

Pancreatic Exocrine Insufficiency (PEI) and Pancreatic Enzyme Replacement Therapy (PERT)

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What is Pancreatic Exocrine Insufficiency?

Pancreatic Exocrine Insufficiency (PEI) can develop when the pancreas doesn't work properly. The pancreas is a key component of our digestive system and has two main functions. Initially it breaks down food into smaller parts that can be absorbed by our body. Once those smaller food parts have been absorbed, the pancreas also ensures they are used appropriately throughout the body. In PEI it is the pancreas' initial function that is impaired. Any disease that destroys pancreatic tissue or blocks the ducts within the pancreas, can cause PEI. In the UK the commonest causes are Cystic Fibrosis, Chronic Pancreatitis and Pancreatic Cancer. PEI may also follow surgery to the pancreas. Severe attacks of acute pancreatitis, where more than a third of the pancreas has been damaged, can also cause PEI.

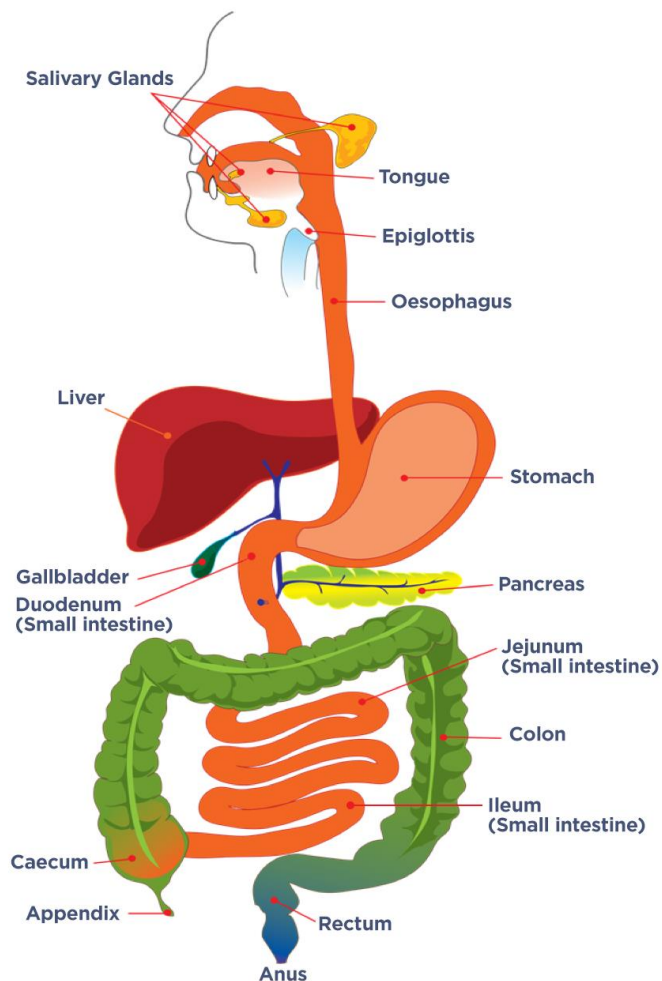
PEI is common in long-term and/or severe chronic pancreatitis. Four fifths of those with severe chronic pancreatitis have PEI and half of those who have had chronic pancreatitis for 5 to 10 years will develop the condition.

What is the role of the pancreas?

To understand PEI it would be helpful to learn more about the role of the pancreas in digestion. The foods we eat are made up of many different constituents at a molecular level. Three of those constituents provide energy to the body: fat, protein and carbohydrate. The pancreas has a crucial role in the digestion of all three.

Most dietary fat, protein and carbohydrate molecules have large and complex structures, which cannot be absorbed through the gut. Some of the carbohydrates in our food, such as sucrose (table sugar) or lactose in milk, have much simpler structures, but even those still need to be broken down before they can be absorbed through the gut.

The pancreas produces a set of specialised molecules (pancreatic enzymes) that can break down fat, protein and some carbohydrates into their smaller parts. Fat is broken down into smaller parts called fatty acids. The pancreatic enzyme responsible for this job is called lipase. Proteins are digested by pancreatic enzymes called proteases which



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break them down to smaller molecules, known as peptides and amino acids. The pancreas also produces an enzyme, amylase, that breaks down starch, a type of complex carbohydrate found in foods such as bread, rice, potatoes, pasta and breakfast cereal.

How does PEI affect digestion?

This breaking down of food into smaller parts releases the nutrients the body needs to function and thrive. Food starts to be broken down in the mouth, with chewing and by mixing with saliva. Stomach acid and its churning motion also break up and mix food. The stomach eventually pumps its contents into the duodenum, the first part of the small intestine. The pancreas, which sits behind the stomach, also reaches the duodenum through a thin tube (the pancreatic duct). The pancreas secretes pancreatic juice through this duct. Pancreatic juice contains pancreatic enzymes, as well as bicarbonate, which neutralises the acid from the stomach.

In a damaged pancreas either not enough enzymes are produced, or the duct that takes them to the duodenum is blocked, or sometimes both. If not enough enzymes reach the duodenum, some of the nutrients in food will not be digested. They will continue to travel along the small intestine and into the large bowel, often triggering unpleasant symptoms. Our gut bacteria might digest some of these nutrients and the rest end up expelled in the stool. This process where nutrients are not absorbed is known as malabsorption. It is important to note that the pancreas has at least five times the necessary capacity to produce enzymes and bicarbonate, so PEI only occurs after prolonged or severe damage (or if the duct is blocked).

Fat malabsorption tends to be the most visible problem in PEI for two reasons. The first reason is that the mouth, stomach and small intestine also produce digestive enzymes, and these may manage to break down proteins and carbohydrates enough to compensate for a malfunctioning pancreas. The digestion of fat, on the other hand, is more reliant on pancreatic lipase (the enzyme that breaks down fat), which means that fat malabsorption tends to be an earlier and/or bigger problem in PEI. The second reason is that fat-malabsorption produces more obvious changes in bowel function than protein-malabsorption, making protein-malabsorption more difficult to diagnose. If there is not enough fat in the diet to trigger the symptoms of fat-malabsorption, the diagnosis of malabsorption is often missed and weight loss, muscle wasting and other symptoms of malnutrition can occur. For this reason, low-fat diets, which only hide the symptoms of PEI and do not treat the real problem, should not be used.

What other roles does the pancreas have?

The secretion of pancreatic enzymes into the small intestine is referred to as its exocrine function and hence the failure to produce enough enzymes is called Pancreatic Exocrine Insufficiency. The other role of the pancreas, which affects the use of nutrients once they have been absorbed into the body, is called its endocrine function. The pancreas endocrine function also requires the use of specialised molecules, such as the hormones insulin and glucagon. These hormones are secreted directly into the blood. Different cells in the pancreas are responsible for its exocrine and endocrine functions, though the bulk of the pancreas is dedicated to producing enzymes for digestion. The cells responsible for producing digestive enzymes are called acinar cells, while those that produce insulin and other hormones are located in the pancreatic islets (or islets of

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Langerhans). These islets are distributed throughout the pancreas, which means that in addition to causing PEI, damage to the pancreas can also lead to problems with insulin production and a special form of diabetes called Pancreatogenic Diabetes.

What are the signs and symptoms of PEI?

PEI can take time to develop and at first the symptoms might be mild. Symptoms can include abdominal discomfort or pain, bloating, flatulence, steatorrhea and weight loss. Steatorrhea appears as fat in the stool, which can look bulky, oily, pale orange/yellow, be foul-smelling and sometimes runny. Stools can float and be difficult to flush and stain the toilet bowl. Fat-soluble vitamins (vitamins A, D, E and K) need fat to be absorbed in the gut so fat malabsorption might lead to deficiencies in these nutrients over time. This can result in bone problems, bruising and poor wound healing, higher rates of infections, visual problems, neurological symptoms, muscle weakness and fatigue.

How is PEI diagnosed?

The diagnosis of PEI is a skilled clinical procedure. The first stage is to ask about symptoms (the history). That may be followed by an examination to look for signs of weight-loss or malnutrition. If PEI is suspected tests will then be suggested to look at the *structure* of the pancreas (usually by X-Rays and scans) and also its *function*. Sometimes the history, examination, structural tests and functional tests agree, in which case the diagnosis is clear. Sometimes however, there is a disagreement between the different tests, or between the tests and the history. When that happens, further tests may be necessary. An experienced clinician will weigh up all these factors in arriving at a diagnosis.

The structural tests are called “imaging techniques” or “scans”. A simple X-Ray may show a severely damaged pancreas, but will miss less severe cases. Although Ultrasound, Computed Tomography (CT) and Magnetic Resonance (MR) scans all aim to look at the pancreas for evidence of damage to its tissue and its ducts, they highlight different features. More than one type of scan may be needed to build up a picture of the type and degree of damage that has occurred. Magnetic Resonance Cholangio-Pancreatography (MRCP) is a special program of the MR scanner which specifically views the ducts of the liver and pancreas. Ultrasound is usually performed by rubbing a probe over the abdomen, but an internal ultrasound (Endoscopic Ultrasound, EUS) may give more detailed information in difficult cases.

It is difficult to test the function of the pancreas because it is buried deep in the abdomen. The method used most commonly in the UK measures the levels of pancreatic enzymes in the stool. During normal digestion some of the enzymes secreted by the pancreas end up in the stool. In PEI the lower levels of enzymes secreted into the duodenum means lower levels also reach the stool. Therefore, measuring levels of pancreatic enzymes in the stool can give an indication of the levels produced by the pancreas. The most reliable enzyme to measure is a protease called elastase-1, because it is not degraded as it travels through the gut and it concentrates in the stool. This test is called the faecal elastase-1 test (or FE-1); the levels of elastase-1 found in the stool can indicate whether pancreatic function is normal, or whether mild to moderate or severe PEI is present. It is relatively convenient to carry out a faecal elastase stool test as it does not require blood tests or invasive examinations, but it can fail to pick up

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cases of mild to moderate PEI. It can also sometimes give false positive results in other causes of diarrhoea.

If further confirmation is needed, an MRCP can be used alongside an injection of the hormone secretin, which stimulates pancreatic secretions. This test gives an indication of the volume of the pancreatic juice that reaches the duodenum, although it cannot give specific amounts of enzymes secreted.

There are other tests that measure, directly or indirectly, the function of the pancreas, though they are not usually carried out in routine clinical practice. The ¹³C mixed triglyceride breath test, which uses a special fat meal labelled with a non-radioactive carbon marker, can give an indication of the amount of lipase (the enzyme that breaks down fat) that is secreted by the pancreas. However, it requires special equipment and is not commonly used in the UK other than in clinical trials. The faecal fat test measures the amount of fat excreted in the stool over 3 days, but it is rarely used because it is unpopular with patients and laboratory staff. Direct tests, in which pancreatic juice is collected via a tube or an endoscope are no longer used in the UK.

How is PEI managed and what is the role of Pancreatic Enzyme Replacement Therapy (PERT)?

Pancreatic enzymes can be taken orally to compensate for the low levels produced by the pancreas in PEI. This is known as Pancreatic Enzyme Replacement Therapy (PERT) and it is the standard treatment for PEI. When taken properly PERT can improve fat, protein and carbohydrate absorption, reduce steatorrhea, flatulence and abdominal pain, increase body weight, and improve nutritional status and quality of life.

Patients take capsules containing pancreatic enzymes (lipase, amylase and proteases) with food. The capsules come in varying strengths so that the dose can be adjusted to suit the different requirements of patients with PEI. They are taken with meals and snacks and release the enzymes in the duodenum, allowing the food to be digested. PERT should be a part of an integrated nutrition strategy, managed by a specialist dietitian, who is a vital part of the team. Patients should avoid seeking other non-registered 'nutritional therapists', as they have variable training and may give poor or dangerous advice. (Read this [British Association of Dietitians leaflet](#) for more information on the differences between a dietitian, a nutritionist, and other roles).

Often patients taking PERT have a poor appetite and, in that case, eating smaller meals more frequently can help. If a patient's weight is stable and they are eating normally, there should be no need to change their meal pattern, just ensure that the PERT dose is adequate and spread out throughout larger meals. There is no need to restrict fat routinely. Occasionally people with pancreatic conditions can develop difficulty tolerating fat. If this is the case the PERT dose should be increased and if this does not help with symptoms, then other conditions should be excluded (such as bile salt diarrhoea). Some people also need vitamin and mineral supplementation.

Many patients are prescribed a standard 'take two capsules three times a day with food' but this doesn't account for the size of the meal or cater for snacks. Successful PERT therapy relies on varying the number and/or strength of capsules taken according to the size and fat-content of the meal. Patients may also be advised to take a part of their dose as they start to eat and the rest halfway through the meal. Some patients take more than two tablets. PERT works directly on food, so it is important the capsules

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are in the stomach at the same time as food. Taking PERT on any empty stomach will not be effective. Some meals take longer to eat (dining out in a restaurant, for instance) and ensuring that PERT is taken with each course will help the capsules mix with the food more effectively. Establishing successful PERT therapy requires a partnership between the patient and their dietitian.

PERT is often prescribed with a proton pump inhibitor (PPI) drug, which reduces acid production in the stomach. In PEI the duodenum is more acidic than usual because the pancreas makes less bicarbonate, which neutralises gastric acid. Pancreatic enzymes do not work in an acidic environment, so PERT capsules have a coating which stops the enzymes being released into acid. If the duodenum is too acidic, the capsules will not release their enzymes in the correct place, and they will not work properly. The PPI drug reduces the amount of acid reaching the duodenum and enhances the action of PERT. The [NICE guideline for pancreatitis](#) recommends that people with chronic pancreatitis are offered monitoring of their pancreatic exocrine function and of their nutritional status at least every 12 months (every 6 months in under 16s). This should be done by clinical and biochemical assessment, to be agreed with a specialist pancreatic centre. Any treatment of vitamin and mineral deficiencies received by the patient should be adjusted according to the results of the assessments. Adults with chronic pancreatitis should also be offered monitoring of HbA1c for diabetes at least every 6 months and a bone density assessment every two years. Hospital staff should inform GPs of the needs for these assessments.

People with chronic pancreatitis and specially those with PEI often learn to manage the food they eat to help their symptoms and improve their nutritional status. Read the section on food and nutrition from Guts UK's [Tips and Suggestions for chronic pancreatitis patients](#) for more information.

Other Guts UK resources:

<https://gutscharity.org.uk/advice-and-information/conditions/chronic-pancreatitis/>
<https://gutscharity.org.uk/advice-and-information/conditions/acute-pancreatitis/>
<https://gutscharity.org.uk/advice-and-information/kranky-panky/tips-and-suggestions-for-pancreatitis-patients/>

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