# Pancreatitis in Dogs

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*Note that clinical references will often use the umbrella term 'pancreatitis' to describe a spectrum of disease affecting the pancreas. However, as outlined in your lecture notes, the term 'acute pancreatic necrosis' is most appropriate to describe the type of pancreatic disease detailed in the case of *Benji the Dog*.

## Overview

From a clinical perspective, pancreatitis can be broadly categorised as acute, recurrent acute or chronic. It can be further classified according to its effect on the patient as mild or severe, non-fatal or fatal. Histologically, acute pancreatitis is characterised by findings that range from pancreatic oedema to necrosis, variable infiltrates of mononuclear and polymorphonuclear cells, and local changes such as peri-pancreatic fat necrosis and thrombosis. Chronic pancreatitis is characterised by fibrosis and low-grade mononuclear inflammation and may be a sequela of recurrent acute pancreatitis or a subclinical disease process that may present as diabetes mellitus or exocrine pancreatic insufficiency (EPI).

## Aetiology and Pathogenesis

The aetiology and pathogenesis of spontaneous pancreatitis is poorly understood. The major factors which have been implicated (by association) as causes of acute pancreatitis in the dog include dietary indiscretion (especially large fatty meals), bile reflux, pancreatic hypoxia, abdominal trauma and drugs/toxins.

Irrespective of the initiating cause, pancreatitis is generally believed to occur when digestive enzymes are activated prematurely within the pancreas. In the normal pancreas, safeguards are present to ensure that harmful pancreatic enzymes are not activated until they reach the intestinal lumen. Enzymes are stored in zymogen granules within the acinar cell in the presence of pancreatic secretory trypsin inhibitor (PSTI) and are released at the apical surface directly into the duct system. They are only activated in the intestine, by trypsin, following the cleavage of trypsin activation peptide (TAP) from trypsinogen by enterokinase. Potential sites for the intrapancreatic activation of pancreatic enzymes can therefore logically be divided into interstitial (within the duct system and interstitium) and intracellular (within the acinar cell).

Experimental pancreatic hyperstimulation and obstruction of the pancreatic duct lead to the formation of large intracellular vacuoles in acinar cells. Vacuole formation is thought to be a consequence of the uncoupling of exocytosis of zymogens and abnormal intracellular trafficking of digestive and lysosomal enzymes. These subcellular alterations are considered to precipitate the intracellular activation of digestive enzymes. Pancreatic hyperstimulation may be of direct relevance to naturally occurring pancreatitis in dogs. CCK is normally released by cells in the duodenum in response to intraluminal fat and amino acids and coordinates and stimulates pancreatic secretion and gallbladder contraction during digestion. It is possible that high fat diets exert their effects via the excessive release of CCK; however, this is not proven.

Often pancreatic inflammation is a self-limiting process, but in some animals reduced pancreatic blood flow and leukocyte and platelet migration into the inflamed pancreas may cause the progression of pancreatic necrosis. Release of active pancreatic enzymes and inflammatory mediators from the inflamed pancreas, such as Tumour Necrosis Factor-α (TNF-α) interleukin-1 (IL-1) and phospholipid platelet activating factor (PAF), amplifies the severity of pancreatic necrosis, and adversely affects the function of many organs (systemic inflammatory response), and cause derangement in fluid, electrolyte and acid-base balance. It is the development of multisystemic abnormalities that separates mild from severe, potentially fatal pancreatitis.