This booklet is part of the Paul Hunter Information Library, a series of patient friendly publications about neuroendocrine tumours, and related conditions treatments and tests, produced in memory of the late snooker player Paul Hunter, 1979-2006.

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The NET Patient Foundation supports people diagnosed with neuroendocrine tumours and their families.

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Glucagonomas

Glucagonomas are rare tumours that develop almost exclusively in the pancreas. There have been few reports of the tumours originating outside the pancreatic gland. The tumours usually develop from pancreatic alpha-cells often found at the base of the pancreas (called the tail) that are responsible for making the hormone glucagon. This hormone helps to regulate the amount of glucose (sugar) circulating in the bloodstream. When the cells develop into tumours the amount of glucagon circulating in the bloodstream can rise dramatically.

What is known about these tumours?

Most cases arise sporadically, although a small percentage (less than 10%) are linked to the genetic, inherited syndrome called MEN1. (For further information about this syndrome see the NET Patient Foundation leaflet on MEN 1).

Like other neuroendocrine tumours (cancers that develop in cells that play a part in the hormonal system) glucagonomas are classically slow growing.

The condition is most often found in patients over 40, although if tumour development is linked to MEN1 it may be picked up at an earlier age.

Like other NETs, glucagonomas may grow ‘quietly’ and without obvious symptoms for some years.

By the time symptoms develop and become troublesome between 60% and 80% of patients may have experienced a spread of the disease beyond the pancreas usually to the liver. However, even when there is disease spread most patients will still be able to look forward to a good quality of life, with the right care and treatment.

What are the symptoms of Glucagonomas?

The larger the tumour grows the more glucagon and other peptides are produced and this can cause a number of key symptoms and conditions to develop. (Looking back, you may find you have been treated for the following conditions separately).

- NME - a striking rash known as necrolytic migratory erythema (NME for short). The rash tends to spread from one part of the body to another migrating from the groin to the buttocks, chest, lower legs and occasionally over areas of minor trauma. In some cases the rash is mistaken for eczema and is treated accordingly to no good effect. The rash can become crusted and blister, and over time may cause a change in skin pigmentation. The affected areas may also be susceptible to infection. The rash can extend to the mouth and create a burning sensation.
- Weight loss
- Diabetes
- Cracked surface of the tongue
- Thickened nails
- Inflammation of the inner lining of the cheeks and lips
- Chapped lips
- Anaemia in 50% of patients
- There is a predisposition to forming blood clots and there may be a history of blood clots in lungs (pulmonary embolism) or legs (deep vein thrombosis)
- There may be some hair loss
- Women may experience inflammation of the vagina or vulva a condition called vulvovaginitis
- Between 20 and 40% of patients may also have raised levels of the hormone gastrin or vasoactive intestinal peptide (known as VIP) that has a role in the digestive process.
How are Glucagonomas diagnosed?

If there is a history of diabetes and evidence of the NME rash, a doctor should suggest a fasting blood test to find out whether you have elevated levels of glucagon in the blood. Patients with glucagonomas can find their levels raised many times above normal. A routine blood test may also detect elevated levels of a neuroendocrine tumour marker called Chromogranin A. Other tests may include scans (for example ultrasound, CT, MRI or an Octreotide scan) to look at the pancreas gland and other organs. A biopsy may be performed of a suspected tumour site in order to confirm the diagnosis and/or to get further information regarding the tumour.

What causes the rash?

The cause of the NME rash is unknown although there is speculation it is associated with a deficiency of certain trace elements such as zinc, or low levels of certain amino or fatty acids, and/or a deficiency in Vitamin B and other nutrients as a result of excessive glucagon in the bloodstream.

Treatment for Glucagonomas

Surgery can offer the possibility of a cure if the disease is localised. Unfortunately, in most patients the disease may have already spread at the time of diagnosis and so it may not be appropriate to perform surgery. However a surgical opinion should always be part of the review process as sometimes a two-stage procedure might be considered, for example, surgery to remove a pancreatic tumour followed by another operation to remove a liver tumour. Additionally, the possibility of ‘debulking’ surgery may be considered if, for example, a surgeon can remove more than 90% of all tumour.

When the tumour is contained and surgery on the pancreas is planned, a surgeon may need to remove the spleen at the same time depending on the position of the tumour. This will generally be done as an open operation although there are some surgeons who are beginning to develop keyhole surgery for pancreatic tumours.

Ideally a surgeon will remove only the part of the pancreas containing the tumour. Sometimes insulin injections are required to control sugar levels. If a large amount of the pancreas has to be removed then it is more likely that insulin will be required.

What if the Glucagonoma has spread?

There are still treatment options.

A surgeon may still consider removing part of the tumour, a procedure called debulking, with the aim of reducing the levels of circulating glucagon that cause the unpleasant symptoms. If the disease has spread to the liver (the most common site for secondaries of this type of tumour to be found) there may be options other than surgery.
Other possible treatments

Every patient’s case is highly individual.

**Medical treatment with somatostatin analogues** - Octreotide or Lanreotide injections are often considered in order to reduce the glucagon hormone release from tumour cells. The injections are either short acting and given daily, or longer acting and administered every 28 days by a health professional.

**Interferon** - Interferon stimulates the immune system to fight cancer cells. However this treatment can be associated with significant side-effects.

**Chemotherapy** - May be given especially if there are signs of the tumours growing.

**Transarterial chemoembolisation** - involves cutting off the blood supply to the tumours, this may be considered with or without the addition of intra-arterial chemotherapy. Occasionally other ablation techniques such as radiofrequency ablation might be used if the tumours in the liver are small and few in number. This involves guiding a special needle electrode to the tumour and then passing a radiofrequency current through it to heat the tumour tissue and ablate, or eliminate, it.

**Radionuclide targeted therapy** – also known as magic bullet treatment is considered for patients who have positive uptake on the Octreotide scan. This treatment carries a radioactive particle such as Yttrium-90 or Lutetium-177 attached to Octreotide to wherever there are tumour cells (which have lit up on the Octreotide scan).

**Drug Trials** – Sometimes patients may be asked to take part in clinical trials of a new drug therapy.

**Blood thinning tablets** - In view of the predisposition to forming blood clots patients are sometimes recommended aspirin or blood thinning tablets.

Improving quality of life

For patients with the NME rash your doctor may also recommend supplementation with zinc and amino acids. Simple measures, such as applying gentle skin creams or emollients to soothe and hydrate any crusting or blistering of the skin, combined with treatment for diabetes, can improve matters considerably.

Patients often feel improved with the reduction in hormone levels resulting from one of the treatments already mentioned.