Neuroendocrine Cancer

…"Medical students are taught when hearing hoofbeats, to think of horses, not zebras. Neuroendocrine tumours are rare, and therefore are considered to be zebras".

London Health Sciences Centre
London Regional Cancer Program

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NS5932 (2008/04/09) Updated May 2014;
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Acknowledgements

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south west regional cancer program
in partnership with cancer care ontario

Reviewed by Patient Education ,
South West Regional Cancer Program,
May, 2014

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This booklet is also available for viewing and printing at:

http://www.lhsc.on.ca/Patients_Families_Visitors/LRCP/Resources/JustDiagnosed.htm

Zollinger-Ellison Syndrome

Zollinger-Ellison Syndrome is a condition caused by some endocrine tumours in the pancreas. These tumours release large amounts of gastrin, a hormone which makes the stomach produce high amounts of acid and pepsin. People with Zollinger -Ellison Syndrome tend to have more ulcers of the stomach and small bowel.

Neuroendocrine System
A system of specialized cells which are located throughout the body.

Non-functional Tumour
A non-functional tumour is one that does not make hormones and other biologically active products.

Pathology
Defines/diagnoses the type of neuroendocrine tumour when examined under the microscope. Often special stains are required to correctly diagnose neuroendocrine tumours.

Portal Vein
A large vein that brings 80% of the blood to the liver.

Pulmonary Embolism
Pulmonary embolism is the term used to describe a blood clot that blocks an artery leading to the lungs. These clots can form in the leg before detaching and traveling through the bloodstream. They cause chest pain, severe shortness of breath, restlessness, anxiety and cough. It is also possible to have blood in the sputum (mucous from the lung) and a low grade fever.

Radioisotope
A radioisotope is a radioactive substance. Nuclear Medicine Physicians use radioisotopes for special types of scans and to treat certain neuroendocrine tumours. These radioisotopes connect to certain receptors on the tumour cells. If the nuclear medicine scan shows that the tumour has the right type of receptors, the same radioisotopes will be used in much higher doses to treat it. The radioisotopes used at LRCP include Indium -111 Octreotide, 177-Lutetium Dotatate, and Indium 131 MIBG.

Neuroendocrine Program of the London Regional Cancer Program

This booklet was written for patients with Neuroendocrine Tumours. We hope to provide you with :

- General information on Neuroendocrine Tumours
- How these tumours are diagnosed
- The three most common Neuroendocrine Tumours
- Treatment options available at London Health Sciences Centre, London Regional Cancer Program (LHSC/LRCP).

The Neuroendocrine Multidisciplinary Team
The complexities of Neuroendocrine Tumours require the collaboration of a team of health care professionals.

Our team includes physicians from London Health Sciences Centre and the London Regional Cancer Program (LHSC/LRCP) who work closely to provide Neuroendocrine patients with a comprehensive evaluation of their individual tumour and recommendations for treatment. Treatment options are communicated to your local health care team. Your oncologist and your family doctor work together to provide treatment.

Our team includes the following health care professionals who may become involved with your care as required. The team is comprised of Medical Oncologists, Radiation Oncologist, Nuclear Medicine Physician, General Surgeon, Hepatobillary Surgeon, Interventional Radiologist, Cardiologist, Cardiac Surgeon, Pathologist, Endocrinologist, Pharmacist, Dietitian, Social Worker, Spiritual Care Specialist and Primary Nurses.

Words that are in bold type are further explained in the Glossary of Terms (see page 33).

What is neuroendocrine cancer?

Neuroendocrine cancer is formed in the neuroendocrine system which is wide spread throughout the body. This system is made up of cells found in the respiratory and digestive tracts. The respiratory tract includes the bronchial tubes and lungs. The digestive tract starts at the mouth and ends at the rectum.

The purpose of the neuroendocrine system is to provide chemical signals to control a number of body functions. These functions include the digestion of food, the movement of food and waste in the small and large bowel (peristalsis), the stress response, thyroid function and many other important processes.

Neuroendocrine cells are also located in endocrine glands, such as the adrenal glands, pancreas, thyroid and pituitary. These cells are also found in the ovaries and the testes.

There are a total of 24 types of Neuroendocrine Tumours:

- Carcinoid
- Glucagonoma
- PPoma
- Corticotrophinoma
- Somatotrophinoma
- Prolactinoma
- Pheochromocytoma
- Ganglioneuroblastoma
- Neuroblastoma
- Paraganglioma
- Gastrinoma
- Insulinoma
- Somatostatinoma
- Gonadotrophinoma
- Thyrotrophinoma
- Parathyroid adenoma
- Ganglioneuroma
- Medulloblastoma
- Medullary thyroid carcinoma
- Vasoactive Intestinal Polypeptide VIPoma
- Non-functioning Islet Cell carcinoma

one organ will make another organ produce or reduce a different hormone.

Interventional Radiologist
The Interventional Radiologist is a specialist physician who is trained to perform highly skilled procedures, like inserting tubes into a person for feeding, drainage, special imaging and embolization.

MEN Syndromes
MEN is an acronym for Multiple Endocrine Neoplasia. These are inherited syndromes. If one parent has MEN, his or her child will have a 50% chance of inheriting the syndrome.

There are two categories:

- MEN-I includes pituitary, parathyroid, and pancreatic endocrine tumours.
- MEN-II
  - MEN-II A includes medullary thyroid cancer, pheochromocytoma, and parathyroid hyperplasia (overgrowth of normal cells).
  - MEN-II B includes medullary thyroid cancer, pheochromocytoma, multiple tumours of the mucous membranes including the lips, tongue and eyelids.

Multiphasic CT Scan
A multiphasic CT scan is a specialized CT scan that shows how blood flows through the liver. Before the scan is started, the patient will take a special drink and have an injection. Both these solutions help make sharper images for the CT scan. This scan is used to see if the patient is able to have a hepatic artery embolization.

Biologically Active
A 'biologically active' substance is one that is both made by the body and has an effect on a bodily function. These functions can include digestion or the control of blood sugar levels. The body makes hundreds of biologically active proteins, hormones and other substances.

Catecholamines
Catecholamines (kat-eh-ko-luh-meens) are biologically active substances made by the adrenal gland. They can be measured in a 24-hour urine collection.

Chromogranin A
Chromogranin A (CgA) is a substance made by tumour cells and is released into the blood-stream. The Neuroendocrine Team measures CgA levels to evaluate tumour growth. CgA is taken at regular intervals.

Deep Vein Thrombosis
Deep Vein Thrombosis (DVT) is a blood clot or *thrombus* that develops in the arm or leg. It usually starts when the lining of a vein is injured or when there is inactivity like sitting for a very long time on an airplane. In some cases, a piece of the clot will break away and travel to the lung, causing a **pulmonary embolism**. Sometimes DVT can happen without any cause.

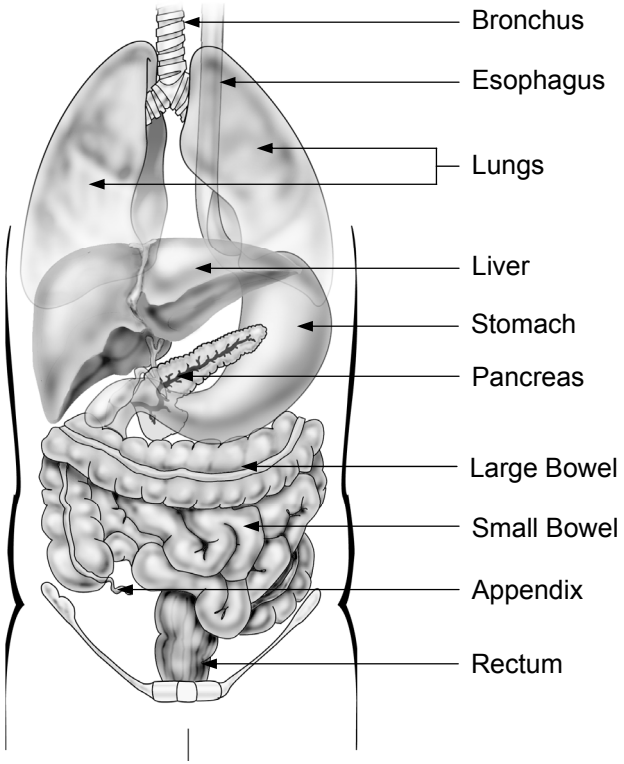
Functional Tumour
A functional tumour is one that makes hormones and other biologically active products.

Hormone
A hormone is a biologically active substance made by an organ. Its function is to tell other organs to increase or decrease an activity like digestion or growth. Sometimes hormones from

- Non-functioning pituitary adenoma
- Prostate tumour with neuroendocrine features
- Breast tumour with neuroendocrine features

The majority of tumours are located in the gastrointestinal (GI) tract and are referred to as the Gastroenterohepatic Neuroendocrine Tumours. Pancreatic Neuroendocrine Tumours (pNET's), are the second most common tumours and named according to the hormone they produce. Rare sites for neuroendocrine tumours are the thymus, adrenal glands, thyroid, skin, ovaries, testes and salivary glands.

Sites where neuroendocrine tumours can appear.



Functional and Non-Functional Neuroendocrine Tumours

Neuroendocrine tumours are classified as **functional** (hormone-producing) or **non-functional** (non-hormone producing).

Functional tumours are often diagnosed sooner because the symptoms felt by the excess production of hormones can make people feel very unwell. However, the symptoms from the hormone production can be quite non-specific.

The most common **functional** tumour is the carcinoid tumour which produces the hormone serotonin in excess and therefore it cannot be broken down by the liver. It is this hormone that causes the carcinoid syndrome. The second most common **functional** neuroendocrine tumour is the Pancreatic Neuroendocrine Tumours (pNET).

Included in the **functional** neuroendocrine tumour category are Phaeochromocytoma (fee-oh-kro-mo-sie-toh-ma) and Paragangioma (pa-ra-gang-oh-ma).

We will address the **functional** neuroendocrine tumours in greater detail later in this book.

Non-functional tumours, in many cases, are slow growing and can go undetected for many years. It is not uncommon for a **non-functional** tumour to have progressed to advanced disease by the time of diagnosis. Often people have severe abdominal pain and a partial blockage of their bowel that leads them to seek medical attention.

What causes Neuroendocrine Tumours?

Most neuroendocrine tumours have no known cause. Neuro-endocrine tumours are usually, but not always, slow growing. They may be present in a person's body for many years before they cause problems.

Q: It is expensive to stay in London for all my tests. Is there any financial support available?

A: You can contact your local Canadian Cancer Society to learn more about funding assistance. Our team's Social Worker can also help you with financial concerns and tell you about sources of financial support. If you come from Northern Ontario, you can apply for the Northern Travel Grant. Ask a member of your local health care team for more information.

Q: Are there any income tax allowances available?

A. You may be able to claim some medical expenses on your income tax return. These expenses include travel costs, drugs and a lot more. If you want to learn more about which items can be claimed, contact a chartered accountant, your financial advisor, or go to www.cra-arc.gc.ca. You can also refer to a resourse called "Claiming Medical Expenses on Your Income Tax Return" published by LRCP .

Glossary of Terms

Amino Acids
Amino acids are the building blocks of protein. They are used in many nutritional therapies for patients who cannot eat or drink. For Indium-111 Octreotide therapy, certain types of amino acids are used to stop special receptors in the kidney. The Indium-111 Octreotide naturally attaches to kidney receptors. This can damage the kidney and can make the therapy less effective.

Q: How much notice will I have for an Octreotide Scan or I-131 MIBG scan booking?

A: Your scan appointments will often be done on short notice too. You must call back and tell us if you are able to come after you have been given dates. We have a very limited number of openings for these scans. We ask that you make every effort to attend the scan on the day provided. Please do not hesitate to call your nurse if you are unavailable for a scan if it has been requested in a specific month.

Q: Are there any support groups for people living with neuroendocrine cancer?

A: A group of patients and families have an email address to which you can send questions or comments. We will give you this address if you wish. There are also some useful websites you can visit:
www.naapnet.org (checked May 2014);
www.carcinoid.org (checked May 2014);
www.cnetscanada.org (checked May 2014).

Q: Where can I stay in London when I come for tests or a clinic appointment?

A: It has been recommended by our patients to stay at the Country Inn and Suites.(www.countryinns.com/london) PHONE # 1-800-456-4000. The direct line to the London location is 519-430-1150. They provide a continental breakfast and are directly across the street from the hospital so you do not have to pay parking on a daily basis. There is also a special rate for hospital patients. There are Bed and Breakfast establishments that are generally less expensive than large hotels as well.

It is rare that neuroendocrine tumours are genetic or inherited. The inherited cancers are referred to as **MEN syndromes** (MEN-I and MEN-II A+B).

Diagnosing Neuroendocrine Tumours

Neuroendocrine tumours are difficult to diagnose. It is common for patients to make many visits to the doctor over several years before an actual diagnosis is made. Symptoms are often very vague and similar to more common health problems such as menopause, irritable bowel syndrome, colitis and asthma. The symptoms can come and go. This makes the diagnosis difficult. Common symptoms of **functional** Neuroendocrine Tumours may include:

- Diarrhea
- Abdominal cramps
- Flushing of the skin
- Wheezing or shortness of breath
- Pounding of the heart
- Skin rash
- Low or high blood sugar
- Stomach ulcers that return when ulcer medication is stopped
- Low or high blood pressure
- Headache

Symptoms will depend on the type of neuroendocrine tumour. A sample of tissue or biopsy from the primary tumour or the liver tumour is the best way to make the diagnosis. Tumours are often found by accident when surgery is done for some other reason.

What kind of tests should I expect?

Often a variety of tests are required to find out the exact type of neuroendocrine cancer. Some of these may be done close to your home. The tests that you may have include:

- CT scan
- Echocardiogram
- Bone scan
- Blood tests
- 24-hour urine collection
- MRI scan

The doctors may also order different x-rays or scopes of the digestive tract. This is to see if the intestine is blocked or narrowed. This test will certainly be done if there has been a problem with severe abdominal pain, vomiting and bloating. An ultrasound to check for gallstones or blockage of the bile ducts may be required. Many of these tests are repeated at various times to evaluate changes in the tumour.

What are nuclear medicine scans?

Two special nuclear medicine scans may be ordered. Nuclear medicine scans use **radioisotopes** to determine if the tumour cells have special receptors. If these special receptors are present and there are enough of them, it is possible that a type of treatment that targets these receptors can be offered. The tests are called:

- Indium-111 Octreotide scan or Octreoscan
- I-131 MIBG scan

These two nuclear medicine tests must be done in London.

Q: Why do my nuclear medicine scans have to be done in London?

Nuclear medicine scans are specialized tests that give a 'test dose' (higher dose then given at other institutions). Special machines are required to do the scan. These machines are located in London. Highly trained and experienced nuclear medicine doctors read these scans.

Q: Who will take care of me when I am not in London?

A: Our team will have close contact with the Oncologist who referred you to London. Notes will be sent after each clinic visit or hospital admission. Your family doctor will also get copies of the notes. This way, both are kept informed of your progress. Your local oncologist and family doctor are your first resources if you feel sick or are having problems. However, we do like to be kept informed about how you are doing.

Q: How far in advance will I be notified of my admission for therapy?

A: You will often be given short notice for therapy dates. Sometimes this notice may be as little as one week .

Q. Why can't I have more notice of therapy dates?

A: Blood counts must be available and they must be above certain minimums for therapy to be given safely. The isotope is not produced on a weekly basis so we can only schedule the treatment when we are guaranteed production.

Frequently Asked Questions

Q: Will these treatments cure my cancer?

A: The only cure is the complete surgical removal of the tumour. This may or may not be possible. The treatments are designed to control your cancer and help you to feel better for as long as possible.

Q: How often will I get treatments?

A: The number of times you will receive treatment depends on how your cancer responds and your overall health. The radioisotope therapies are usually given in a series of 3 or 4 treatments.

Q: Are the radioisotope therapies painful?

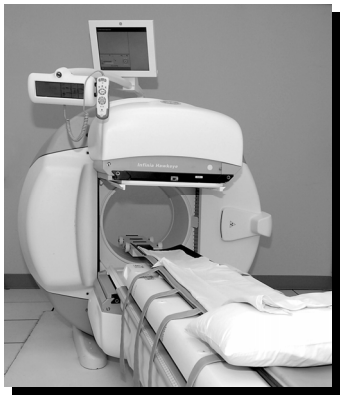
A: There is no pain with the radioisotope injections. Occasionally people can experience a heavy feeling in the liver area if this is where the majority of the Neuroendocrine tumour is located.

Q: Can I go to work during treatment?

A: Many people work during their treatment, however, they may need to discuss reduced hours or duties with their employer if fatigue is a problem.

Q: Will I ever be able to stop taking Octreotide?

A: Most people must use Octreotide for the rest of their life .



Hawkeye Spect CT Scanner

Types of Neuroendocrine Tumours

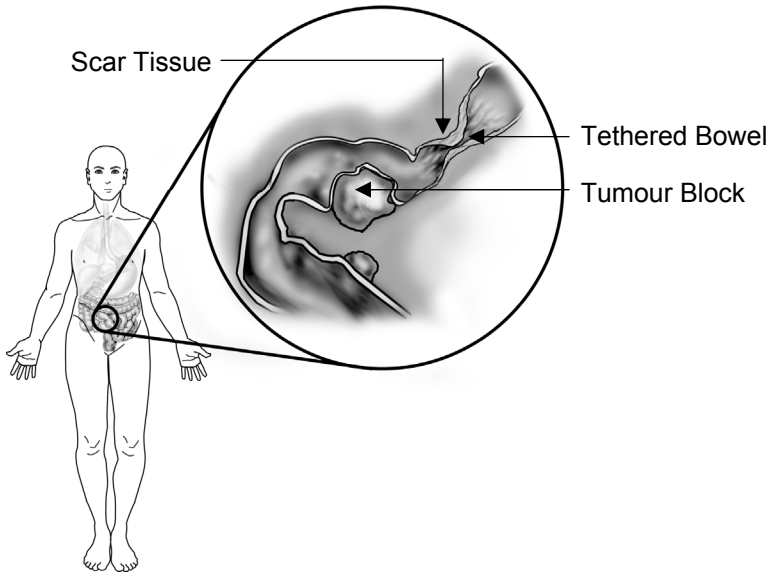
Functional Neuroendocrine Tumours

Carcinoid tumour is the most common **functional** type of Neuroendocrine Tumour. The medical community is moving away from the term 'carcinoid' because it does not take into account the makeup of this particular group of Neuro-endocrine Tumours. Carcinoid tumours are now associated with the **neuroendocrine system** where the majority of these tumours are found. The gastrointestinal tract is their most common location.

It is important to note that carcinoid tumours can also be **non-functional**.

Neuroendocrine Tumours most often occur in the small bowel and appendix, followed by the large bowel, rectum, stomach and lung. They are typically a slow growing cancer. Neuroendocrine tumours often have spread to the liver before the cancer is diagnosed.

Examples of Bowel Blockage



Carcinoid tumours of the bowel tend to produce a lot of scar tissue around the tumour. This may block the bowel because the scar tissue pushes directly on the wall of the bowel. This causes a bottleneck effect. The scarring may cause "tethering" or sticking down of the bowel or lining around the bowel. The scarring may also trap waste and narrow blood vessels.

What is carcinoid syndrome?

Carcinoid Tumour Symptom Chart

Tumour	Hormone/ Peptide	Major Symptoms
Carcinoid	Serotonin Substance P Histamine Bradykinin Kallikrein	Flushing, watery diarrhea, stomach cramps, asthma-like wheezing, heart palpitations, heart problems.

If one of your doctors has not been receiving your notes, their secretary can call the London Regional Cancer Program at 519-685-8600 and speak with a member of the Heath Records Team. They will fax the required information.

In Summary:

It is not uncommon for individuals to question the response rate to the various treatments provided for Neuroendocrine Tumours. Majority of people are referred to our program when the tumour has already spread to other parts of their body. The goal of treatment is to improve your quality of life rather than cure the Neuroendocrine Tumour. The common terms you will hear from the doctors are clinical benefit or response.

Clinical Benefit is the term used when the tumour has not grown in size (remained stable) and an improvement in symptoms caused by the tumour is reported.

Response is the term used when the diameter of the tumour has decreased in size by more than 30%.

Remission is not a useful or valid statement when evaluating Neuroendocrine Tumours.

The number of individuals presenting with a diagnosis of a Neuroendocrine Tumour is increasing. World wide the medical community continues to increase their collective knowledge about these unique tumours. The increase in knowledge is reflected by an increase in the variety of treatment options available.

Improvement in your quality of life is a measurement of success.

tumour. The addition of the chemotherapy drug increases damage to the tumour cells.

What happens after the treatment ends?

When you finish your treatment, you will have blood tests and x-rays at different times to see how the tumour responds to the therapy. You will have a **Plasma Chromogranin A** blood test to determine the size and activity of the tumour. This test must be done in London or you can pay a fee of $65.00 at a private lab.

Telemedicine conferences can be arranged for individuals who live a significant distance from London.

CT scans will be done at regular intervals to measure tumour size. It will be compared to the baseline CT done before treatment. Sometimes these can be done at your home hospital, especially if the original CT scan was done there.

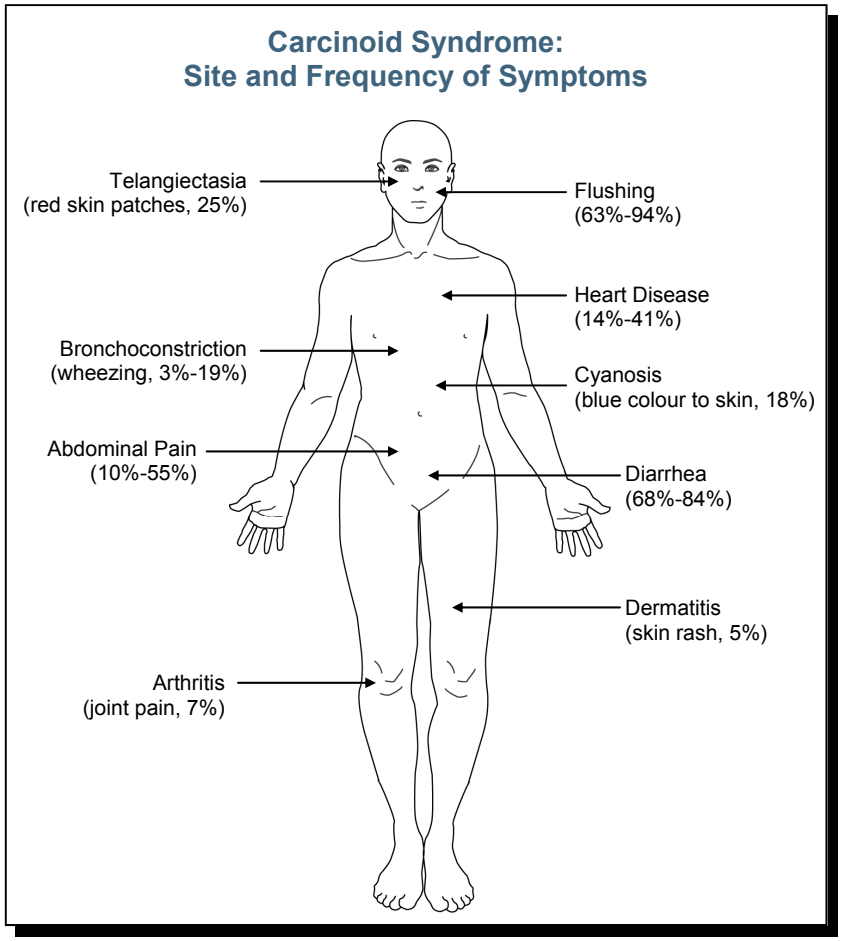
At various times you will need an Indium-III Octreotide Scan and/or an I-131 MIBG scan. These specialized scans must be done at London Health Sciences Centre. When they are scheduled, it is important to keep these appointments. Only 16 of these scans are done each month.

The team in London will involve your doctor and specialists to provide the best possible care. Notes are sent to them every time you are seen in London, which will keep them informed of your progress.

London Regional Cancer Program

Carcinoid syndrome occurs when a **functional** carcinoid tumour makes or secretes large amounts of **hormones** and **biologically active** substances like peptides. When this happens the most common symptoms experienced are:

- Flushing of the face and upper body
- Watery diarrhea
- Cramps
- Heart palpitations



High amounts of hormones may also cause memory problems and make it difficult to think clearly. Generally, carcinoid syndrome happens when tumour cells spread to the liver. Lung carcinoids can also cause the syndrome even if the cancer has not spread to the liver.

Not everyone with carcinoid syndrome will have all of these symptoms. For example, some people may only have flushing.

Carcinoid syndrome may be triggered by certain foods such as smoked, salted or pickled meats or fish, tomato dishes in large quantities, after eating a large meal and caffeine. Alcohol can also cause the carcinoid syndrome as well as stress, exercise and surgery. Carcinoid syndrome can also happen for no reason.

Over time, high hormone levels can damage the valves on the right side of the heart. High hormone levels may also thicken the lining of the heart muscle on the right side. This can lead to heart failure. It is important to lower hormone levels so that damage to the heart is delayed or prevented.

Carcinoid syndrome can be controlled with daily or monthly injections of a drug called Octreotide (awk-tree-oh-tide). The amount and timing of the injections are based on hormone levels and the severity of symptoms. Some people will need an intravenous infusion (IV) to help control the carcinoid syndrome.

MSN.com

Radiofrequency Ablation (RFA)

Radiofrequency Ablation (RFA) is a procedure that uses radio waves to destroy liver tumours. It is done on a small number of patients in very select cases. RFA depends on the location, size and number of liver tumours. A Radiofrequency Ablation can be done at the time of surgery or as an outpatient by the Interventional Radiologist. If appropriate, a referral to a liver surgeon or an Interventional Radiologist will be arranged by the Neuroendocrine Team.

mTOR Inhibitors

This is a new group of medications that has shown a favourable response in the treatment of Pancreatic Neuroendocrine Tumours in some individuals. These medications are in pill form and interfere with various pathways that are needed for the growth of tumour cells and blood vessels. They are less harmful to the normal cells. These medications are very expensive and may not be covered by all private drug plans.

Will I have to go to London for all of my treatments?

All radioisotope treatments must be given in London. At times, your local oncology team will assist in giving you chemotherapy if indicated. The goal is to minimize the number of trips you have to make, especially if you live far from London.

Hepatic Artery Chemoembolization must be done in London. This is because we inject a chemotherapy drug mixed with lipiodol into the liver tumour. Other hospitals do 'bland' embolizations. This means gel foam is placed by the interventional radiologist to cut off the blood and oxygen supply to the

you have a functional tumour, you will be closely watched for symptoms of the syndrome that is associated with your tumour.

If you have a functional tumour, you may feel some discomfort in the area of your liver or have increased symptoms a few days after treatment. You may not feel hungry and you may feel tired. Your nurses and doctors will order medicine to help manage these symptoms.

Some people cannot have this treatment because of certain conditions. Embolization is not safe if you have had any of the following:

- Previous surgery that has changed the bile system (such as stents or shunts)
- Too much tumour growth in the liver
- Abnormal liver tests
- Not enough blood flowing through the **portal vein**
- Excess fluid in the abdomen (ascites)

If you receive this treatment, more information will be given to you before you start the treatment.

Interventional Radiology Suite

Holding Area in Radiology Department

What is carcinoid crisis?

A carcinoid crisis is a severe form of the carcinoid syndrome. It is a medical emergency. Sometimes it is called malignant carcinoid syndrome.

Carcinoid crisis causes low or high blood pressure, a fast or slow heartbeat, or narrowing of the breathing passages. It should be treated with high doses of the drug, Octreotide. This will quickly relieve these symptoms.

Why must 24-hour urine samples be collected?

People who have a **functional** carcinoid Neuroendocrine Tumour require 24 hour urine collections to measure their hormone levels. The 24 hour urine sample measures the amount of a substance called 5-hydroxyindoleacetic acid (5-HIAA).

This substance is a break-down of the hormone serotonin which is made by the tumour cells. The doctor uses the 5-HIAA results to adjust the dose of Octreotide. The doctor will determine the frequency of the urine collections and arrangements will be made by your nurse.

Functional Pancreatic Neuroendocrine Tumours

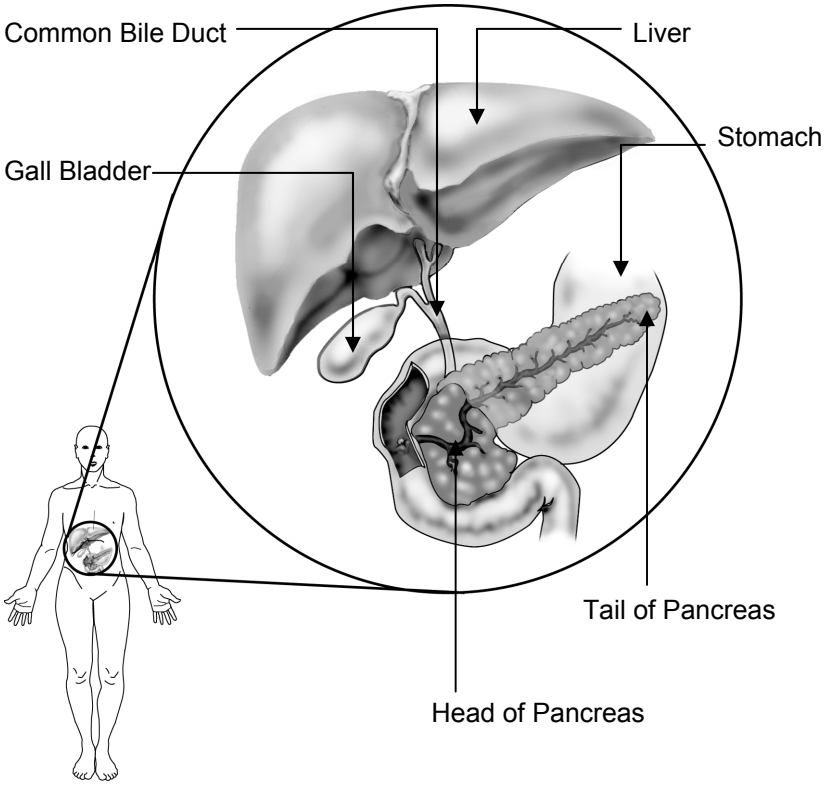
Pancreatic Neuroendocrine Tumours (pNET's) are the second most common Neuroendocrine Tumour. These tumours are very different from the more common Pancreatic Cancer that develops from the digestive enzyme producing cells. These tumours start in the pancreas from specialized cells that cause an over production of hormones like insulin, gastrin, glucagon and vasoactive intestinal peptide (VIP).

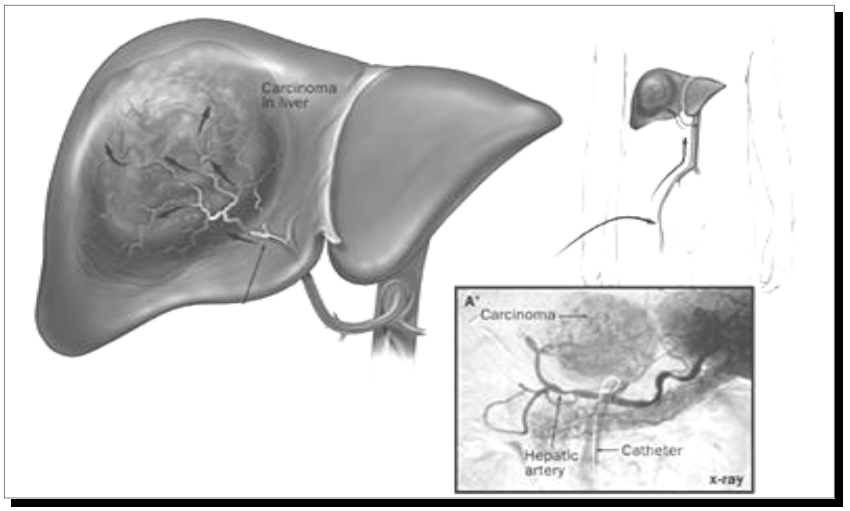
The 4 common pNET's are named after the hormone they produce.

- Insulinoma
- Gastrinoma
- Glucagonoma
- VIPoma, Vasoactive Intestinal Peptide

Pancreatic Neuroendocrine Tumours that are functional or hormone secreting cause changes in blood values which can make people feel sick. Octreotide can be used to block these hormones. When hormones are blocked, people tend to feel better. Changes in the dose of octreotide is often required.

Pancreas and Nearby Organs





The following tests must be done in London:

- **Multiphasic CT scan**
- **Blood tests**

At some point, it is not uncommon to arrange the CT scan at your local hospital once it is determined you have received the maximum benefit from the chemoembolizations.

How will I feel after chemoembolization?

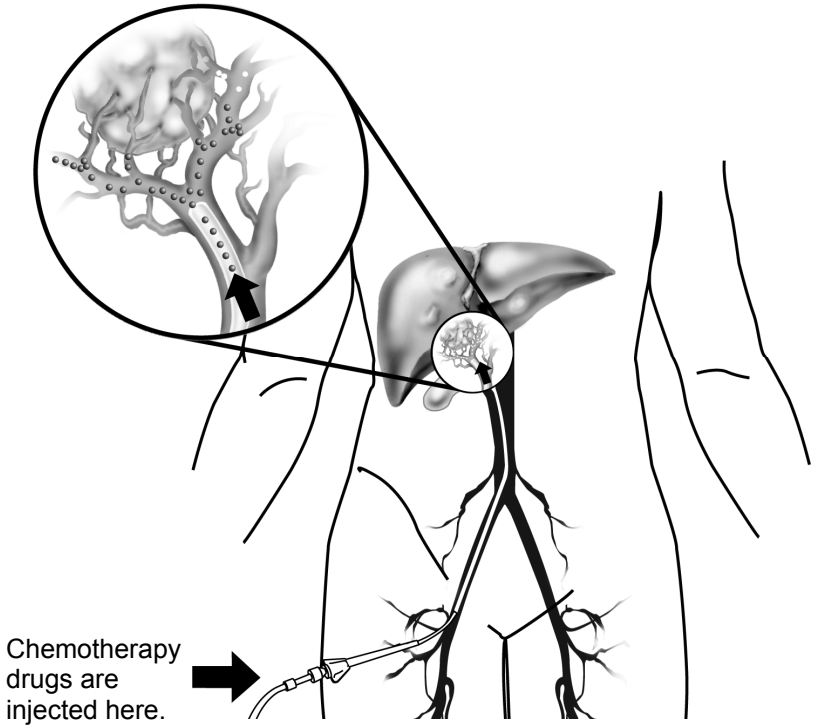
Most people feel some discomfort during the procedure. This might include feelings of warmth, flushing, pain and nausea. You will be able to manage your pain during and after the procedure by using an intravenous pain pump. Anti-nausea drugs will be given before, during and after the treatment.

When the chemoembolization is complete, you will be cared for in a recovery room for at least 2 hours. Nurses will watch for bleeding from the site in your groin where the catheter was inserted and they will check your blood pressure and pulse. If

It is not uncommon for an individual to require several chemoembolization treatments. This will be evaluated and determined approximately 6-8 weeks after each chemoembolization by the Interventional Radiologist.

Many people with carcinoid and pancreatic tumours need an adjustment of Octreotide. If it is required, this adjustment will be done in hospital. It is not unusual to need short-acting Octreotide for a short period of time.

Hepatic Artery Chemoembolization



Pancreatic Neuroendocrine Tumours can alter blood sugar levels. Medication to help control blood sugar levels are often required. There may be frequent adjustments of these medications. Your family doctor or an endocrinologist can manage this part of your care.

Pancreatic Neuroendocrine Tumour Symptom Chart

Tumour	Hormone/ Peptide	Major Symptoms
Insulinoma	Insulin	Low blood sugars which can cause confusion, visual disturbances, sweating, weakness, seizures, very high levels of insulin, occasional neurological or psychiatric disturbances.
Gastrinoma	Gastrin	Recurrent stomach ulcers and multiple ulcers, diarrhea, high stomach acid, abdominal pain, **Zollinger-Ellison Syndrome** with MEN.
Glucagonoma	Glucagon	High levels of glucagon, mild glucose intolerance, itchy rash, weight loss, diarrhea, anemia, tendency to form clots in the veins (e.g., **Deep Vein Thrombosis**).
VIPoma	Vasoactive Intestinal Polypeptide	Watery diarrhea, low potassium, low salt, anemia, dehydration, weight loss.

If part of your pancreas has been removed, it may be necessary to take pancreatic enzyme capsules to help digest the fat in food and fat produced by the liver. Short-acting octreotide and the long-acting formula (Sandostatin LAR) can block the pancreatic enzymes that help digest fat. This can result in your stools becoming pale in color, foul smelling, urgency and the stool often will float in the toilet. If this occurs, pancreatic enzymes may be helpful. These can be prescribed by your family doctor.

About 33 to 50% of pancreatic tumours are **non-functional**. This means they do not secrete hormones. Over time, however, they can change and become hormone secreting.

Pheochromocytoma & Paraganglioma

Pheochromocytoma (fee-oh-kro-mo-sie-toh-ma) and paraganglioma (pa-ra-gang-glee-oh-ma) are very rare tumours that start in the central part of the adrenal glands or in specialized nerve cells called the paraganglia. The adrenal glands sit on top of the kidneys. Para-g-an-glia are found throughout the body. In some cases these tumours are part of the MEN-II hereditary syndrome.

The hormones made by these tumours are called **catecholamines**. They include epinephrine (epp-uh-nef-rin) and norepinephrine. These hormones help with the "fight or flight" reaction to stress or threats.

What are the symptoms of pheochromocytoma and paraganglioma?

Very high blood pressure is a symptom that occurs in 90% of people with this cancer. It may be constant or it may come and go. In some people, the blood pressure drops to very low levels when they stand up.

Your kidneys also need protection when you receive Indium-111 Octreotide or 177-Lutetium therapy. This is done by giving you an infusion with IV fluids and **amino acids** a few hours before and after the radioisotope.

The radioisotope I-131 MIBG tends to collect in the thyroid gland. To prevent damage to your thyroid, you will get tablets of Potassium Iodide before the treatment. You will also need to take these tablets for 9 to 10 days after the radioisotope treatment ends.

The prescription must be filled at the LHSC Outpatient Pharmacy. Potassium Iodide tablets are not available in outside pharmacies.

Hepatic Artery Chemoembolization

Hepatic artery chemoembolization is a treatment that delivers chemotherapy directly to the liver. This therapy may be the best option when the tumours are mostly found in the liver. In this procedure, a skilled radiologist inserts a small tube called a catheter into a large artery located in the groin. The tube is moved into a specific artery leading to the liver. Once in place, the Radiologist injects the chemotherapy mixed with lipiodol, a thick poppy seed oil, into the artery where it targets the tumours in the liver. The artery is then blocked with a substance (gel foam) that will dissolve after a short period of time. The tumour is deprived of blood and oxygen, plus has the chemotherapy, which helps to kill off the cancer cells. If you get this treatment, you will stay in the hospital for 3-4 days. You will be given a prescription for an antibiotic to take at home for 10 days to prevent infection.

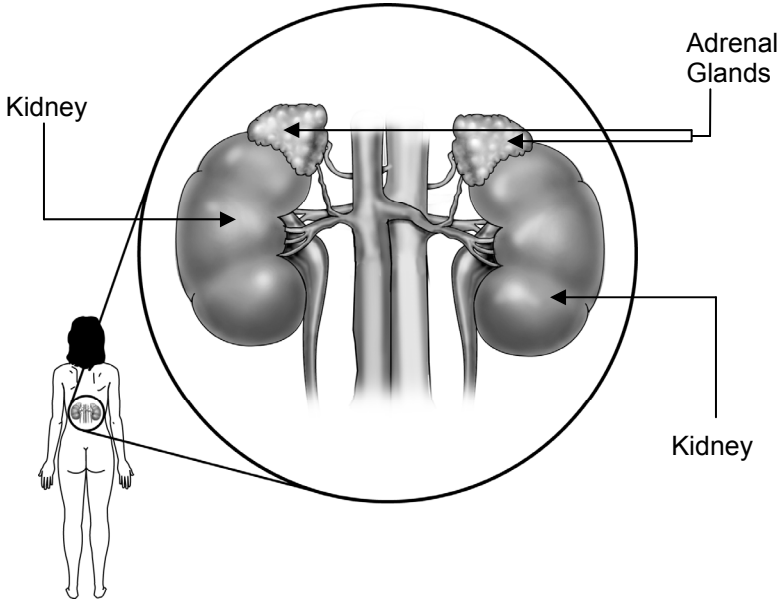
Private Room

Will I have side effects from radioisotope therapy?

Normally patients do not feel any side effects from radio-isotope therapy. In very few cases, some people experience nausea for 2 to 3 days after treatment. It is common for people to have increased fatigue, a full feeling in the abdomen and decreased appetite for up to 10-14 days after the therapy.

Radioisotope therapy does suppress the bone marrow. This means that your body is slower to make blood cells. It is absolutely necessary to have blood tests done every week at a lab close to your home. We will give you a Ministry of Health requisition form when you are discharged from the hospital.

Kidneys and Adrenal Glands



Exercise, emotional upset, drinking alcohol, urination, or a physical exam in the area of the tumour may cause these symptoms to happen.

Medicines for high blood pressure and anxiety may be prescribed. You may also be referred to an endocrine specialist.

Pheochromocytoma and Paraganglioma Symptom Chart

Tumour	Hormone/ Peptide	Major Symptoms
Pheochromo-cytoma Paragan-glioma	Epinephrine Norepin-ephrine	Headache, high blood pressure, sudden changes in blood pressure, rapid heart beat, sweats, paleness, nausea, feelings of impending death.

Why are 24-hour urine samples collected?

People who have a phaeochromocytoma and paraganglioma will have urine collections to measure hormone levels (epinephrine, nor-epin-ephrine, and vanillylmandelic acid). Hormone levels in the urine show how active the tumour cells are and when treatment may be indicated.

Treatment of Neuroendocrine Tumours

The Neuroendocrine Team at the London Regional Cancer Program/London Health Sciences Centre will discuss your particular situation and will inform you of the recommend-ations. The team may recommend several different methods to treat your particular type of Neuroendocrine Tumour. You may have one or more treatments depending on where the cancer is located and how far it has spread. **We share your care with your local health care team as much as we possibly can.**

More information will be given to help you decide which treatment is best for you.

Surgical Treatment of Neuroendocrine Tumours

Surgery can be very important in the treatment of neuroendocrine tumours. Surgery is used to :

- Remove the primary tumour
- Reduce tumour size (debulking)
- Reduce unpleasant symptoms

Surgery is also helpful in the relief of blocked, scarred, and tethered (sticking down) bowels. In these cases, surgery can

Some Neuroendocrine Tumours have receptors for both Indium -111 Octreotide and I-131 MIBG . If this is the case, both radioisotopes can be administered to treat the tumour.

In a way, the radioisotope therapy is a “targeted therapy”.

The London Health Sciences Centre/London Regional Cancer Program has access to three radioisotopes: Indium-111-Octeotide, 177-Lutetium and I-131 MIBG.

How are radioisotope treatments given?

Radioisotope treatments are considered “systemic” treatments. This means that the treatment is given into the bloodstream through an IV. The radioisotopes attach to the tumours where they deliver the radiation. If you receive this type of therapy, you will be admitted to a private room in the Inpatient Oncology unit at Victoria Hospital (LHSC). You will be isolated because you will be radioactive for 1 to 5 days, depending on the radioisotope used. This may sound scary but it is not harmful to you; however, it can be harmful to others, especially pregnant women and children.

If this treatment is suggested, you must be able to care for your own needs. You will have an IV running most of the time during your hospital stay. This might make going to the bathroom a little difficult. It is important to tell staff if you need help.

More detailed instructions will be given to you at the time of treatment. Visitors are allowed, but there will be some restrictions which will be explained to you when you are admitted.

Radioisotope Therapy

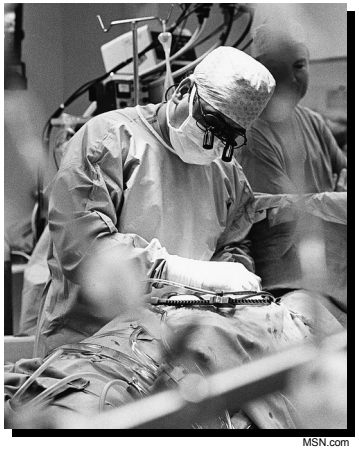
A radioisotope is sometimes called a radiopharmaceutical. When injected into the bloodstream, the radioisotope attaches to special parts of the tumour called receptors. This is the term used when the tumour lights up on the octreotide scan. Indium-111 Octreotide and I 131 MIBG scans give you a test dose of the radioisotope which can determine if your tumour is 'avid' for the radioisotope. If your tumour lights up for a radioisotope, then we can offer you treatment with the specific radioisotope in a much higher dose.

There are two categories of radioisotopes: **Peptide receptor isotopes** and **non-peptide receptor isotope.**

Peptide Receptor Isotopes are given to treat tumours that have **somatostatin receptors.** These receptors are identified by the Indium-111 Octreotide scan. Tumours in this category which light up for the isotope can be treated with either Indium-111 Octreotide or 177-Lutetium Dotatate, both available at London Health Sciences Centre. The tumours with the Peptide Receptors can also be treated with Yttrium 90 Dotatoc, but this is only available in Europe.

When the Indium-111 Octreotide or the 177- Lutetium Dotatate attach to the tumour they deliver damaging radiation to the tumour cells.

Non-Peptide Receptor Isotopes is the treatment recommended for individuals who have a Neuroendocrine Tumour that **do not** have **somatostatin receptors**. Tumours in this category which light up for the isotope, can be treated with I-131 MIBG (iodine-131-meta-iodobenzlyguanidine). I-131 MIBG is a radiotracer similar to the hormone norepinepherine which is commonly found in Phaeochromocytoma and Paraganglioma Neuroendocrine Tumours.



improve the quality of a person's life by decreasing the periods of pain and vomiting.

If the surgeon finds that the cancer has spread, sometimes the secondary tumours or metastases can be reduced.

Medical Treatment of Neuroendocrine Tumours

What does Octreotide do?

Somatostatin is a hormone that our body naturally produces. It plays an important role in many of our body's internal processes. It also blocks the hormones made by certain tumours. It is the over-production of hormones caused from a **functional** neuroendocrine tumour that make a person feel sick.

Octreotide is a man-made form of somatostatin. Octreotide helps control the hormones that cause diarrhea, flushing, low blood sugar, pounding of the heart, and changes in blood pressure. Octreotide is used for **functional c**arcinoid tumours that produce excess serotonin measured by the 24 hour urine for 5-HIAA. The extra circulating serotonin can damage the heart over time. Octreotide can protect the heart from damage even if you have no symptoms of carcinoid syndrome. The goal is to reduce the serotonin production to the lowest possible level.

Octreotide is used in **functional** Pancreatic Neuroendocrine Tumours to control the symptoms of extra hormone production

(refer to Pancreatic Neuroendocrine symptom chart). Octreotide is not only recommended for individuals who have a **functional** tumour, but also for individuals who have a **non-functional** Neuroendocrine Tumour. In these situations, the goal is to prevent the tumour from growing. Once you are started on Octreotide injections, you will be on them for the rest of your life.

Octreotide is available in short-acting and long-acting form. These may be prescribed as subcutaneous (under the skin) injections, intramuscular (in the muscle) injections or intravenous (in the vein) infusions.

The team will arrange to have injections given to you in your home by a nurse. In some cases, you may be taught how to give injections to yourself by a home care nurse.

Is chemotherapy helpful?

Chemotherapy drugs are often given to treat cancer. There are many combinations of drugs used to treat different types of cancer. The type of chemotherapy depends on how the tumour looks under a microscope (**pathology)**.

Some Neuroendocrine Tumours respond well to chemo-therapy, but for others chemotherapy has a limited effect.
For Neuroendocrine Tumours that do not respond well to chemotherapy alone, the chemotherapy may be combined with radioisotope therapy or only radioisotope therapy will be used for treatment.

Your treatment schedule will depend upon the type of therapy recommended. If chemotherapy is recommended, more detailed information will be given to you.

What are the side effects of chemotherapy?

Some people do experience side effects from chemotherapy. The most feared side effect associated with chemotherapy is nausea and vomiting. This side effect can be managed with specific anti-nausea medication that targets the nausea and vomiting caused by chemotherapy. Fatigue is the side effect that all patients struggle with and it can be frustrating. This is when you must take 'me' time, slow down and accept the generous offers from friends and family.

If you have chemotherapy, the Team will talk to you about the specific chemotherapy drugs. They will provide you with written material on the medication and discuss the management of potential side effects. This will help you understand your journey through this part of your treatment for your Neuroendocrine Tumour.

Biologically Targeted Therapies (mTOR Inhibitors)

This is a new group of medications that, in some individuals, has been effective in the treatment of Pancreatic Neuroendocrine Tumours. These medications are in pill form and interfere with various pathways that are needed for the growth of tumour cells and blood vessels. They are less harmful to the normal cells. These medications are very expensive and may not be covered by all private drug plans.