromorphone (Dilaudid®)
- Morphine immediate release (MSIR)
- Morphine oral solution (Roxanol®)
- Fentanyl lozenge (Actiq®)
Suggestions for people on sustained release/long-acting pain medications AND immediate release pain medications:

- Continue the sustained release medication on a regular basis, whether you are having pain or not at that time. Do not change this schedule without talking to your doctor.
- Use your "breakthrough" pain medication as needed. Do not wait until pain becomes severe or it will become difficult to get good control.
- Keep a record of the breakthrough medications taken over a 24 hour period. This information is helpful when you talk to your doctor about your pain control.

Remember

If breakthrough pain medication is needed 4-6 times a day
or
If pain keeps you up consistently at night
then
Notify your doctor who may consider increasing your sustained release pain medication.

Other ways to reduce pain

In addition to medications, a number of other treatment strategies can be used to relieve pain. Although on their own, these tools might not be enough to eliminate moderate to severe pain, they are often helpful when used in combination with medication. Some of these strategies commonly referred to as "complementary therapies" include:

- Relaxation, guided imagery
- Hypnosis
• Biofeedback
• Creative therapies such as music and art
• Prayer, meditation
• Massage
• Acupressure and acupuncture
• Application of heat or cold
• Therapeutic exercise

Many pain medications cause constipation. If you are taking pain medications on a regular basis, you will need to review the section “What Can be Done to Prevent Constipation” on page 36.

Information about complementary therapy programs offered at the Rogel Cancer Center can be found at http://www.rogelcancercenter.org/support or by calling 1 (877) 907-0859.

What can I do to maintain my weight and increase my appetite?

Why does this happen?
Weight loss can be a problem for patients with adrenal cancer. You may see your appetite decrease or feel bloated after eating. It may be hard to eat normally because foods taste different to you. You may have times when you feel nauseated, or have constipation or diarrhea.

Cancer can also cause changes in your body that affect your metabolism and will contribute to weight loss.

What can be done?
The overall goal during treatment is to keep your weight stable. We will monitor your weight throughout your treatment.

Talk to your medical team about your symptoms.
There are medications available to reduce or treat pain, nausea, constipation or digestion problems you may be experiencing. Your doctor can order these for you.
Also, dietitians are available at the cancer center to offer suggestions and guidance, and will prepare a dietary plan during your treatment. The Nutrition Clinic is open Monday through Friday from 8:00am to 4:30pm.

Appointments can be made in advance at your clinic checkout area or you can call 1 (877) 907-0859.

There are some steps you can take to improve your diet and prevent weight loss. These include:

- Eat 5 to 6 small meals or snacks throughout the day.
- Choose foods that are high in protein and calories.
- Try new foods regularly as taste can change from day to day. Limit fluids at meals and drink liquids in-between to avoid fullness at meals.
- Increase protein and calories by using supplements such as Carnation Instant Breakfast®. There are several flavors to choose from and you can add ice cream, whole milk, yogurt and fruit to increase calories.
- Take anti-nausea medications as prescribed by your doctor during your chemotherapy treatments.
- Appetite stimulating medications such as megestrol acetate (Megace®) or dronabinol (Marinol®) may be recommended by your doctor.

If you need additional nutrition information, you may contact the Rogel Cancer Education Program:

- Telephone: (734) 647-8626
- E-mail: CCC-PERC@med.umich.edu
- Visit the https://www.rogelcancercenter.org/
The most important thing to remember is that weight loss should be addressed and we will work with you to help prevent and treat this problem.

**What can be done to prevent constipation?**

**Why does this happen?**

Constipation is common during cancer treatment. Constipation is a decrease in the number of bowel movements combined with hard stool, excessive straining, bloating, increased gas, and/or abdominal cramping.

Adrenal cancer patients are at risk for constipation because they are often treated with pain medications, receive chemotherapy and anti-nausea medications, have decreased their physical activity and have had a change in their eating and drinking habits – all of which can cause constipation. Other causes of constipation include dehydration, a lack of fiber in your diet, and the changing hormone levels in your body.

**What can be done?**

There are a number of preventative things to do. These include:

- Increase the fiber in your diet with foods high in fiber such as fresh, raw fruits and vegetables, whole grains, prunes, nuts and dates.
- Increase fluids in your diet (drink at least 2 quarts of non-caffeinated fluid daily).
- Avoid cheese products.
- Get regular exercise every day if possible - keep up your activity as much as you are able.
- Go to the bathroom whenever you have an urge to go.

For people taking narcotic pain medications, we recommend a combination of stool softener and laxative on a regular basis. Here are some suggestions:
• Take Senokot-S®, 2 to 6 tablets daily in divided doses to keep regular bowel movements every day. This can be decreased or increased according to results and your tolerance. Generic versions of Senokot-S® can be substituted. Ask your pharmacist for information about generic versions. They are often cheaper.

• If no bowel movement in any 24 hour period (1 day), take 2 tablespoons of Milk of Magnesia® (MOM) at bedtime with a full glass of water.

• If no bowel movement in any 48-hour period (2 days), take 3 Senokot-S® tablets twice a day (total of 6 tablets per day) plus 2 tablespoons of MOM at night before bedtime.

• If no bowel movement in any 72-hour period (3 days), add one of the following:
  ◦ Take Magnesium Citrate 8 oz. (1/2 bottle) once, then repeat in 6 hours.
  ◦ If still no bowel movement, then take 2-3 Dulcolax® tablets.

**How do I cope with my feelings?**

If you have been diagnosed with cancer, it is normal for you and your family to experience a wide range of emotions. Important issues in the life of any person with cancer may include the following:

• Fear of death.
• Interruption of life plans.
• Changes in body image and self-esteem.
• Changes in social role and lifestyle.
• Money and legal concerns.
Everyone who is diagnosed with cancer will react to these issues in different ways. Many people experience feelings of anxiety, depression, sadness, stress, and have difficulty sleeping or eating. It is important to know when and where to seek help for these feelings. These symptoms and fears usually lessen as a person adjusts to the diagnosis.

There are many misconceptions about cancer and how people cope with it, such as the following:

- All people with cancer are depressed.
- Depression in a person with cancer is normal.
- Treatment does not help the depression.
- Everyone with cancer faces suffering and a painful death.

**Seeking support**

Being diagnosed with cancer is a scary and isolating experience for most people. It is even more difficult when diagnosed with a rare cancer. This makes it difficult to speak to others who don't know what you are going through. It makes the isolation even more profound, and you may feel even more alone.

For this reason, you may want to reach out in different ways than patients with common cancers. You may find it difficult to locate resources in your community, but there are many resources available to patients through the internet, national organizations, and the American Cancer Society. You may try an online support group or a telephone group hosted by one of these organizations. You can also participate in lectures online or via the telephone and receive information about cancer related issues.

These resources are listed in the last section of this booklet (Page 41). We suggest you connect with others during your cancer treatment. Research
has found this to be helpful in reducing anxiety and depression, as well as improving your knowledge and overall quality of life.

A person who cannot adjust to the diagnosis after a period of time, and who loses interest in usual activities, may be depressed. Mild symptoms of depression can be distressing and may be helped with counseling. Even patients without obvious symptoms of depression may benefit from counseling; however, when symptoms are intense and long-lasting, or when they keep coming back, more intensive treatment is important. These are often signs of what is called “major depression.”

Major depression is not simply sadness or a blue mood. Major depression has been found to affect about 25 out of 100 (25%) of cancer patients and has common symptoms that can be diagnosed and treated. Symptoms of depression that are noticed when a patient is diagnosed with cancer may be a sign that the patient had a depression problem before the diagnosis of cancer. Anyone experiencing these symptoms, or who has a history of depression should talk to their healthcare team.

It is important to remember that depression can, and should be treated. The symptoms of major depression include the following:

- Having a depressed mood for most of the day and on most days.
- Loss of pleasure and interest in activities that you usually enjoy.
- Changes in eating and sleeping habits.
- Nervousness or sluggishness.
- Tiredness.
- Feelings of worthlessness or guilt.
- Poor concentration.
- Thoughts of suicide or thinking constantly about death.
Depression can affect caregivers too

Just as patients need to be evaluated for depression throughout their treatment, so do family caregivers. Caregivers have been found to experience a good deal more anxiety and depression than people who are not caring for cancer patients.

If the family of a patient diagnosed with cancer is able to express feelings openly and solve problems effectively, both the patient and family members will have less depression. Good communication within the family reduces anxiety.

Seeking help

The Multidisciplinary Adrenal Cancer Team believes that helping patients cope with their cancer diagnosis is an essential part of providing care. A social worker is an essential member of the team who provides evaluation, counseling, and referral to additional resources such as support groups, the PsychOncology clinic and community resources. Remember, our team is here to help address any emotional needs you or your family may have. Do not hesitate to contact us at (877) 907-0859.
Resources

It is important to us that every patient receives the right support at the right time. However, resources specific to adrenal cancer are uncommon in the general community. Adrenal cancer affects 500 Americans annually, but they are spread throughout the country.

Therefore, you will find adrenal cancer resources most commonly on the internet and in large academic healthcare centers that have specialized adrenal cancer clinics.

Web Resources

• The Rogel Cancer Center Multidisciplinary Endocrine Oncology Clinic at the University of Michigan —
  http://www.rogelcancercenter.org/adrenal-cancer

  This site has information about the Multidisciplinary Adrenal Cancer Clinic at the University of Michigan. The "Resources" pages have links to additional sources that may be of interest to people with cancer.

• Adrenal Gland Tumor — Doctor-Approved Information from ASCO (American Society of Clinical Oncology)
  https://www.cancer.net/cancer-types/adrenal-gland-tumor

• All About Adrenal Cortical Cancer — Information from the American Cancer Society (ACS)
  • From the ACS Home page click on “Cancer A-Z”
  • Scroll down and click on "View All Cancer Types"
  • Select then Click on “Adrenal Cancer” from the list.
  www.cancer.org
• **Adrenocortical Carcinoma - Patient Version** — An overview of adrenocortical carcinoma from the National Cancer Institute.
  

• **Your Adrenal Glands** — A Section of EndocrineWeb.com site, this page reviews the anatomy of the adrenal glands and links to information on pheochromocytomas and adrenal cancer.
  

• **ACC C.U.R.E. Adrenal Cortical Carcinoma Crusade Until a Resolution Exists** — A nonprofit organization for Adrenal Cancer Research.
  
  [http://www.accure.org](http://www.accure.org)
  [http://www.facebook.com/adrenalcancerawareness](http://www.facebook.com/adrenalcancerawareness)

• **Uptodate Adrenal Cancer** — *UpToDate* is an online medical information resource where patients can go to learn about a medical condition, better understand management and treatment options, and find information to have a better dialogue with their healthcare providers. From the link below, you can type in adrenal cancer and select from the list.
  
  [http://www.uptodate.com](http://www.uptodate.com)

• **American Cancer Society video. ACS Research Grantee: Dr. Hammer's Story** — Dr. Gary Hammer, the director of the Rogel Cancer Center Endocrine Oncology Program at the University of Michigan, shares how his lab was first funded by the ACS and the importance of investing in young researchers.
  
  [http://www.youtube.com/watch?v=qcsnvpxxJUc&feature=youtu.be](http://www.youtube.com/watch?v=qcsnvpxxJUc&feature=youtu.be)
E-mail Groups (Listserves)

- RARE-CANCER is an e-mail discussion group for patients with rare cancer types and their families, hosted by the Association of Cancer Online Resources (ACOR)
  
  [http://www.acor.org](http://www.acor.org)
Pheochromocytomas fast facts

- Pheochromocytomas are tumors that come from the adrenal medulla or inner layer of the adrenal gland.
- They are rare and occur in about five people in every million.
- Pheochromocytomas have been clearly associated with several hereditary disorders including Type MEN Type 2 (multiple endocrine neoplasia), Von Hippel-Lindau disease, Neurofibromatosis Type 1, and the Familial Paraganglioma Syndrome. Therefore, physicians regularly recommend genetic testing for everyone with a pheochromocytoma.
- **Symptoms:** Primary symptoms are paleness, high blood pressure, fast heartbeat, headache and high blood sugar. Symptoms can be episodic, occurring suddenly, or constant and persistent.
- **Diagnosis:** Diagnosis is made by measuring hormones that are secreted by the pheochromocytoma in the blood or urine. Once the doctors know a pheochromocytoma is present, they proceed with further radiological and nuclear medicine imaging to find out more about the localization and extent of the tumor.
- **Treatment:** Surgery is the treatment of choice. Before surgery, the blood pressure of pheochromocytoma patients needs to be well controlled with special medications. There are also treatment options for advanced pheochromocytoma such as chemotherapy. They are mainly available through clinical trials.
- **Prognosis:** Pheochromocytomas have a 98 out of 100 (98%) percent cure rate with surgery alone. People with a history of a genetic mutation or whose pheochromocytomas developed outside of the adrenal gland have a higher risk of recurrence (the cancer returning).
- **Follow-up:** People with pheochromocytomas are followed annually for the rest of their lives. Follow-up involves imaging and blood tests to evaluate presence of recurrent disease.
Disclaimer: This document contains information and/or instructional materials developed by Michigan Medicine for the typical patient with your condition. It may include links to online content that was not created by Michigan Medicine and for which Michigan Medicine does not assume responsibility. It does not replace medical advice from your health care provider because your experience may differ from that of the typical patient. Talk to your health care provider if you have any questions about this document, your condition or your treatment plan.

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