Insulinomas

NET Patient Foundation
Insulinomas

Insulinomas are a rare type of functional neuroendocrine tumour usually found in the pancreas. They are called functional because they produce insulin and cause blood sugar levels to drop, often quite dramatically and in ‘episodes’.

Even the smallest tumours can cause symptoms connected to hypoglycaemia (the medical term for low blood glucose levels).

The vast majority are benign (with no spread beyond the pancreas). However, 10% are malignant and by the time of diagnosis will have spread elsewhere in the body, usually the liver. The tumours are generally diagnosed in middle age and slightly more women are affected. If an insulinoma is suspected you may also be screened for a genetic condition called MEN1.

(for more information on this, see A.M.E.N.D.’s booklet on MEN1, available under Patient Resources at www.netpatientfoundation.org).

The role of the pancreas

In a healthy person the pancreas produces both insulin and glucagon. When blood sugar rises after a meal, beta cells in the pancreas release insulin. The insulin helps sugar from food to enter the blood cells and lowers levels of glucose to normal.

If blood sugar falls too low then alpha cells in the pancreas produce glucagon that triggers the liver to release glycogen. This is converted into blood glucose, thereby lifting levels of blood sugar to normal.
What is known about insulinomas?

In most cases a single tumour develops in the beta cells (the insulin producing cells) within the pancreas. In a very small number of cases (1-3%) the tumour will develop in insulin producing cells that have ‘escaped’ into the abdomen. The reason why the tumours form is not yet fully understood. They may be present for many years prior to diagnosis as the symptoms they cause can be confused with other conditions.

What are the key symptoms?

The tumours are associated with episodes of low blood sugar (hypoglycaemia) that can cause an array of symptoms.

Low blood sugar levels can affect the central nervous system (the brain) causing episodes of confusion, panic attacks and even personality change.

The insulin producing tumours can also affect the autonomic nervous system (that controls many of the organs, muscles and systems in the body, such as heart rate) causing palpitations, sweating and a trembly feeling.

Patients with an insulinoma will find eating or drinking something sugary can quickly alleviate their symptoms.

Diagnosis

Insulinomas can be diagnosed through a simple fasting blood test. Your NET specialist will look for a certain combination of:

- low blood sugar (less than 2.8 mmol/l)
- high insulin (6 microunits/ml or higher)
- and high levels of C peptide (0.2 nmol/l or higher), an inactive amino acid that in a healthy body will be produced in equal amounts to insulin.

The doctor may also use a ‘rule of thumb’ guide called the Whipple’s Triad. Under this guide an insulinoma will be considered if you experience:

- Symptoms and signs of hypoglycaemia
- Blood sugar levels below 2.8 mmol/l
- Recovery from an attack after eating something sugary

If you are on medication for diabetes you can still be tested for insulinomas:

- If someone takes insulin, doctors will be looking at the levels of C peptides in the blood. Commercially used insulin does not contain C peptides, so a test will look for certain levels that might suggest a tumour is present.

- If someone takes sulphonylurea tablets (that lower blood glucose levels) the doctor will be looking at the level of sulphonylurea in the blood in relation to insulin, blood sugar and C peptide levels. If it is normal an insulinoma will be suspected.

The long fast

If further confirmation is needed you may be invited into hospital for a special fasting test that can take between 48 and 72 hours. You will not be allowed to eat or drink, apart from water, throughout this period. You will have blood tests at intervals of between three to six hours, and also whenever you show symptoms of low blood sugar, to look at the key levels of blood glucose, insulin, C peptides and sulphonylurea. This hospital fasting test will diagnose insulinomas in more than 90% of cases.

Low blood sugar levels caused by the tumour can trigger

- Confusion, anxiety, personality disorders and even aggressiveness
- Rapid heartbeat, sweating, palpitations, feelings of hunger, dizziness and drowsiness. You may look pale, have a headache, feel irritable and suddenly weak.
- If blood sugar drops very low or very suddenly it is possible to lose consciousness and it can even lead to seizures (fits).

Note: Insulin normally helps to lower blood sugar, and when it gets to the right level the body gets a signal to stop the insulin production. In people with insulinomas the body does not get this signal and high levels of insulin continue to be released leading to the hypoglycaemic episode.
Further tests

SRS Somatostatin Receptor Scintigraphy (Octreotide scan) – this is a common scan for NET patients. It can help to detect tumours that might be missed on other conventional scans. Around 50% of insulinomas have special receptors on their surfaces called somatostatin receptors. Octreotide is a somatostatin analogue, a substance that mimics the action of naturally occurring somatostatin. When Octreotide is combined with a mildly radioactive agent and then injected via a vein in the arm, it sticks to somatostatin receptors on the tumour surface and the tumours ‘light up’ on the screen as hot spots. This is a useful test to find out more about your tumours, where they are positioned, and also whether you would be suitable for certain treatments that use Octreotide or another chemical called Lanreotide as a carrier agent.

Ga-68 octreotate/octreotide PET scan – this is a new type of molecular imaging for NETs. It is much more sensitive than Octreotide scan, especially for small size tumours such as insulinomas. Also, it can be completed and provide very good quality images within hours, whereas Octreotide scan needs two days to be completed. Unfortunately, this new imaging modality is not widely available in UK yet.

CT scan – a computerised tomography (CT) scan provides a three dimensional picture of the inside of the body. It can be used to determine the position and size of tumours, and regular scans are useful to find out more about the rate of tumour growth and how your tumour is responding to treatment. When you arrive at the clinic you will probably be asked to drink a litre of fluid that contains a contrast agent that helps to highlight tumours, and you may also have a cannula inserted through which a special contrast dye is administered during the scan. These both help your specialists to read the scans more clearly as the tumours are highlighted.

MRI scan – this is a whole body scan. Magnetic resonance imaging (MRI) scans can help reveal where tumours are positioned. It uses magnetism rather than X rays to take pictures of inside the body. Scans can take up to one hour to complete and you have to stay very still inside the scanner, lying on a couch. MRI is often used in conjunction with CT and SRS scans. They have a good value when detecting liver metastases (spread of tumour into the liver).

Endoscopic ultrasound (EUS) – is a technique that uses a special endoscope that has an ultrasound machine at the tip. Endoscopy refers to the procedure of inserting a long flexible tube via the mouth or the rectum to see the digestive tract, whereas ultrasound uses high-frequency sound waves to produce images of the organs and structures inside the body such as the liver and pancreas. Using the EUS scope, doctors can place the ultrasound probe in the GI tract, close to the area of interest, so that a very detailed image of the deeper layers of the GI tract, surrounding lymph nodes, blood vessels, and organs can be obtained. Biopsies can also be taken at the same time. EUS is performed under sedation in the endoscopy unit. For detection of the primary tumour this procedure has a high sensitivity and accuracy level.

Portal vein sampling - there are other interventional tests that can be done if there is still doubt. A procedure that involves testing blood taken from the portal vein (that carries blood from the GI tract to the liver) following an injection of calcium (that stimulates insulin secretion) can reveal insulinomas smaller than 1cm. This test is called PVS (portal vein sampling) and is done under sedation.

Once the diagnosis of insulinoma has been made, it is likely you will be screened for the presence of MEN1 (Multiple Endocrine Neoplasia, type 1) syndrome, a condition that includes tumours of parathyroid glands, pancreatic neuroendocrine tumours and pituitary tumours.

What does screening for MEN1 involve?

A blood test to estimate levels of calcium and certain hormones in the blood.

TREATMENT FOR INSULINOMAS

Benign tumours (with no spread beyond the pancreas)

Complete surgical removal of the insulinoma from the pancreas can provide a cure. Most patients have single tumours that can be totally removed – “enucleated” – without even the need to cut away any part of the healthy pancreas. Often this can be performed via keyhole surgery.

During surgery the specialist may perform an intraoperative ultrasound to ensure there are no other small tumours close by or any affected lymph nodes.

Malignant tumours

There are treatment options if you have a malignant tumour that can lead to an improved quality of life and good control of symptoms

Surgical - surgery may still be considered. It may be possible to resect (surgically remove) part of the pancreas containing the tumour and also surgically remove any tumour which may have spread to the liver, which tends to be the main secondary site for these tumours.

Medical management - if surgery is not possible you may be prescribed a tablet called diazoxide that can help to elevate and control blood sugar levels.

Other treatments

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

Transarterial chemoembolisation - may be considered if there has been spread of disease to the liver. This procedure involves cutting off the blood supply to the tumours 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 radio frequency current through it to heat the tumour tissue and ablate, or eliminate, it.

Chemotherapy – can be helpful for highly aggressive tumours that do not respond to other measures. Your NET specialist will advise you. The combination usually used is 5-fluorouracil plus cisplatin and streptozotocin.

New molecular treatments – Everolimus. Everolimus is a new oral agent, which belongs to the group of drugs that inhibit the ability of the neuroendocrine tumour to produce new vessels. There is now evidence that the drug is beneficial in patients with pancreatic neuroendocrine tumours and, according to two small published series of patients, it can improve the blood sugar levels, if other treatments have failed to do so. However, as this treatment may some side effects, your NET specialist will advise you whether you are suitable for this drug.
What about somatostatin analogue injections?

Some NET patients are helped with regular injections of octreotide or lanreotide. But in the case of people with insulinomas this injection can make symptoms worse by decreasing blood sugar further. You will need to seek specialist advice from a NET consultant to find out whether this treatment would be suitable for you.

Diet for Insulinoma

Insulinomas are rare tumours, therefore there is very little research or existing evidence regarding diet in this condition. Although diet cannot control the release of insulin from the tumour, it can help prevent low blood sugars. People with insulinomas tend to suffer from low blood sugar levels until the tumour has been treated to stop it releasing excess insulin. If you are losing weight, please ask to see a dietician.

Glycaemic index

The glycaemic index (GI) is a measure of how quickly foods that contain carbohydrates will raise blood sugar levels. Foods are given a GI number or classed as low, medium or high GI.

Low GI carbohydrates are released slowly into the blood and therefore are able to maintain blood glucose levels for longer. It is recommended that you try to choose low GI carbohydrates as much as possible during the day to prevent sharp peaks and troughs in your blood sugars.

High GI carbohydrates are released very quickly into the blood and are very useful when you are experiencing a hypoglycaemic (very low blood sugar) episode.

How to switch to a low GI diet

- Eat breakfast cereals based on oats, bran and wholegrain wheat e.g. All Bran Flakes, porridge.
- Use breads with wholegrain, stone ground flour or sour dough e.g. multigrain, wholemeal, soya and linseed, pumpernickel.
- Include pasta, noodles, pearl barley or quinoa.
- Choose new potatoes, sweet potatoes or yam in preference to other potatoes. Leave the skins on if you can.
- Eat plenty of vegetables and salads.
- Add beans, lentils and other pulses to soups, stews, salads and other dishes.
- Use basmati or long grain rice, rather than Thai, jasmine, sticky or short grain rice.
- Choose grainy crackers and crisp breads e.g. Ryvita Seeded, oatcakes.

Tips for Low GI meal choices:

**Breakfast**
- Muesli*, All Bran, Sultana Bran, Special K
- Oat-based breakfast cereal and fruit

**Lunch**
- Baked beans with jacket potato
- Lentil-based soup
- Variety of breads: pitta bread, breads made with mixed grains and pumpernickel
- Grilled chicken, salad, basmati rice and peas

**Evening meal**
- Basmati rice, sweet potato, buckwheat, bulgar wheat, pearl barley, noodles
- Vegetables with meal
- Pasta-based meals
- Beans and pulses (dahl)

**Snacks**
- Fruit
- Yoghurt (low fat)
- Popcorn
- Rye bread, fruit loaf*
- Nuts*

* These foods can have a higher fat content, therefore consume in moderation if you are trying to lose weight.

Hypoglycaemia

Hypoglycaemia is low blood sugars. Hypoglycaemia or ‘hypos’ can make you feel unwell and can be dangerous. Diet can help in preventing hypoglycaemia.

Tips:
- Use low or medium GI foods when possible.
- Have a bedtime snack to prevent hypos while asleep. Some people may need to set an alarm to wake up for a snack during the night too if they have hypos during the night.

High GI - suitable food and drinks for hypos:
- Jelly babies, Liquorice Allsorts, Wine Gums, jelly beans
- Dextrose tablets
- Lucozade (1/3 bottle)
- Lucozade Sport (1/2 bottle)
- Ribena (1/2 carton)
- Coca Cola, Fanta (1/2 can)
Multidisciplinary teams

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

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

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

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

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

Clinical Research

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

Research goals include:

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

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

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

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

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

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

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

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

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

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

**ClinicalTrials.gov**
This is a register of federally and privately supported clinical trials conducted in the United States and around the world.
clinicaltrials.gov
You can also search for research trials available to patients in the UK and Europe on these websites:
www.macmillan.org.uk
www.cancerhelp.org.uk
www.ctu.mrc.ac.uk (The Medical Research Council Clinical Trials Unit)
www.ncr.org.uk (National Cancer Research Network)
www.eortc.be/ (European Organisation for Research and Treatment of Cancer)

**Useful Organisations**

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

**AMEND (Association for Multiple Endocrine Neoplasia Disorders)**
Support and information for people affected by Multiple Endocrine Neoplasia Disorders and associated endocrine tumours and syndromes
01892 516076
www.amend.org.uk

**Insulinoma Support Network**
Sharing knowledge and experience of insulinomas
www.insulinoma.co.uk
Further support

NET Patient Foundation
From diagnosis, throughout treatment and beyond, our services are here every step of the way. Here is an overview of all the services we offer to people living with and beyond NET cancer.

Helpline - 0800 434 6476
Our free, confidential helpline is here for anyone who has questions about NET cancers (neuroendocrine tumours). Your call will be answered by one of our nurses or trained staff members with experience of NET cancer. Whatever your concern, you can be confident we will understand the issues you might be facing, and that the information you receive is clear and up-to-date. We will also let you know where else you can go for further support.

The helpline is open 10am-2pm Monday to Friday. We also operate a call-back service for those who wish to leave a message out of hours.

Website – www.netpatientfoundation.org
We know how important it is to understand as much as possible about your NET cancer. Our website is here round-the-clock giving you instant access to information when you need it. As well as clinical information, you’ll find real life experiences and access to the largest online NET cancer community in the UK, so you can share your questions or concerns with other people in a similar situation.

Discussion forums
Through our discussion forums you can exchange tips on coping with the side effects of treatment, ask questions, share experiences and talk through concerns online. Our dedicated areas for popular topics should make it easy for you to find the information you’re looking for. The discussion forums are easy-to-use. If you’re feeling anxious or just need to hear from someone else who’s been there, they offer a way to gain support and reassurance from others in a similar situation to you.

Ask the nurse
If you find it difficult to talk about your cancer, we can answer your questions by email instead. Our ‘ask the nurse’ service is available on the website – complete a short form that includes your question and we’ll get back to you with a confidential, personal response.

Information and support sessions
We run information and support sessions for people living with NET cancer. These meetings include talks from some of the country’s top NET specialists, invaluable Question & Answer sessions, as well as an opportunity to meet other NET patients. For information about meetings in your area, please see our website or call our helpline.

Information resources
Our free information resources are for anyone affected by NET cancer. They are here to answer your questions, help you make informed decisions and ensure you know what to expect. All of our information is written and reviewed regularly by healthcare professionals and people affected by NET cancer, so you can trust the information is up-to-date, clear and accurate. You can order our publications by sending us an email or calling the helpline. All our publications can also be downloaded from our website.

Other organisations

Macmillan Cancer Support
89 Albert Embankment London SE1 7UQ
General enquiries: 020 7840 7840
Helpline: 0808 808 0000
Website: www.macmillan.org.uk
Textphone: 0808 808 0121 or Text Relay

Macmillan Cancer Support provides practical, medical, emotional and financial support to people living with cancer and their carers and families. Over the phone, its cancer support specialists can answer questions about cancer types and treatments, provide practical and financial support to help people live with cancer, and are there if someone just wants to talk. Its website features expert, high-quality information on cancer types and treatments, emotional, financial and practical help, and an online community where people can share information and support. Macmillan also funds expert health and social care professionals such as nurses, doctors and benefits advisers.

The NET Patient Foundation incorporating Living with Carcinoid was formed at the start of 2006 and has Charity Commission status.

The Foundation has the following aims:

- To provide accurate and up-to-date information for people living with, or affected by, NET cancers
- To provide support for patients and others affected by NET cancers
- To provide education for healthcare professionals in the treatment and care of NET patients
- To raise awareness of NET cancers within the medical community, and amongst the general public
- To improve access to care for NET patients
- To raise funds, which will help to support research around the UK & Ireland

Did you know?
• 50% of patients are diagnosed when the cancer has already spread
• Early diagnosis significantly improves outcomes for patients
• Help us to make a difference. Donate now at www.netpatientfoundation.org

Why the moth?
We have chosen the moth as our logo to symbolise this ‘camouflaged’ condition. We aim to encourage medical professionals to consider an uncommon alternative when symptoms persist (i.e. a NET rather than IBS).

“We see an insect beating its brightly patterned wings against your window, don’t assume it’s a butterfly. It could be a moth.”
This booklet has been compiled with the assistance of:

Dr Christos Toumpanakis MD PhD
Consultant in Gastroenterology & Neuroendocrine Tumours
Honorary Senior Lecturer UCL
and Caley Schaid
Royal Free Hospital, London