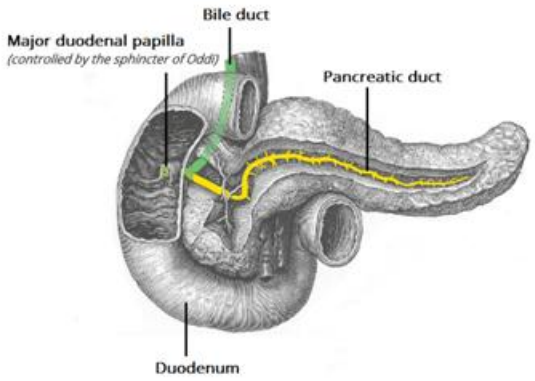
Physiology

The pancreas is an abdominal glandular organ, with an **digestive** (exocrine) and **hormonal** (endocrine) function.

90% of the pancreas is composed of **exocrine** cells, and the remaining 10%, of **endocrine** cells. These different cell types are distinct in their function, and can be considered separately.

The Exocrine Pancreas

The Duct System



The exocrine compartment is classified as a **serous gland**. It is composed of approximately a million 'berry-like' clusters of cells called **acini**, connected by short **intercalated ducts**. Intercalated duct cells beginning within acini are called **centroacinar cells**. The intercalated ducts drain into a network of **intralobular collecting ducts**, which in turn drain into the main **pancreatic duct**.

The pancreatic duct runs the length of the pancreas and unites with the common bile duct, forming the **hepatopancreatic ampulla of Varter**. This structure opens into the duodenum. Secretions into the duodenum are controlled by a muscular valve – the **sphincter of Oddi.** It surrounds the ampulla of Varter, acting as a valve.

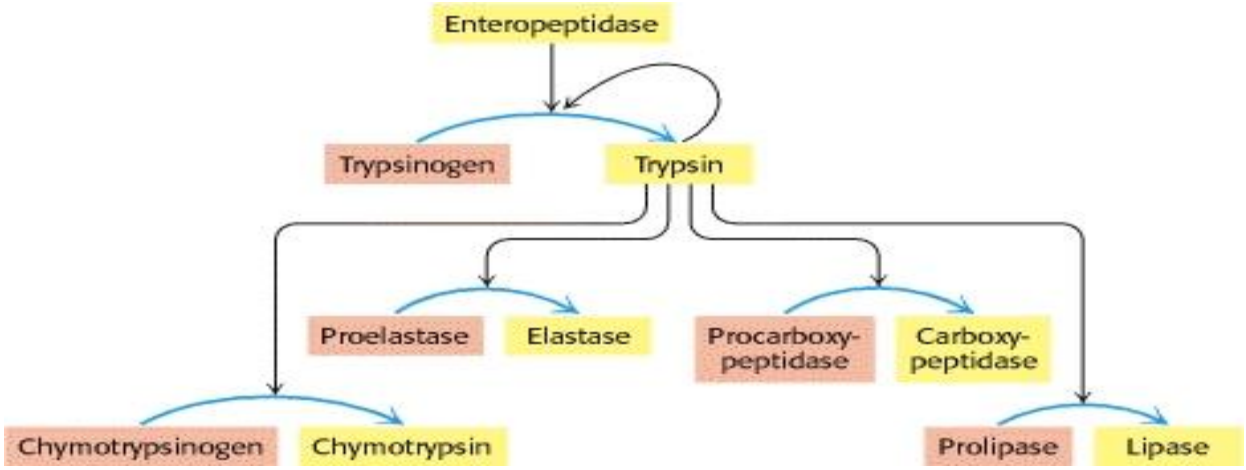
Functions of the Exocrine Pancreas

The main function of the exocrine pancreas is to synthesise and secrete **digestive enzyme precursors** into the duodenum in an **alkaline, protein-rich fluid**.

The pancreas secretes 1.5 litres of this fluid a day. Its alkalinity **neutralises** the acidic chyme entering the duodenum from the stomach and creates an **optimal pH** for pancreatic enzyme activity.

Secretion of Enzymes: Pancreatic enzymes can be produce already active, or as zymogens. **Zymogens** are inactive precursors of enzymes, with are then activated in the small intestine.

1. Zymogens are produced by secretory **acinar** cells, and are stored in **zymogen** granules.
2. Upon stimulation, enzymes are secreted from the acinar cells to form a **primary secretion**, with alkaline fluid later added by intercalated duct cells.
3. This pancreatic juice is released into the duodenum.
4. Here, **trypsinogen** (a zymogen) is activated to **trypsin.** Trypsin is highly proteolytic and activates the remaining zymogens.



The zymogen activation pathway. After activation, typsin causes further activation of the remaining zymogens

Clinical Relevance: Pancreatitis

Inflammation of the pancreas, or **pancreatitis**, is caused by the activation of pancreatic enzymes in the pancreas rather than the small intestine. It is most commonly caused by alcohol or gall stones.

Pancreatitis is characterised by an intense **burning pain in the epigastric region** that **radiates towards the back** and is relieved by sitting forwards. Symptoms include **nausea** and **vomiting** which worsen on eating. Treatment is dependent on the cause of inflammation but includes analgesia and nutritional support.

Regulation of Exocrine Secretion

Exocrine secretion is under both **hormonal** and **neural control**.

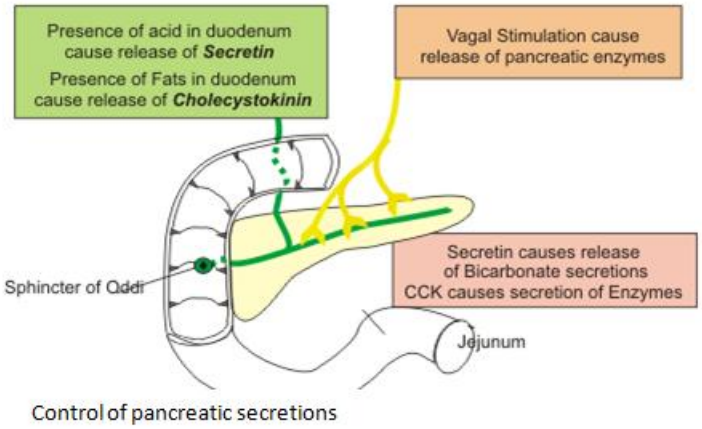
<u>Hormonal:</u>

Enteroendocrine cells of the duodenum secrete the hormones **secretin** and **cholecystokinin (CCK)** into the blood upon entry of acidic chyme into the duodenum.

- Secretin stimulates **intercalated duct cells** to secrete large volumes of bicarbonate-rich fluid.
- CCK stimulates **acinar cells** to secrete enzymes.

Neural:

The pancreas receives autonomic innervation; **parasympathetic** nerve fibres stimulate acinar and centroacinar cells to secrete **pancreatic juice**, whilst **sympathetic** fibres regulate pancreatic **blood flow**.



Control of pancreatic secretions

Clinical Relevance: Pancreatic Carcinoma

Pancreatic carcinoma usually affects the exocrine pancreas, and rarely the endocrine. Its prevelance is increasing in the UK, with risk factors including smoking, diabetes and alcohol. Diagnosis has a poor outcome, with survival often less than 6 months, due to **early metastasis** and **late presentation** of the disease.

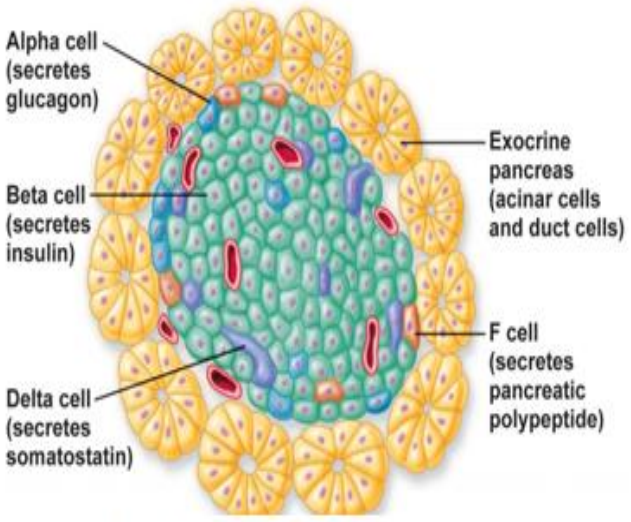
60% of cases affect the **head of the pancreas**; these present with **painless obstructive jaundice**. Carcinoma in the body or tail of the pancreas usually presents with **epigastric pain radiating to the back** and relieved by sitting forwards. Diabetes, weight loss and acute pancreatitis are all common complications arising with pancreatic carcinoma.

The Endocrine Pancreas

Functions of the Endocrine Pancreas

The endocrine pancreas synthesises and secretes **hormones** involved in the regulation of glucose, lipid and protein **metabolism**. In this way, the endocrine pancreas regulates the availability of metabolic substrates.

Endocrine cells are found scattered throughout the pancreas in clusters called **islets of Langerhans**. The islets are made up of at least **5 cell types**. Each cell type is associated with the synthesis and secretion of a different hormone, as discussed below:



The endocrine cells of the pancreas

A (alpha) cells: Make up ~15% endocrine cells and are located around the periphery of the islets. Alpha cells synthesis **glucagon**- this stimulates gluconeogenesis and release of glucose into the bloodstream.

B (beta) cells: Make up ~75% endocrine cells and are located in the centre of the islets. Beta cells secrete **insulin**, the hormone responsible for decreasing blood glucose levels.

D (delta) cells: Make up ~5% endocrine cells. They secrete **somatostatin**, the hormone responsible for the inhibition of insulin and glucagon secretion.

PP (gamma) cells: Make up <5% endocrine cells. PP cells secrete **pancreatic polypeptide** which functions to self-regulate exocrine and endocrine pancreatic secretions.

Epsilon cells: Make up <1% endocrine cells. They produce **ghrelin**, a hormone stimulating appetite.

Regulation of Endocrine Secretion

Endocrine secretion is regulated by **hormones** and input from the **autonomic nervous system.**

The extensive capillary network of the pancreas is such that endocrine cells are in direct contact with blood vessels and/ or other endocrine cells. This facilitates **autocrine** and **paracrine** signalling between islet cells. In this way, endocrine cells receive **positive/ negative feedback**, which directly influences their secretion activity.

Alpha cells: Stimulated by **low blood glucose** and fatty acid levels, and by **glucagon** (positive feedback). **Insulin** inhibits glucagon secretion from alpha cells.

Beta cells: Stimulated by **high blood glucose** and fatty acid levels, and by **glucagon** and **insulin** (positive feedback).

Delta cells: Stimulated by **glucagon**. Somatostatin subsequently inhibits release of digestive hormones including **insulin, glucagon, CCK** and **secretin**.

The islets of Langerhans also receive sympathetic and parasympathetic innervation.

- ***Parasympathetic:*** **Increases insulin** and **glucagon** secretion.

- ***Sympathetic:*** **Increases glucagon** secretion, **inhibits insulin** secretion.

Clinical Relevance: Diabetes Mellitus

Diabetes mellitus is caused by the lack of, or diminished effectiveness of, endogenous insulin. This may be due to the selective destruction of pancreatic beta cells (**Type 1** diabetes), or due to the development of insulin resistance and/ or reduced secretion of insulin (**Type 2** diabetes).

Patients often present with symptoms of **hyperglycaemia** including polyuria, polydipsia, unexplained weight loss and lethargy, and diagnosis is confirmed by consistently **high venous glucose** levels.

Type 1 diabetes is an **autoimmune** disease requiring lifelong treatment with insulin. Type 2 diabetes is largely associated with lifestyle factors such as **lack of exercise, obesity** and **poor diet**. It is initially managed through lifestyle and diet modifications if possible, then with oral hypoglycaemics and failing all else, with insulin.

Source: http://teachmeanatomy.info/abdomen/physiology/pancreas/