

Digestive System

Exocrine Pancreatic Insufficiency

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Form and Function of the Exocrine Pancreas

The pancreas is an L-shaped organ located underneath the stomach and next to the duodenum (the beginning portion of the small intestines). The pancreas has both endocrine functions, secretion of substances into the bloodstream and exocrine functions, secretion of substances into a ductal system, leading to local effects. For the purposes of this chapter, we will focus on the exocrine portion of the pancreas, which is heavily involved in the breakdown of food products.

The exocrine pancreas produces digestive enzymes that play critical roles in breaking down fat, proteins, and carbohydrates into smaller components so they can be

absorbed by the intestinal cells and enter the bloodstream. The pancreas also secretes bicarbonate, which is a buffer that is important in neutralizing the acids that flow into the duodenum from the stomach (see **Figure 6.1**). Pancreatic digestive enzymes are inactive when initially formed but become activated after they are secreted into the intestinal tract. The digestive enzymes are formed in little sacs within the pancreas called acinar cells. These inactive enzymes are secreted into the pancreatic ducts and are then transported into the duodenum, via openings called the major and minor duodenal papilla. While the minor duodenal papilla serves as an opening for the pancreatic duct, the major duodenal papilla also serves as an entryway for the common bile duct from the gall bladder and liver. Bile passes down this duct into the duodenum.

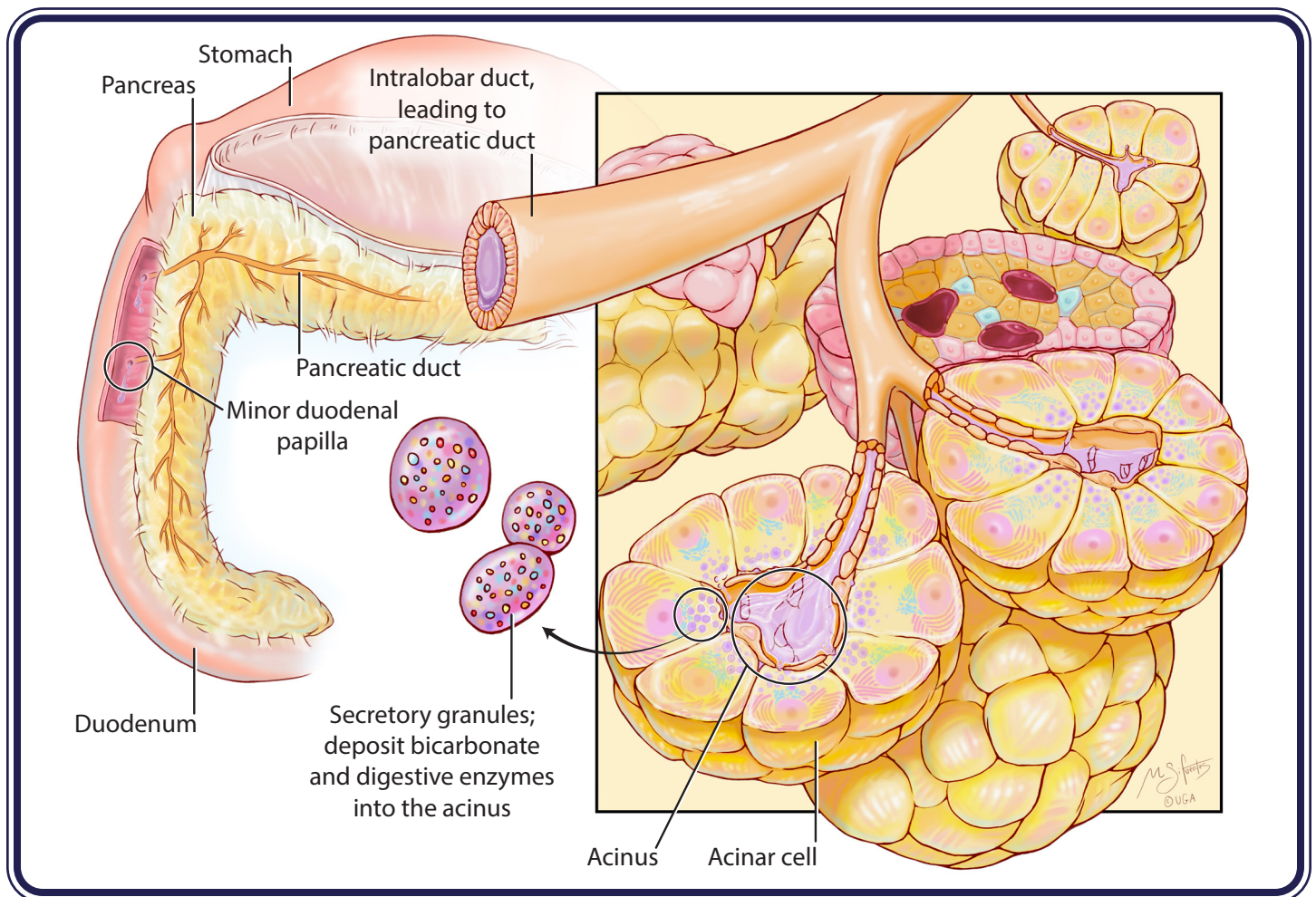


Figure 6.1 - Illustration showing acinar cells of the pancreas which create digestive enzymes

Exocrine Pancreatic Insufficiency

When there is inadequate production and secretion of digestive enzymes from the exocrine pancreas, exocrine pancreatic insufficiency results. This is one of the most common pancreatic diseases in dogs, second only to pancreatitis (i.e., inflammation of the pancreas). Dogs with exocrine pancreatic insufficiency are unable to break down food they eat, which prevents its absorption by the intestines. This leads to overall malnourishment, as vital nutrients are not processed for use by the body. Exocrine pancreatic insufficiency most often develops either as a primary breakdown of the acinar cells that produce the digestive enzymes or as an effect of chronic pancreatitis. In West Highland White Terriers, this disease most commonly is the end result of chronic pancreatitis. In most cases of exocrine pancreatic insufficiency, there is a reduction in the production of all pancreatic enzymes. As a result, the breakdown of fats, carbohydrates, and proteins are all affected. More than two-thirds of affected dogs have a concurrent deficiency in vitamin B12, otherwise known as cobalamin. Cobalamin is necessary for a variety of processes throughout the body including formation of red blood cells and maintenance of cells in the nervous and gastrointestinal systems. The pancreas normally secretes intrinsic factor, a protein required for intestinal absorption of cobalamin. When an inadequate amount of intrinsic factor is produced, cobalamin is not able to be absorbed appropriately, leading to an overall deficiency.

Most patients with exocrine pancreatic insufficiency develop it secondary to other disease processes and begin showing clinical signs when they are middle-aged or older. Breeds, such as German Shepherds, that are predisposed to development of pancreatic acinar atrophy often begin showing clinical signs early in life. The most common clinical sign is weight loss, as affected dogs are unable to

properly digest dietary nutrients that normally would be used to build up fat or muscle. Their stools may be loose or watery, and often have a greasy appearance because they contain excess fat. Many affected dogs will have an increased appetite and a dull, thin hair coat. When exocrine pancreatic insufficiency is mild, patients may not show any outward evidence of disease. In fact, more than 90% of functional pancreatic mass is usually lost before dogs begin showing clinical signs.

A definitive diagnosis is made by measuring trypsin-like immunoreactivity, which evaluates blood concentrations of two digestive enzymes produced by the pancreas, namely trypsin and trypsinogen. Low blood concentrations of these enzymes are considered diagnostic for exocrine pancreatic insufficiency. However, the blood concentrations of these enzymes may be on the low end of the normal range in some dogs who have the disease but are not yet demonstrating clinical signs. This makes it difficult to make a definitive diagnosis in dogs with 'subclinical' disease. In these cases, repeated testing or additional diagnostics may need to be performed to determine if they have exocrine pancreatic insufficiency.

As exocrine pancreatic insufficiency progresses, the pancreas often begins to atrophy and its diminished appearance may be identified with abdominal ultrasound. It is important to know that the pancreas can be difficult to image in healthy dogs, and the pancreas may appear normal in dogs with early-stage exocrine pancreatic insufficiency. Elastase, another digestive enzyme produced by the pancreas, can be measured in feces. However, while dogs with exocrine pancreatic insufficiency have low levels of fecal elastase, dogs with other intestinal diseases can have similarly low levels. Consequently, this test is not considered diagnostic for exocrine pancreatic insufficiency. While the results of these tests may be suggestive of the

Common Clinical Findings

Vomiting

Diarrhea

Weight Loss

Reduced Serum Cobalamin

disease, they cannot independently be used to definitively diagnose it or rule it out. To help reach a diagnosis, your veterinarian will evaluate test results along with a dog's clinical signs.

Finally, some dogs with exocrine pancreatic insufficiency will also have additional diseases such as diabetes mellitus or chronic enteropathy (disease of the gastrointestinal tract). Therefore, dogs should also be evaluated for concurrent diseases as some may also affect their ability to digest and absorb nutrients appropriately, and therefore may require additional therapies.

Treatment and Prognosis of Pancreatic Insufficiency

The mainstay of treatment for exocrine pancreatic insufficiency is replacement of the missing pancreatic enzymes. Your veterinarian will provide options for the correct products. The most commonly used products include dried pancreatic extract from a pork pancreas. This extract typically contains all components of pancreatic enzymes that are needed to properly digest food. They are packaged as a powder that will need to be mixed into each meal. Once a dog's weight is stabilized, the amount of enzyme that is added is gradually reduced until a minimally effective dose is determined. Dogs are typically fed a high-quality maintenance diet that is low or moderate in dietary fiber.

As mentioned earlier, most dogs with exocrine pancreatic insufficiency are also deficient in cobalamin. Dogs with this deficiency tend to have lower rates of survival when compared to dogs that have adequate levels of

cobalamin. Therefore, if a cobalamin deficiency is present, supplementation is highly recommended. Evaluating cobalamin concentrations requires a simple blood test, and supplementation is either provided by daily pills or weekly injections underneath the skin for a certain amount of time. Recent studies demonstrate that either supplementation method is effective.

It is possible that some portions of the pancreas may regenerate over time and that enzyme supplementation may be tapered or discontinued. In most cases, however, management is lifelong, and dogs require consistent supplementation with pancreatic enzymes. Thankfully, with appropriate management, dogs with exocrine pancreatic insufficiency can regain weight and have resolution of their other clinical signs. Well managed dogs usually have a normal quality of life and a normal lifespan.

Summary

Exocrine pancreatic insufficiency is a disease process in which production and release of digestive enzymes is disrupted. The disease leads to inadequate breakdown of food products for digestion and subsequent malnutrition. It typically occurs secondary to chronic inflammation of the pancreas, though it can be a genetic-based disease in some breeds. Clinical signs may or may not initially be present. When they do, they usually manifest as chronic weight loss, changes to stool consistency, or changes to the hair coat. Diagnosis of the disease is usually straightforward, and treatment involves supplementation with the digestive enzymes. When properly managed, many dogs with exocrine pancreatic insufficiency can live normal, healthy lives.

Current Research About Exocrine Pancreatic Insufficiency

There has been a fair amount of research performed in recent years evaluating additional monitoring and treatment methods for dogs with pancreatic insufficiency. Of particular interest is the focus on the prevalence of cobalamin deficiency and its effect on the overall prognosis in dogs with pancreatic insufficiency. Summarized below are two studies; the first evaluated the effect of cobalamin deficiency on prognosis, while the second evaluated the efficacy of oral cobalamin supplementation on increasing serum cobalamin concentration in dogs with exocrine pancreatic insufficiency.

Soetart N, Rochel D, Drut A, Jaillardon L. Serum cobalamin and folate as prognostic factors in canine exocrine pancreatic insufficiency: An observational cohort study of 299 dogs. Vet J. 2019 Jan;243:15-20. doi: 10.1016/j.tvjl.2018.11.003. Epub 2018 Nov 12. PMID: 30606434.

Exocrine pancreatic insufficiency results in inadequate nutrient absorption and has been associated with decreased serum concentrations of cobalamin and folate. Cobalamin is important for a variety of bodily functions, and inadequate concentrations may lead to increased morbidity. This study measured serum cobalamin and folate concentrations in 299 dogs with exocrine pancreatic insufficiency as well as the animals' long-term survival rates. Of these dogs, 67% had low serum cobalamin concentrations, which were determined to be a significant risk factor for decreased survival in dogs with exocrine pancreatic insufficiency. Also significantly associated with decreased survival were decreased appetite at diagnosis, male sex, and not receiving enzyme replacement therapy. The investigators concluded that decreased serum cobalamin concentrations were associated with a worse prognosis.

Toresson L, Steiner JM, Spodsberg E, Olmedal G, Suchodolski JS, Lidbury JA, Spillmann T. Effects of oral cobalamin supplementation on serum cobalamin concentrations in dogs with exocrine pancreatic insufficiency: A pilot study. Vet J. 2021 Mar;269:105619. doi: 10.1016/j.tvjl.2021.105619. Epub 2021 Jan 18. PMID: 33593499.

Cobalamin deficiency has a high prevalence rate in dogs with exocrine pancreatic insufficiency. Supplementation of cobalamin involves either weekly injections or daily oral administration. This study evaluated 18 dogs with documented exocrine pancreatic insufficiency and cobalamin deficiency. All dogs were administered oral cobalamin according to a standard protocol, and a significant increase was noted in serum cobalamin concentrations. The authors concluded that oral cobalamin supplementation is a potential alternative to the weekly injectable protocol.

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