Neuroendocrine Tumors

Neuroendocrine tumors arise from cells that release a hormone in response to a signal from the nervous system. “Neuro” refers to the nervous system. “Endocrine” refers to the hormones. These tumors may secrete large amounts of hormones. This release of hormones can cause a range of symptoms. Neuroendocrine tumors can arise in many sites, such as the gastrointestinal (GI) tract, lung, and brain.

Neuroendocrine tumors may be fast growing, or high grade tumors. Tumors such as small cell cancers, pheochromocytomas and Merkel cell cancer are high grade tumors. There are also slower growing, or low grade tumors. Tumors such as carcinoid (cancer-like) tumors and islet cell tumors are low grade tumors. As a rule, the treatment and prognosis for high grade tumors are much alike. This also true for most low grade tumors.

High Grade Neuroendocrine Tumors
There are many types of high grade tumors. We will address two types of high grade tumors here.

Pheochromocytoma
This is a cancer of the chromaffin cells that release the hormone adrenalin during times of stress. These cells are found in the adrenal glands. These glands are on the top of the kidneys. Most of these tumors are found in one adrenal gland. A few are found in both or outside of the adrenal glands.

Risk Factors
- **Age** – The tumor most often occurs between the ages of 40 and 60.
- **Gender** – Men are more likely than women to get the tumor.
- **Family history** – Ten percent of the tumors have genetic links.
- **Immune suppression** – People with suppressed immune systems because of HIV/AIDS or an organ transplant have a higher risk of getting a tumor.
- **Family history of multiple endocrine neoplasia, type 1 (MEN1)** – MEN1 is a hereditary condition that increases the chance of getting a cancer of the endocrine system.

Symptoms
- High blood pressure
- Fast pulse and heart rate
- Palpitations
- Anxiety attacks
- Fever
- Headaches
- Nausea and vomiting
- Clammy skin

Diagnosis
- A biopsy removes a small sample of tissue. The tissue is looked at under a microscope.
- **Urine tests** look for a high level of adrenalin in the body.
- **Blood tests** include a glucagon stimulation test and a clonidine suppression test. These tests measure adrenalin levels in the body.
- **CT/MRI I-131-MIBG scan** special scans. They provide detailed images of the body.
Staging
There is no standard staging system for pheochromocytoma. The tumors are placed in one of two groups. The tumors are either
- Localized and benign
- Malignant and metastatic

Treatment
The standard treatment is surgery to remove the tumor. If the tumor has spread, surgery can still be used to remove all visible disease. Doing this will decrease the extra hormone produced. This will decrease symptoms. Closely watching blood pressure before, during, and after surgery is vital.

Targeted radiation therapy may be an option for some patients. Patients whose tumor cannot be removed, has recurred, or has spread, may receive this treatment. Clinical trials are taking place to find a useful chemotherapy treatment.

Merkel cell cancer
Merkel cell cancer is an aggressive and very rare cancer. It starts in the hormone-producing cells just beneath the skin and in the hair follicles of the head and neck.

Risk Factors
- **Age** – Merkel cell cancer is most common in people after the age of 70.
- **Gender** – Men are more likely to get this cancer than women.
- **Race** – White people are most likely to get Merkel cell cancer.
- **Immune suppression** – People infected with HIV/AIDS and people whose immune systems are suppressed because of an organ transplant have a higher risk of getting a tumor.
- **Arsenic exposure** – Exposure to the poison arsenic may increase the risk.
- **Sun exposure** – Some doctors believe that the amount of time spent in the sun may be a risk factor.

Symptoms
- Painless, firm, shiny lumps on the skin that are red, pink, or blue in color. They are found in the head and neck region.

Diagnosis
- **Biopsy** – A biopsy removes a small sample of tissue. The tissue is looked at under a microscope.
- **CT/MRI scan** – These special scans provide detailed pictures of the body. The scans help find the extent of the disease.

Staging
- **Stage IA** – The tumor is smaller than 2 cm. There is no spread to the lymph nodes or distant sites.
- **Stage IB** – The tumor is larger than 2 cm. There is no spread to the lymph nodes or distant sites.
- **Stage II** – The cancer has spread to the lymph nodes close to the tumor, but has not spread to distant sites.
- **Stage III** – The cancer has spread to distant sites.

Treatment
Surgery is the most helpful treatment. To destroy any cancer cells that may remain, radiation might be used. Clinical trials are taking place to find a useful chemotherapy treatment.
Low Grade Neuroendocrine Tumors
There are many types of low grade neuroendocrine tumors. We will address these two types of low grade tumors here.

Gastrointestinal (GI) Carcinoid
These tumors arise from neuroendocrine, hormone-making cells in the GI tract. The GI tract includes the stomach, small intestine, large intestine, and rectum. These cells produce hormones that help control digestive juices. They also affect muscle activity in the GI tract. A GI carcinoid tumor may produce these hormones in large amounts. This can cause a group of symptoms. This group of symptoms are called carcinoid syndrome. More than half of carcinoid tumors are found in the GI tract. They are found most often in the stomach, appendix, small intestine, and rectum. Twenty-five percent are found in the lungs. Most often, these types of tumors are slow growing.

Risk Factors
- **Family history of multiple endocrine neoplasia, type 1 (MEN1)** – MEN1 is a hereditary condition. It is linked to an increased chance of getting cancers of the endocrine system.
- **Having certain conditions that affect how well the stomach is able to produce stomach acid.** This includes atrophic gastritis, pernicious anemia, or Zollinger-Ellison Syndrome.
- **Smoking tobacco**
- **Age** – The average age at diagnosis is 61

Symptoms
There may be no symptoms in the early stages of the tumor. Carcinoid syndrome is caused by high levels of serotonin produced by the tumor. The syndrome may occur if the tumor has spread to the liver. It occurs most often when tumors are found in the small intestine or the right side of the large intestine (ascending colon).

Symptoms of Carcinoid Syndrome
- Flushing, redness, or a feeling of warmth in the face and neck
- Diarrhea or cramping
- Shortness of breath
- Rapid heart rate
- Fatigue
- Wheezing
- Heart disease
- Swelling of the ankles or feet
- Pain or a feeling of fullness in the abdomen

Diagnosis
- **A Biopsy** removes a small sample of tissue. The tissue is looked at under a microscope.
- **Blood tests** can point to the presence and extent of the tumor.
- **A 24-hour urine collection** can help confirm a diagnosis of carcinoid. It may also be used to check its progress.
- **CT/MRI scans** – These special scans give detailed pictures of the body. These scans help find the extent of disease.
- **Octreoscan** – A small amount of octreotide (Somatostatin®) is given intravenously (IV) along with a short-lived radioactive tracer. This medicine will attach itself to tumor cells only. The tumor cells can then be seen on the scan. It is useful in finding the extent of disease.
Staging
There is no standard staging system. Tumors tend to be grouped by where they are found in the body.

- **Localized** – Cancer found in the stomach, appendix, rectum, or small intestine only.
- **Regional** – Cancer has spread from the stomach, appendix, rectum, or small intestine to nearby tissues or lymph nodes.
- **Metastatic** – Cancer has spread to other parts of the body, for example, the liver.

Treatment
- **Surgery** to remove the tumor is the standard treatment for cure. Since these types of tumors are often slow growing, repeat surgery for tumors that return may be an option.
- **Radiation therapy** may be used to ease symptoms caused by disease that has spread to other parts of the body.
- **Chemotherapy** has seen little success in the treatment of these tumors. Clinical trials are looking for better treatments. Ask your doctor if there is a clinical trial you could be a part of.
- **Octreotide (Sandostatin®)** injections may be helpful to ease the symptoms of carcinoid syndrome. It helps by lowering the amount of serotonin made.
- **Radiofrequency Ablation (RFA)** uses a special probe. The probe releases high-energy radio waves that kill cancer cells. This treatment may be used to treat metastatic disease in the liver or lung.
- **Cryosurgery** uses a device to freeze the tumor.
- **Hepatic Artery Embolization** blocks the hepatic artery. This is the main blood vessel that brings blood to the liver. Blocking the flow of blood to the liver and tumor, kills cancer cells growing there.

Islet Cell Tumors
These tumors are found in the pancreas and are very rare. Other names for islet cell tumors include:
- Pancreatic islet cell tumor
- Pancreatic endocrine tumor
- Islet of Langerhans tumor
- Neuroendocrine tumor.

Islet Cell Tumors can be either **benign** (not cancer) or **malignant** (cancer). The Islets of Langerhans are special cells in the pancreas. These cells produce hormones, the most important being insulin. Insulin helps control the amount of sugar in the blood.

Islet cell tumors can be **functioning** or **nonfunctioning**. Functioning islet cell tumors produce hormones which cause symptoms. There are five main types of functioning islet cell tumors.

- **Gastrinoma** also called Zollinger-Ellison syndrome. With this syndrome large amounts of **gastrin** are produced. This hormone causes large amounts of acid to be made in the stomach. As a result of the excess acid, ulcers may form and severe diarrhea may occur. Other symptoms may be abdominal pain and weight loss.
- **Insulinomas** make too much insulin. This causes **hypoglycemia** (low blood sugar). Weight loss, fatigue, lightheadedness, and weakness are common symptoms. Confusion can also occur. These tumors are rarely malignant.
- **Glucagonomas** produce too much glucagon. This causes hyperglycemia (high blood sugar). Symptoms of include frequent urination, increased thirst, skin rash, and sore tongue.

- **VIPoma**, (Verner-Morrison syndrome) occur when too much vasoactive intestinal peptide (VIP) is made. This is a hormone that affects water transport in the intestine. Too much VIP causes large amounts of watery diarrhea, flushing, fatigue, nausea, and low potassium.

- **Somatostatinoma** is a tumor that most often occurs in the head of the pancreas. This type of tumor makes too much of a hormone called somatostatin. This hormone slows the secretion of other hormones, including insulin and gastrin. Too much somatostatin can cause electrolyte imbalances, diabetes, weight loss, loss of gastric acid, and poor absorption of food in the intestine.

Most islet cell tumors are **nonfunctioning**. This means they do not produce large amounts of hormones. These types of tumors do not cause the symptoms mentioned above. As a result, they are often found at a more advanced stage.

**Diagnosis**
- The tests listed under Carcinoid Tumors are the same tests used to diagnose islet cell tumors.

**Staging**
There is no standard staging system for islet cell tumors. Often these types of tumors are placed into one of three groups:
1. Tumors within the pancreas, and only occur in one site
2. Tumors within the pancreas, and occur in many sites
3. Tumors that have spread to lymph nodes or other parts of the body

**Treatment**
- **Surgery** to remove the tumor is the standard treatment for cure. In cases where a cure can not be achieved through surgery, **debulking** may be done. Surgery in these cases serves to reduce the amount of tumor. Doing this may be helpful to ease symptoms.

- **Radiation** therapy has not been shown to work well in treating islet cell tumors.

- **Chemotherapy** has seen only some degree of success in the treatment of islet cell tumors. Clinical trials are looking for treatments that will work better. Ask your doctor if a clinical trial is an option for you.

- **Octreotide (Sandostatin®)** injections may be helpful to ease the symptoms of an islet cell tumor. It helps because the amount of serotonin produced is decreased.

- **Radiofrequency Ablation (RFA)** uses a special probe. This probe releases high-energy radio waves. These waves kill cancer cells. This treatment may be used to treat disease that has spread to the liver or lung.

- **Cryosurgery** uses a device to freeze the tumor.

- **Hepatic Artery Embolization** blocks the hepatic artery. This is the main blood vessel that brings blood to the liver. Blocking the flow of blood to the liver and to the tumor kills cancer cells growing there.
If you have questions of concerns about this handout please discuss them with your doctor or nurse.