Pathology testing and Neuroendocrine tumours (NETs)
NETs are probably far more common than we think.

Most grow so slowly and produce such widely varied and non-specific symptoms, or no symptoms at all, that it is not unusual for someone to have spent years seeking answers to their health problems before a diagnosis is made.
NEUROENDOCRINE TUMOURS (NETs)

NETs are relatively uncommon tumours that develop from neuroendocrine cells. These cells are present in many organs throughout the body and their job is to release hormones – chemical messengers that regulate bodily functions.

There are several different types of NET depending on where they occur. However, they all share similar cellular characteristics that can be seen under the microscope.

NETs can be benign or malignant. Most arise in the digestive system, including the bowel, appendix, pancreas and stomach and are referred to as gastroenteropancreatic neuroendocrine tumours (GEP NETs). They can also develop in the lungs; the better known include small-cell lung cancer, large-cell neuroendocrine carcinoma, and typical or atypical carcinoid tumours. Very rarely, they form in other organs such as the liver, gallbladder, bile ducts, kidneys, ovaries or testicles. The largest sub-group of NETs are carcinoids, which account for more than half of those diagnosed.

NETs are uncommon and also underdiagnosed. They can overproduce hormones such as serotonin, insulin, gastrin and catecholamines. This can be continuous or intermittent and lead to symptoms and syndromes (groups of symptoms) that can be characteristic of the particular NET. Symptoms are often vague and non-specific and vary widely according to the type, size and location of the tumour(s). Common symptoms include diarrhoea, flushing of the skin, wheezing, weight loss, anaemia, low blood sugar (headaches, confusion), stomach cramps and occasionally skin rash. Some NETS do not produce hormones and cause minimal symptoms. These are referred to as ‘non-functioning’ NETs.
DIFFICULTIES IN DIAGNOSIS

Because NETs are generally slow-growing, and any symptoms they produce are varied and non-specific, they can be notoriously difficult to diagnose. NETs often present a diagnostic challenge for doctors.

It is not unusual for someone with a NET to have spent years seeking answers to their health problems before a diagnosis is made.

PATHOLOGY TESTS

Your doctor may start by referring you for some blood and urine tests called tumour markers. These are substances such as proteins and hormones in the blood and urine that are known to increase when certain tumours are present. Although they cannot be relied upon alone to identify a particular tumour, these markers are very useful in confirming a diagnosis in someone strongly suspected of having a tumour. They are also important in monitoring for tumour recurrence or progression after treatment.

Chromogranin A (CgA)
CgA is a protein released by neuroendocrine cells and is seen in increased amounts in the blood of most people with NETs. CgA is especially useful because it is also elevated by non-functioning NETs. This means CgA is one of the most widely used markers for NETs. Serum CgA levels are also elevated by the use of proton pump inhibitors (PPIs), used for gastro-oesophageal reflux or peptic ulcers. These must be stopped for at least two weeks before the blood sample is collected.

Platelet serotonin
Most of the serotonin in the blood stream is stored in platelets. This blood test is often used in combination with CgA and 5-HIAA.
5-Hydroxyindoleacetic acid (5-HIAA)
Serotonin is broken down by the liver into a chemical called 5-HIAA and then passed out of the body in the urine. A urine test detects raised 5-HIAA levels. Because serotonin may be secreted intermittently, a 24-hour urine collection is needed. Serotonin-rich foods such as bananas, avocados, tomatoes, pineapples and nuts can cause temporary elevations of 5-HIAA and should be avoided for at least three days before the test. Some medications and other health conditions can affect 5-HIAA levels and need to be discussed with your doctor.

Hormones
As well as CgA, 5-HIAA and platelet serotonin, pathology tests may be used to find out if you have increased blood levels of particular hormones. These include insulin, gastrin, pancreatic polypeptide (PP) vasoactive intestinal peptide (VIP) and glucagon.

Microscopic investigation (histology)
By examining a sample under the microscope the pathologist can identify the precise type of tumour and assess how advanced it is so that treatment decisions can be made. This requires surgery and/or a biopsy to obtain the sample.

Observing a sample of the tumour microscopically provides the only definitive diagnosis of a NET.
How can I have tests for NETs?
Pathology is a medical specialty, so your doctor will need to complete a pathology request form to refer you for tests.

Are there any special things I have to do?
Because hormones may be released only intermittently by NETS, some samples for hormone tests may need to be collected when symptoms are present. Your doctor will advise you on this.

The fasting blood tests and the 5-HIAA 24-hour urine test may also have special conditions attached. Your doctor or pathology collector can advise you.

Where can I have my test collected?
Locate our collection centres
For a full list of collection centres and their opening hours, visit snp.com.au. With your web-enabled camera, phone-scan the QR code with a QR code reader application.