PATHOLOGY OF PANCREATIC DISORDERS IN CANINES

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Thesis submitted in partial fulfilment of the requirement for the degree of

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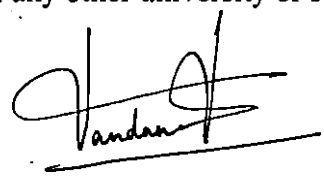
DECLARATION

I hereby declare that this thesis entitled **"PATHOLOGY OF PANCREATIC DISORDERS IN CANINES"** is a bonafide record of research work done by me during the course of research and that this thesis has not previously formed the basis for the award to me of any degree, diploma, associateship, fellowship or other similar title, of any other university or society.



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Certified that the thesis entitled **"PATHOLOGY OF PANCREATIC DISORDERS IN CANINES"** is a record of research work done independently by **Dr. Vandana Vijayachandran** under my guidance and supervision and that it has not previously formed the basis for the award of any degree, diploma, fellowship or associateship to her.

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Introduction

1. INTRODUCTION

The pancreas is a unique organ possessing large reserves of both exocrine and endocrine functions. The gland with the duodenum is tucked away in the upper abdomen where it is relatively well protected against trauma and where it is not readily accessible to the clinician. For these reasons, destructive processes of the pancreas with exception of acute pancreatic necrosis, which can be shockingly painful usually go undetected in pets.

Due to its multiple physiological functions, pancreatic diseases are revealed as metabolic disturbances and digestive abnormalities and can cause confusions in diagnosis. The exocrine pancreas is one of the largest extra intestinal gland secreting digestive enzymes. Exocrine pancreatic secretions also influence the functions of the small intestine by neutralisation of gastric juice, inhibiting bacterial proliferation, contributing to the normal degradation of exposed brush border enzymes and by exerting a tropic effect on the mucosa. When exocrine pancreatic function is severely impaired in conditions such as pancreatic acinar atrophy and hypoplasia, clinical signs of malabsorption occur. Several of the malabsorbtion, vomition and diarrhoea cases of dogs presented to veterinarians remain uncured as the association of pancreatic disorders is often overlooked.

The islets of Langerhans of pancreas consists of 1.5 gm of tissue subdivided into about one million specks and forms the most important part of the gland. Each islet by itself is a fully functioning multihormonal endocrine system, sensing and responding to chemical gradients and neural impulses in an integrated and homeostatic fashion. It is now known that the islets are a collection of more that five types of cells, each liberating a hormone mainly involved in metabolic activities. The cells being alpha, beta, delta, gamma and enterochromaffin cells which secrete glucagon, insulin, somatostatin, pancreatic polypeptide and serotonin respectively. Dysfunctions involving any of these cells ultimately

results in either an excess or a deficiency of the respective hormone in the circulation. In dogs the most common disorder of the endocrine pancreas is diabetes mellitus due to lack of hormone insulin. The incidence of diabetes mellitus in dogs is reported to vary from 1 in 100 to 1 in 500, but a few number of cases are diagnosed before animals exhibit the complications of diabetes.

Like a nuclear power plant, the pancreas operates effectively and quietly when all its synthetic and conveyance systems are in order but is capable of rampant self-destruction and regional catastrophe whenever these normal mechanisms go astray. There are several mechanisms that discourage the autodigestion of the pancreas by the enzymes that it secrets (Williams, 2000). The damaged pancreas can be literally destroyed by its own synthetic products, the digestive enzymes of great potency. The pancreas apparently has poor regenerative capacity and responds to injury with replacement fibrosis and atrophy of persisting parenchyma (MacLachlan and Cullen, 2001). Thus, ongoing destruction of pancreatic tissue will cause progressive loss of glandular tissue without replacement. Besides the effect on itself the release of proteolytic enzymes to the vascular space can result in rapid death due to intravascular coagulation and shock as the free proteases activate the kinin, coagulation, fibrinolytic and compliment cascade systems. (Williams, 2000). The intimate anatomical relationship of the pancreas with adjacent organs can result in extensive damage of these organs through direct contact with pancreatic ferments during pancreatitis and pancreatic necrosis. An understanding of the disorders and timely action are required to limit this catastrophe.

Disorders of the exocrine and endocrine pancreas are relatively common in dogs and are exhibited as digestive disturbances and diabetes. These often go misdiagnosed due to its associated systemic responses, which in severe cases can result in multiple organ failure. An awareness of typical abnormalities in dogs with pancreatic disorders, classification of the lesions identified and documentation of these will serve as a valuable guide to the clinician for

formulating strategies for proper diagnosis and treatment. Eventhough there are a number of parallels in the embryologic and cytodifferentiation of pancreas and liver, pancreas has not received a commensurate share of attention given to liver and its response to injury. Taking all these into consideration this study was undertaken with the following objectives.

1. Establish the incidence of pancreatic disorders.
2. Study the gross and histopathological lesions and to classify them.
3. Correlate the lesions of the exocrine and endocrine pancreas with the general post mortem findings.

Review of Literature

2. REVIEW OF LITERATURE

Pancreas is an organ of much importance placed well protected within the upper abdomen tucked away with the duodenum. It plays a significant role in the maintenance of normal metabolic homeostasis in animals and human beings.

2.1 ANATOMY AND HISTOLOGY

Frappier (1998) stated that pancreas is an encapsulated, lobulated, compound tubuloacinar gland containing both exocrine and endocrine parts. The capsule of pancreas gives rise to delicate connective tissue septa separating the parenchyma into distinct lobules. The lobules are composed of secretory units of tubuloacinar type. The cells of these are pyramidal in shape with spherical nucleus towards the base.

The endocrine pancreatic islets are cluster of cells, which are variously shaped. Generally they are spherical or ovoid and intermingled with exocrine pancreatic tissue. The islet cells are arranged in irregularly anastomosing cords composed of five different cell types A, B, C, D and F cells (Dellmann, 1998).

Williams (2000) stated that the pancreas of dogs consists primarily of right and left lobes with a small central body where lobes join together. There are two ducts, which usually intercommunicate within the gland, the pancreatic duct (Wirsung's duct) and the accessory pancreatic duct (Santorini's duct). Microscopically each pancreatic lobule is composed of acinar cells and the branching duct system that forms the exocrine part. The endocrine tissue is composed of islets of Langerhans, which accounts for only one to two per cent of the gland.

Nelson (2000) reported that endocrine pancreas is composed of islets of Langerhans, which are depressed as small islands in a sea of exocrine secreting

acinar cells. These are composed of four distinct types of cells, α cells, β cells, D cells, and F cells.

2.2 PHYSIOLOGY

The normal pancreas is protected against autodigestion by synthesising and storing proteins as inactive precursors called zymogens in zymogen granules (Rinderknecht *et al.*, 1978).

Dworken (1982) found that the functional status of pancreatic acinar cells was dependent on the existing milieu. Further, pancreatic secretion was stimulated hormonally by cholecystokinin (CCK) and neurologically by acetylcholine released from vagus. Acetylcholine and gastrin produced hypertrophy of acinar cells, but CCK produced both hypertrophy and hyperplasia.

Murtaugh and Jacobs (1985) experimentally demonstrated that there was a significant decline in the serum antiprotease concentration in dogs in both experimentally induced acute pancreatitis and spontaneous acute pancreatitis. This indicated escape of significant amount of proteolytic enzymes into systemic circulation during acute pancreatitis resulting in extrapancreatic complications of acute pancreatitis.

Pancreatic secretions contain enzymes for digesting all the major types of food proteins, carbohydrates and fats. It also contains large quantities of bicarbonate ions that play an important role in neutralizing the acid chyme passing from the stomach into the duodenum (Guyton and Hall, 2000).

2.3 PREVALENCE OF PANCREATIC DISORDERS

Duffell (1975) conducted a survey of pancreatic diseases seen in cats over two years period and of the 17 cases reported three suffered from diabetes mellitus, 11 from pancreatitis and three had neoplastic lesions.

A survey of pancreatic lesions in primates revealed a variety of pathological conditions viz., focal parenchymal or periductal accumulations of mononuclear cells with varied degrees of periductular fibrosis in 77 cases, hyalinized islets (amyloidosis) in 29, acute or chronic pancreatitis in 18, neoplasms in 11, haemorrhage in eight, parasites in seven, lymphoid nodules in the parenchyma in six, acinar ectasia in six, focal parenchymal fat in six, ectopic pancreas in four, parenchymal cysts without fibrosis in three, acinar cell atrophy in one and cystic fibrosis like change in one (McClure and Chandler, 1982).

Steiner and Williams (1999) stated that pancreatitis was the most common exocrine pancreatic disorder in felines. Pancreatic pseudocyst, pancreatic abscess, pancreatic parasites and nodular hyperplasia were the less common exocrine pancreatic disorders. According to him pancreatic adenocarcinoma was the most common neoplastic condition of the exocrine pancreas.

Princy (2000) screened the pancreas of 100 cattle over a period of one year, among these 17 per cent had prominent lesions consisting of pancreatic tumour (two per cent), parasitic infestation (two per cent), chronic pancreatitis (four per cent), atrophy of pancreas (four per cent), fat necrosis (three per cent), islet cell hyperplasia (one per cent) and pancreatolith (one per cent). The remaining 14 per cent revealed moderate lesions and 20 per cent mild changes.

2.4 PATHOLOGY OF EXOCRINE PANCREAS

2.4.1 Hypoplasia

2.4.1.1 Prevalence

Hypoplasia was observed in several breeds of dogs but was more frequent in German shepherd indicating a genetic predisposition and breed susceptibility (Jubb, 1993).

2.4.1.2 Pathology

Baker (1955) reported a rare case of congenital hypoplasia of pituitary and pancreas with resultant retarded growth, unthriftness, diabetes and cirrhosis of liver. At necropsy pancreas was pale, small and moist and in the region of the anterior pituitary gland only a mucino-gelatinous mass could be seen.

Jubb (1993) stated that usually in hypoplastic pancreas the duct system was prominent and the acinar tissue was seen as a thin veil or sheet surrounding the axial duct. Some hypoplastic pancreas appeared normal grossly but microscopically contained only nodules of acinar tissue in gland with abundant fat.

2.4.2 Pancreatic Acinar Atrophy (PAA)

2.4.2.1 Prevalence

Westermarck *et al.* (1989) noticed that the German shepherd and the rough coated Collie were the most commonly diagnosed breeds of dogs in Finland with pancreatic degenerative atrophy (PDA). The incidence of PDA in the Collie breed in Finland was close to one per cent. Of the 51 cases diagnosed in the Collie

breed, 44 could be placed in one composite pedigree. An affected dog in that pedigree had, on average, 17 affected relatives distributed in 11 different litters. This clustering strongly suggested that PDA was a hereditary disease. The pedigree data indicated that PDA could be an autosomal recessive trait.

Westermarck *et al.* (1993) recognised that exocrine pancreatic atrophy was more common in the German shepherd and that the clinical disease was mostly seen when the animals were six to eight months of age.

Williams (2000) reported that PAA could occur at any age in a wide variety of breeds, with a high prevalence in German shepherds.

Shridhar and Yathiraj (2004) stated that exocrine pancreatic insufficiency could occur at any age although it appeared to occur more commonly in younger dogs, but was common in older German shepherd.

2.4.2.2 Etiology

Churg and Richter (1971) demonstrated that atrophy of exocrine secreting acinar cells occurred following ligation of the pancreatic duct.

The studies conducted by Westermarck *et al.* (1989) in Finland indicated a strong familial clustering suggesting that PDA was a hereditary disease. The pedigree data indicated that PDA could be an autosomal recessive trait.

Weiberg *et al.* (1999) demonstrated that pancreatic acinar atrophy was preceded by infiltrative lymphocytic inflammation suggesting an autoimmune reaction.

Williams (2000) attributed nutritional deficiencies like essential amino acids and copper deficiency, gastrointestinal disturbances affecting absorption,

pancreatic duct obstruction, congenital abnormality of the pancreas, toxicosis, ischemia and viral infections as the causes of pancreatic acinar atrophy.

2.4.2.3 Pathology

2.4.2.3.1 Gross

Prentice *et al.* (1980) reported autopsy finding of small, diffuse and gelatinous pancreas with organ weight lower in comparison to normal dogs in six beagle dogs with pancreatic atrophy.

Westermarck and Rimalia-Parnanen (1989) observed very thin pancreas, almost transparent surrounded by large amount of fat in exocrine pancreatic insufficiency.

Boari *et al.* (1994) reported that in a family of English setters with history of exocrine pancreatic insufficiency, puppies at two months of age lacked pancreatic acinar tissue at necropsy. This could be secondary to early onset of juvenile atrophy of pancreatic acinar cells or congenital deficiency.

2.4.2.3.2 Histopathology

Hashimoto *et al.* (1979) found that the pancreas of a dog with juvenile acinar atrophy showed degranulation and loss of acinar cells.

Prentice *et al.* (1980) reported two types of atrophy histologically. In type I atrophy, the acinar lobules were few and scattered surrounded by adipose tissue. Zymogen granules were rare in the small acinar cells. The interlobular and intercalated ducts were prominent and no evidence of inflammatory reaction or fibrosis was seen. Type II atrophy had more acinar tissue with larger acinar cells

containing detectable granules, interspersed with fat cells. The size of acinar cells varied. Like type I, ducts were prominent.

Westermarck and Rimalia-Parnanen (1989) studied the histology of pancreas in exocrine pancreatic insufficiency and noticed pancreatic atrophy with ductal proliferation and lymphocytic infiltration.

Westermarck *et al.* (1993) conducted sequential assessments of pancreatic structure and function on female dogs bred from parents with exocrine pancreatic insufficiency (EPI). Till the 22 months of age no gross or histologic abnormalities could be detected. Typical features of pancreatic acinar atrophy, including scattered and disorganised exocrine cells were visible only by 25months.

Weiberg *et al.* (1999) scanned the histological sections of 12 dogs with sub clinical exocrine pancreatic insufficiency (SEPI) and found both normal and atrophied acinar structures. The main finding was a marked lymphoid cell inflammatory reaction that was more extensive in the border zone area. There was no associated increase in fibrous connective tissue. Whereas the sections of clinical exocrine pancreatic insufficiency revealed totally atrophied exocrine tissue consisting of disorganized cells, ductal structures and adipose tissue. Fibrosis was slightly increased than the subclinical phase but replacement by adipose tissue was more prominent than fibrosis.

2.4.3 Cystic Fibrosis

Abdul-Karim *et al.* (1986) observed that in subjects with cystic fibrosis there was advanced acinar atrophy and fatty infiltration. Small groups of acinar cells and isolated islets of Langerhans were seen as islands surrounded by mature adipose tissue. Quantitative analysis of insulin producing cells in the islets revealed that the mean surface area occupied by beta cells in patients with cystic

fibrosis and diabetes was significantly less than those with cystic fibrosis and normoglycemia and this was again less than the controls.

Tucker *et al.* (2003) demonstrated that the early acinar plugs seen in cystic fibrosis were inspissated zymogen granules of pancreatic acini.

2.4.4 Pancreatic Cyst

Steer *et al.* (1995) stated that pseudocysts of pancreas were collections of pancreatic secretions surrounded by non-epithelial-lined fibrous walls of granulation tissue. This was seen in ten per cent of patients with chronic pancreatitis

Hines *et al.* (1996) noticed a hypoechoic mass arising from the left lobe of the pancreas in a 13-year-old neutered female domestic shorthair cat. The mass was identified as a cyst during explorative celiotomy. The resected portion on histological examination revealed a pancreatic pseudocyst.

Horky *et al.* (1998) reported a case of enteric duplication cyst palpated as a discrete, round mass in the posterior pancreatic head which on sectioning revealed unilocular thin walled cyst tensely filled with thick mucoid material. The cyst was lined by ciliary, pseudostratified columnar epithelium.

VanEnkevort *et al.* (1999) diagnosed pancreatic pseudocyst in four dogs. The cyst size ranged from 2x2 cm to 7x6 cm. The pseudocystic fluid had high lipase activity in each case.

Princy (2000) observed cystic spaces in nine percent of the bovine pancreas examined. Among these two cases were grossly identifiable which appeared as raised, fluid filled, fluctuating masses. Microscopically, the cysts had

a wall of fibro-collagenous tissue without an epithelial lining and lumen was filled with pink staining material.

Coleman *et al.* (2005) published a case of true pancreatic cyst in a five-year-old neutered male Cornish Rex cat, first of the kind, presented with a history of vomiting over a period of five days. The cyst was associated with chronic active inflammation.

Pho *et al.* (2005) provided the first pathological evidence of benign epithelial cyst formation in the pancreas caused by fibromatosis invasion of the organ as a part of familial adenomatous polyposis (FAP).

2.4.5 Pancreatitis

2.4.5.1 Prevalence

Cook *et al.* (1990) conducted a study on the risk factors associated with acute pancreatitis and identified that dogs greater that seven years had an increased risk of developing acute pancreatitis. He found a greater chance in spayed female and castrated male dogs than sexually intact males. Among the breeds, terriers and non-sporting breeds appeared to be at greater risk.

Strombeck and Guilford (1991) reported acute pancreatitis as a disease of middle-aged obese dogs, with higher incidence in female dogs. According to him, Dachshunds were most prone to develop pancreatitis. Incidence over a period of six years at the Veterinary Medical Teaching Hospital in Davis was 3.2 out of 1000 cases. Ten percent of the cases were seen in the age group of six months to two years.

Hess *et al.* (1999) found dogs with fatal pancreatitis were largely middle to old aged. Yorkshire terriers were at increased risk while Labrador retrievers and

Miniature poodles were at decreased risk. Males and neutered females appeared to have increased risk.

Animals affected with pancreatitis were middle aged or older and the onset signs usually followed ingestion of large amount of fatty food (Williams, 2000).

2.4.5.2 Etiology

Feldman *et al.* (1981) recognised the predisposing factors of pancreatitis as hyperlipoproteinemia, blunt agent abdominal trauma and a variety of gastrointestinal inflammatory problems.

Frick *et al.* (1987) demonstrated that the dogs, which have high levels of pancreatic butrylcholinestrase when administered diazinon with or without secretin, developed acute edematous pancreatitis within two hours of treatment.

Experimental and clinical studies indicated that activation of progressively large amounts of proteases and phospholipases within the gland was associated with transformation of mild oedematous pancreatitis to haemorrhagic and necrotic pancreatitis (Williams, 1994).

Steer *et al.* (1995) identified that chronic pancreatitis may be initiated by high proteinacious diet and obstruction of pancreatic duct due to various reasons like post traumatic ductal stricture, pseudocysts or periampullary tumours. Pancreatic divisum can also result in chronic pancreatitis. Thirty to 40 percent of the cases had no apparent reason and were considered idiopathic chronic pancreatitis.

Williams (2000) described the causes of pancreatitis as malnutrition, hyperlipoproteinemia, administration of certain drugs, toxins, hypercalcemia, pancreatic duct obstruction due to tumour, parasite, biliary calculi, trauma or

surgical interference, duodenal reflux and pancreatic ischemia. He also stated that certain viral, mycoplasmal and parasitic infections might be associated with pancreatitis.

Nigwekar and Casey (2004) stated that pancreatitis could occur as a rare adverse effect of metronidazole administration.

Touzios *et al.* (2005) observed cholangitis or pancreatitis due to exercise following biliary bypass or pancreatoduodenectomy.

2.4.5.3 Clinical Signs

Kelly *et al.* (1975) reported a case of combined inflammation of bile duct, gall bladder and pancreas in a Siamese cat with clinical signs of pyrexia, anorexia, weight loss and jaundice.

Hill and Van Winkle (1993) observed that in some cases of pancreatitis there were two stages in the progression of the disease, first characterised by anorexia, weight loss and lethargy and second stage characterised by acute deterioration and development of shock.

Hess *et al.* (1999) reviewed 70 cases of fatal acute pancreatitis and the clinical signs reported by them were anorexia, vomiting, weakness, diarrhoea, polyuria, polydypsia, neurologic abnormalities, melena, weight loss, hematemesis and passage of frank blood in faeces.

Williams (2000) stated that dogs with pancreatitis usually have depression, anorexia, vomiting and in some cases diarrhoea, some dogs exhibited signs of abdominal pain assuming prayer position and anterior abdominal mass could be palpated in some cases.

Ferreri *et al.* (2003) reported that antemortem differentiation of acute necrotizing pancreatitis and chronic pancreatitis in cats could not be made solely on the basis of clinical, clinicopathological, radiographic or ultrasonographic findings. Histological examination remained the only dependable method of differentiating acute necrotizing pancreatitis and chronic pancreatitis.

2.4.5.4 Pathology

2.4.5.4.1 Gross

Duffell (1975) reported that appearance of pancreas varied from little departure from normal to nodular hyperplasia in pancreatitis.

In interstitial pancreatitis, the nodularity of the pancreas was accentuated and cut surface appeared firm, pale and nodular (Kelly *et al.*, 1975).

Princy (2000) stated that grossly the pancreas revealed no recognisable changes in the ten cases of chronic pancreatitis encountered in cattle that ranged from mild to severe chronic pancreatitis.

Pezzilli *et al.* (2004) reported a case of autoimmune pancreatitis resembling pancreatic carcinoma which could be differentiated only histologically.

2.4.5.4.2 Histopathology

Duffell (1975) reported that the histological lesion in pancreatitis might be focal accumulation of lymphocytes or focal necrotizing inflammation.

Kelly *et al.* (1975) demonstrated that the nodularity in interstitial pancreatitis was associated with interlobular fibrosis and the fibrous tissue extrusion into the interlobular areas of the gland.

Feldman *et al.* (1981) stated that extensive pancreatic necrosis and peripancreatic fat tissue necrosis was a prominent feature in pancreatitis.

Suda and Miyano (1985) studied bile pancreatitis in cases with abnormal pancreatic cholechoductal junction in which histological alterations like degeneration and disappearance of the pancreatic ductal epithelium, intraluminal aggregation of bacilli and diffuse intralobular fibrosis were found.

Salisbury *et al.* (1988) reported that acute necrotizing pancreatitis was characterised by coagulative necrosis of pancreatic parenchyma and neutrophilic infiltration and chronic active pancreatitis by multifocal, chronic abscess and interlobular fibrosis.

Hill and Van Winkle (1993) studied the histological sections of 40 cats with acute pancreatitis and two distinct groups were established based on histological analysis of tissue, group one had acute pancreatic necrosis (APN) and group two had suppurative pancreatitis.

Steer *et al.* (1995) described the morphological changes of chronic pancreatitis as varying degrees of oedema, acute inflammation, and necrosis superimposed on a background of chronic changes that included fibrosis, inflammation and loss of exocrine tissue. Ductal elements appeared to be dilated with calcified protein plug.

Hess *et al.* (1998) classified acute pancreatitis into acute pancreatic necrosis, acute pancreatic necrosis with fibrosis and acute suppurative pancreatitis. Acute pancreatic necrosis was defined as moderate to severe acute

pancreatic acinar and peripancreatic fat necrosis with minimal to moderate inflammatory infiltrates of neutrophils and macrophages. Interstitial fibrosis was minimal to mild. When along with necrosis extensive interstitial fibrosis and infiltration of lymphocytes and plasma cells were noticed it was termed acute pancreatic necrosis with fibrosis. In acute suppurative pancreatitis, there was moderate to severe, acute to subacute inflammation with minimal acinar or fat necrosis.

Princy (2000) noticed that in chronic pancreatitis there was narrowing of the pancreatic duct due to fibro-collagenous tissue cuffing and infiltration of mononuclear cells and lymphocytes along with focal areas of fibrosis and inflammatory cell infiltration between the acinar parenchyma.

Pezzilli *et al.* (2004) reported a case of autoimmune pancreatitis confirmed histologically by the presence of ductocentric lymphoplasmocytic infiltrates with germinal centres. Periphlebitis in the pancreatic and peripancreatic tissue and dense interstitial fibrosis were also observed.

2.4.6 Pancreatic Abscess

2.4.6.1 Clinical Signs

Clinical signs of anorexia, lethargy, vomiting and pain on abdominal palpation have been associated to the pancreatic abscess (Salisbury *et al.*, 1988).

2.4.6.2 Pathology

2.4.6.2.1 Gross

Salisbury *et al.* (1988) reported that the pancreatic abscesses appeared as gray masses with petechial or ecchymotic hemorrhagic areas, which may be firm

and fibrotic or friable. Cavity of abscess contained greenish brown mucopurulent exudate.

2.4.6.2.2 Histopathology

Histological examination of pancreatic abscess in six dogs revealed acute necrotizing pancreatitis in two dogs and chronic-active pancreatitis in the other four (Salisbury *et al.*, 1988).

2.5 PATHOLOGY OF ENDOCRINE PANCREAS

2.5.1 Diabetes Mellitus

2.5.1.1 Prevalence

Of the fourteen cases of diabetes mellitus described by Dixon and Sanford (1970), eleven were in bitches, indicating a greater predisposition for females and the average age at diagnosis was seven years.

The study conducted by Foster (1975) showed that the probability of diabetes mellitus in cats was higher in neutered females, whereas entire bitches appeared to be more predisposed in case of dogs especially during immediate post-oestrous stage. According to him the miniature and toy Poodle and miniature, standard, wire haired and longhaired Dachshunds were more prone to the condition and the tenth year of life was the greatest point for diabetic onset.

Ling *et al.* (1977) analysed 59 dogs with diabetes mellitus and noticed that most of the affected dogs were of age greater than or equal to seven years with females affected about twice as frequently as the male dogs. In his study dachshunds and poodles were more in number in the diabetic group, which reflected a breed predisposition.

According to Doxey *et al.* (1985) the mean age of onset of diabetes in dogs is nine years. The breeds commonly affected were crossbred terriers and miniature and toy poodles. They too reported a higher incidence in unspayed females than uncastrated males.

Panciera *et al.* (1990) studied retrospectively medical records from 333 cats with diabetes mellitus and concluded that breed had no effect on risk for diabetes mellitus whereas, body weight, age, gender and neutering had significant effect. Body weight of 6.8 kg and age of seven years were predisposing. According to him male cats were at 1.5 times greater risk for developing diabetes mellitus than females and neutered cats twice the risk than sexually intact cats.

2.5.1.2 Clinical Signs

The four most likely presenting signs were polydypsia, polyuria, weight loss and polyphagia (Dixon and Sanford, 1970; Foster *et al.*, 1975; Ling *et al.*, 1977; Bansal *et al.*, 1994).

2.5.1.3 Pathology

Cotton *et al.* (1971) reported that acute and chronic pancreatitis was found in high percentage of dogs having diabetes mellitus.

Duffell (1975) conducted histopathology of the pancreas of three diabetic cats and reported no reduction in the size or number of islets in the first, hydropic degeneration of islet cells in the second, while the third showed subacute pancreatitis having areas of necrosis with large number of neutrophils surrounded by fibrinous exudate and numerous leucocytes were scattered through out the interstitium. Amyloid like substance surrounded many blood vessels.

Carpenter and Novilla (1977) studied a case of diabetes mellitus in a black-footed ferret. Histopathological examination showed that pancreas had adequate number of beta cell granules in the islets of Langerhans.

Lee *et al.* (1978) demonstrated in a colony of guinea pigs with an occurrence of diabetes mellitus that the urine contained virus like particles and this was the means of transmission of diabetes from one guinea pig to another.

Insulinopenia in diabetes mellitus in a family of keeshond dogs was the result of aplasia of the β cell of islet of Langerhans (Kramer, 1981).

Yano *et al.* (1981) reported that incidence of insular amyloidosis was not significantly different between diabetic and age-matched non-diabetic cats. However mean percentage of islet with abundant amyloid deposit was greater in diabetic than non-diabetic.

According to Nakayama *et al.* (1986), pancreatic changes in diabetes in dogs were necrosis, islet atrophy, vacuolation of islet cells and chronic inflammation.

A comparative study done on the presence of islet amyloid polypeptide (IAPP) immunoreactivity and islet amyloid deposition in normal, impaired glucose tolerant and overtly diabetic cats showed that the proportion of animals with IAPP immunoreactivity and deposition were higher in the impaired glucose tolerant group and overtly diabetic than normal (Johnson *et al.*, 1989).

Ono *et al.* (1989) demonstrated that the islets of a cow with spontaneous diabetes consisted mostly of glucagon cells and had few insulin cells, while the glucagon cells were sparsely located in the peripheral area of islets in normal cows.

Experimental study on alloxan induced diabetes in dogs revealed degeneration of beta cells of islets of langerhans while the exocrine pancreas had normal histoarchitecture (Bansal *et al.*, 1994).

Root *et al.* (1995) studied a case of diabetes mellitus in a kitten and concluded that diabetes was due to pancreatic endocrine insufficiency.

Minkus *et al.* (1997) reported a case of diabetes mellitus with hypoplasia of islets of Langerhans showing vacuolar degeneration and areas of ductuloendocrine proliferation suggesting a regenerative phenomenon.

A comparative study of diabetes mellitus in dogs given alloxan alone and alloxan in combination with ethylene glycol revealed that lesions such as vacuolations and necrosis of pancreatic islet cells along with hyalinisation and degeneration were more severe when alloxan ethylene glycol combinations were used (Sandhu *et al.*, 2000).

Govindarajan *et al.* (2001) conducted a study on fibrocalous pancreatic diabetes patients and demonstrated pancreatic exocrine tissue and islet cell atrophy in many areas in addition to ductal dilatation and intraductal calculi.

2.6 PARASITIC CONDITIONS OF PANCREAS

Sastry and Kumar (1979) reported a case of involvement of pancreas in dracunculosis in a 30 years old man. The guinea worm was calcified and presented beneath the capsule of pancreas. It did not seem to evoke any pathology to the pancreas itself.

Anderson *et al.* (1987) described a case of *Eurytrema procyonis* in a domestic cat. The pancreas appeared diffusely white and firm. Microscopically there was atrophy, fibrosis and extensive loss of lobular architecture. The reaction

was more severe towards the pancreatic duct. Major pancreatic duct was lined by hyperplastic smooth to papillary epithelium and contained a mild scattered infiltration of mononuclear inflammatory cells and eosinophils. Numerous cross sections of trematodes were seen within the duct.

Georgi and Georgi (1992) suggested that pancreatic duct in dogs might be involved in hyperplastic and fibrotic changes in response to parasites similar to that seen in red fox and cats.

Jubb (1993) had stated that ascaris might invade the pancreatic ducts from the intestine in dogs. Other parasites viz, *Dicrocoelium dentriticum, Opisthorchis sinensis* could occur in the pancreatic ducts. Of the genus Eurytrema species *Eurytrema fastosum* was seen to infest carnivores animals. Infestations could result in chronic interstitial pancreatitis with almost total destruction of acinar tissue by fibrofatty tissue.

2.7 HYPERPLASTIC CONDITIONS

2.7.1 Nodular Hyperplasia

Nodular hyperplasia is a common finding in old dogs, cats and cattle. Macroscopically, the hyperplastic nodules projected as flat elevations, whiter and harder than surrounding tissue. Microscopically, these nodules were not encapsulated and did not compress the surrounding parenchyma. Cells appeared enlarged counterparts of normal acinar cells with a bulky brightly acidophilic cytoplasm, or they may be of indifferent character, producing a low cuboidal lining for glandular spaces or they may be small indifferent clusters without lumen (Jubb, 1993).

Princy (2000) described nodular hyperplasia in four cattle, which appeared greyish white, focal, circumscribed, raised, smooth nodules of two millimetre

diameter which were hard in consistency. Microscopically circumscribed focal aggregates of hyperplastic acinar cells that were separated from the adjacent acinar cells by thin band of fibrocollagenous tissue were seen.

MacLachalan and Cullen (2001) reported that nodular hyperplasia is common in older dogs and cats. The nodules were multiple, raised, smooth, uniform grey or white on cut surface and could be firmer than adjacent normal pancreas. Microscopically, these nodules consisted of unencapsulated aggregates of acinar cells.

2.8 NEOPLASTIC CONDITIONS

2.8.1 Benign

2.8.1.1 Adenoma

Love *et al.* (1977) examined pancreatic acinar adenomas that occurred in several rats maintained under standard conditions. Grossly, these were similar in colour to the rest of the pancreas and presented a smooth surface.

Lloyd *et al.* (1981) reported two cases of islet cell adenomatosis or nesidioblastosis. The pathological abnormality on histological section of pancreas was islet cell adenoma or increased amount of islet tissue. The size of most islets ranged between 80 and 120 μm with less than one percent of islets at about 250 μm.

Adenomas of exocrine pancreas were extremely rare. The acinar adenomas shared all the features of hyperplastic nodules but were single and larger than the normal pancreatic lobules (MacLachalan and Cullen, 2001).

2.8.2 Adenocarcinomas

2.8.2.1 Prevalence

Jubb (1993) reported that pancreatic carcinomas were rare in canines. These were seen usually in older animals and Airedale terriers were more prone.

The age range of 11 cases of insulin-secreting tumours studied by Dunn *et al.* (1993) ranged from seven to 11 years. Three of these dogs were Springer spaniels, two were Golden retrievers and two were Irish setters.

Beta cell neoplasms were seen most frequently in dogs of five to twelve years of age, with a mean of nine years (Capen, 2001). In dogs, carcinomas of the pancreatic islets were more common than adenomas.

The median age at the time of diagnosis of an insulin-secreting tumour in a series of 71 cases screened by Nelson (2000) was ten years, with a range of three to 14 years. There was no sex predilection and insulin-secreting tumours were diagnosed in a wide variety of dog breeds.

2.8.2.2 Pathology

Caywood *et al.* (1979) reported six cases of pancreatic islet cell adenocarcinoma in dogs. Histologically, the pancreatic tumour nodules were comprised of ribbons of well-differentiated columnar cells separated by partitions of fibrous connective tissue.

Chang *et al.* (1980) reported a case of cystadenocarcinoma in the pancreas of a female infant. Grossly, the tumour appeared as a multinodular cystic mass composed of cysts of varying diameter. Histological examination revealed cysts

lined by single layer of columnar or cuboidal epithelium separated by narrow myxomatous fibrous septa.

Kapur *et al.* (1985) reviewed six cases of insulinoma in dogs treated over a period of ten years. Five of them showed pathology of pancreatic adenoma and one of them a malignant tumour of islet.

Xu (1985) reported three tumours of pancreas in canines, an exocrine undifferentiated carcinoma, exocrine adenocarcinoma and well-differentiated islet cell carcinoma. Exocrine undifferentiated carcinoma was composed of pleomorphic cells with an oval or round nucleus, fine nuclear chromatin, inconspicuous nucleolus, plentiful lightly eosinophilic cytoplasm and generally indistinct cell outline. Exocrine adenocarcinoma of small tubular (ductal) pattern was composed of cells with small, oval, round or intended dark staining nucleus and moderate amount of eosinophilic cytoplasm arranged either as sheets of cells or a distinct small tubules with a lumen of varying size.

Banerjee *et al.* (1985) discussed about an unusual presentation of a malignant non-functioning pancreatic islet cell tumour, as a pseudocyst of the pancreas with ulceration into the stomach. The tumour cells were arranged in solid nests and ribbons separated by highly vascular stroma. The cells had large irregular nuclei and some showed abundant granular cytoplasm.

Dunn *et al.* (1993) reported that five of the ten insulin-secreting tumours of canine pancreas examined histologically were clearly demarcated from the surrounding tissues by a capsule of mature fibrous tissue. On the other extreme, three tumours showed no evidence of encapsulation. The internal morphology showed little variation regardless of their growth. They consisted of numerous solid lobules of closely packed epithelial cells separated by delicate fibrous tissue septa. The cells had abundant acidophilic cytoplasm, with very indistinct cytoplasmic boundaries and a pale staining nucleus with prominent nucleoli. The

mitotic count for individual tumours varied from zero to 45 per ten high power fields.

Hoorens *et al.* (1993) observed that a common feature of pancreatic adenocarcinoma was lobulation of the neoplastic tissue by fibrous tissue strands with very scanty stroma within the large lobules. Invasion into the adjacent pancreatic tissue, the spleen or the duodenum was often seen. Histologically there were three patterns of differentiation, the typical acinar pattern, the mixed acino-trabecular pattern and a solid pattern. The acinar pattern was a reminiscent of normal pancreatic acinar tissue, the cells had round nuclei of uniform size with abundant eosinophilic cytoplasm and mitotic figures were low. In the mixed pattern, the trabecular and solid pattern alternated and nuclei were somewhat irregular and larger than the acinar category and mitotic figures were high. Solid pattern was a reminiscent of low-grade endocrine tumours; cells had scant cytoplasm with vesicular nuclei containing distinct nucleoli.

Capen (2001) observed that the carcinomas of pancreatic islets could be differentiated from adenomas by their large size, multilobular appearance, extensive invasion of adjacent parenchyma and lymph vessels and metastases to extrapancreatic sites.

Itani *et al.* (1999) identified fourteen cases of squamous cell carcinoma of pancreas between 1988 and 1997 at the Houston Veterans Affairs Medical Centre. The microscopical picture was keratinising cells with eosinophilic cytoplasm forming whorls or pearls with intercellular bridges.

Dzaja *et al.* (2000) diagnosed a case of progredient seizures in a dog to be insulinoma. Pancreas showed several indurated oval grey white masses of 1.5 cm size scatted throughout the parenchyma.

Geener *et al.* (2000) reported two cases of papillary cystic tumour of pancreas composed of small uniform round to oval cells arranged in sheets and nests forming pseudopapillary areas and myxomatous areas. The metastasising tumours showed capsular invasion, infiltration to surrounding tissue and vascular invasion with metastasis to lymphnode.

Adsay (2002) reported that intraductal papillary mucinous neoplasms were characterized by intraductal proliferation of neoplastic mucinous cells that formed papillae and led to cystic dilation of pancreatic duct.

Adenocarcinoma of ductal origin accounts for 80 per cent to 90 per cent of all pancreatic tumours. Ray *et al.* (2004) reported a case of clear cell ductal adenocarcinoma of pancreas which grossly appeared as a vaguely circumscribed, firm, white tumour, measuring 5 x 4 x 3 cm which replaced much of the pancreatic parenchyma, extended into peripancreatic soft tissue and infiltrated well into the spleenic parenchyma. Microscopic examination revealed highly atypical glands composed of pleomorphic cells with abundant clear cytoplasm and well defined borders.

Ben-david *et al.* (2004) reported a case of moderately well-differentiated infiltrating pancreatic adenocarcinoma in an adult human being with annular pancreas, a congenital abnormality.

2.8.3 Zollinger-Ellison Syndrome

Zollinger-Ellison syndrome is characterised by severe hypersecretion of gastric acid with fulminating peptic ulceration at atypical sites such as the distal duodenum and jejunum associated with non-insulin-producing tumours of the pancreas.

2.8.3.1 Clinical Signs

Happe *et al.* (1980) noticed that the clinical signs of Zollinger-Ellison syndrome in dogs were similar to that in humans viz., vomition, intermittent diarrhoea, poor appetite and weight loss.

2.8.3.2 Histopathology

Happe *et al.* (1980) observed three basic patterns of tumours of pancreas in Zollinger-Ellison syndrome in dogs. In one, cells were arranged in solid masses with delicate, highly vascularised stroma and a connective tissue capsule. The second pattern was a ribbon or trabecular pattern, in which the tumour cells were arranged in bonds intimately related to capillaries. The third form was an acinar pattern with cuboidal cells around a central lumen. Immunohistochemistry revealed scattered cells of weak moderate gastrin immunoreactivity in all three tumours.

2.9 EXTRA PANCREATIC LESIONS IN PANCREATIC DISORDERS

Cotton *et al.* (1971) reported that fatty degeneration of liver, various types of nephritis and infections of urinary and respiratory tracts were found in a high percentage of dogs having diabetes mellitus.

Lee *et al.* (1978) reported pulmonary oedema associated with acute pancreatitis in dogs as in humans under conditions where cardiac functions and central venous pressure was normal.

Tahamont *et al.* (1982) examined the role of proteases in mediating lung vascular injury after acute haemorrhagic pancreatitis. The studies showed that increase in pulmonary lymph flow and protein clearance were due to increased vascular permeability as a result of injury due to release of proteases.

Nakayama *et al.* (1986) studied the renal glomerular lesions in dogs with hyperglycaemia and concluded that the glomerulopathy seemed to have resulted from hyperglycaemia due to pancreatic changes.

Boomsinger *et al.* (1988) reported ulcers in duodenum and atrophy of villi in multihormonal pancreatic endocrine tumours.

Strombeck and Guilford (1991) stated that in pancreatitis there could be associated dehydration and shock, alteration in gastrointestinal motility, peritonitis, renal complication, respiratory complications, blood-clotting disorders, cardiomyopathy and hepatic lesions.

Brown *et al.* (1994) were able to associate three cases of multiple necrotizing steatitis in dogs to the presence of pancreatic carcinoma.

Paterson (1994) associated a sterile nodular panniculitis with a bile duct carcinoma leading to pancreatic necrosis.

Sottiaux (1999) reported atherosclerosis affecting the abdominal aorta and medium sized arteries in a dog with diabetes mellitus.

A study conducted on risk factors associated with acute pancreatitis in dogs, revealed that most dogs in this study had intercurrent diseases, including diabetes mellitus, hyperadrenocorticism, chronic renal failure, neoplasia, congestive heart failure and autoimmune disorders (Hess *et al.*, 1999).

Williams (2000) reported that dogs with pancreatic acinar atrophy commonly had overgrowth of bacteria in the small intestine.

Nezelof *et al.* (2002) observed that multifocal myocardial necrosis was seen in association with various pathological conditions including cystic fibrosis of the pancreas and pancreatic lipomatous hypoplasia or atrophy.

Materials and Methods

3. MATERIALS AND METHODS

The present study was undertaken at the Centre of Excellence in Pathology (CEP), College of Veterinary and Animal sciences, Mannuthy to investigate the pathological conditions affecting the pancreatic gland in canines, to classify the lesions encountered and correlate it with other post mortem findings.

3.1 MATERIALS

3.1.1 Data collection

The history and other details regarding the carcasses such as age, breed and sex, brought for autopsy to the CEP during the period of study (January 2004-June 2005) were documented after getting the information from the owners. The individual weights of the carcasses were recorded

Data regarding the symptoms and treatment were obtained from the Veterinary Hospital, Mannuthy for those cases referred from the hospital for postmortem examination.

3.1.2 Sample Collection

One hundred samples of the pancreas obtained from the carcasses of dogs brought for autopsy to CEP between (January 2004-June 2005) were utilised for the study.

3.2 METHODS

3.2.1 Gross examination

A detailed systematic postmortem examination of the canine carcasses brought for autopsy was conducted. The pancreas was dissected out separately and carefully examined for gross lesions like changes in size, nodularity and

presence of cyst, abscess or tumours. The weight and length of individual pancreas were measured and recorded. The gland was bisected by a longitudinal incision along the mid axis and the cut surface examined. Pancreatic duct was examined for changes in colour and presence of parasites. All the other organs were examined in detail and the gross lesions were recorded with the objective of correlating the pancreatic disorders with the general post mortem findings.

3.2.2 Histopathological examination

Representative samples from the head, body and tail of the pancreas, pancreatic duct and duodenum obtained from the carcasses were fixed in ten per cent neutral buffered formalin. The tissues were processed by routine paraffin embedding techniques (Sheehan and Hrapchak, 1980). Sections were cut at four-micron thickness and stained with routine Haematoxylin and Eosin stain (Bancroft and Cook, 1995) for histopathological studies. Duplicate sections were stained using Gomori's' chromium haematoxylin phloxin for studying the changes in the islet cells, wherever necessary. Special staining techniques like Gomori's trichrome, pearls staining and von Kossa silver staining were used wherever necessary as per the method described by Luna (1968). The stained sections were examined in detail under light microscope and the lesions were classified.

3.2.3 Analysis of Data

The relative weight of the pancreas was determined. Incidence of pancreatic disorders in canines with respect to breed, sex and age was determined.

Results

4. RESULTS

Comprehensive gross and histopathological examinations were carried out on pancreas obtained from one hundred cases of canines autopsied at the Centre of Excellence in Pathology, College of Veterinary and Animal Sciences, Mannuthy between January 2004 and June 2005. The carcasses were grouped based on age and breed. Lesions were classified according to age, sex, breed and pathological findings. Seventy-two per cent of the pancreas revealed pathological changes on gross and histopathological examination. The prominent lesions were seen in 21 per cent of the cases, which included adenocarcinoma of acinar pancreas (1), suppurative pancreatitis (1), acute pancreatitis (2), chronic pancreatitis (2), parasitic pancreatitis (1), pancreatic abscess (1), haemonecrosis (5), pancreatic atrophy (3), ductular adenoma (1), duct obstruction due to squamous metaplasia (1), islet cell hyperplasia (1) and hyalinisation (2). The moderate and mild lesions that were 20 and 31 per cent respectively consisted of congestion, haemorrhage, oedema, degeneration, lipomatosis, ductular changes like fibrosis, hyperplasia, hypoplasia, lymph stasis and islet changes like degeneration and necrosis. The lesions were graded as mild, moderate and severe (Fig.1).

4.1 INFLUENCE OF AGE AND BODY WEIGHT ON THE PANCREAS

The age wise incidence of pancreatic disorders in canines is shown in table.1. A higher incidence was seen in the age group of one to three years, which was 79.44 per cent whereas the group below one year of age showed only a prevalence of 55.55 per cent. The age group of three to five and above five years also revealed high prevalence of disorders to the tune of 76.93 and 68.18 per cent respectively.

The relation of pancreas weight to body weight is shown in table. 2. The average pancreas weight in grams per kilogram bodyweight was higher in the

younger age group (3.2). In all other groups the average pancreas weight in grams per kilogram body weight was approximately two.

The age wise distribution of pancreas length is given in table. 2. The average pancreas length was highest in older dogs of more than five years of age. The average pancreas lengths for age groups below one year, between one and three years, between three and five years and above five years were 17.66 cm, 14.53 cm, 21.41 cm and 22.78 cm respectively.

4.2 INFLUENCE OF BREED ON THE PANCREAS

The distribution of pancreatic lesions based on the breed of the dog is given in the table 3. German shepherd was identified as the breed with greatest prevalence of pancreatic disorders. Of the 27 cases examined 25 revealed pancreatic disorders (92 per cent). The average pancreas weights in gram per kilogram body weight were in the range of 1.5 to 2.5 in all the breeds (Table. 4).

4.3 INFLUENCE OF SEX ON THE PANCREAS

The comparison between prevalence of pancreatic disorders among males and females is given in Fig. 2. The study revealed that there was a higher prevalence of pancreatic disorders among females (79 per cent) when compared to males (62 per cent). Among the seven cases of pancreatitis encountered during the period of study, two were in males while the rest five cases were in females.

4.4 CLASSIFICATION OF LESIONS

Based on the histopathological findings, pancreatic lesions were classified as vascular changes, degenerative changes, atrophic changes, ductular changes, inflammatory changes, pigmentation, proliferative changes and neoplastic changes. Each was graded as mild, moderate and severe (Fig. 3)

4.4.1 Vascular Changes.

4.4.1.1 Congestion

Forty-two cases (58.3 per cent) of pancreas screened showed congestion. Congestion was severe in seven cases, moderate in 16 and mild in 19. Grossly the organ was slightly enlarged and dark brown. The blood vessels were dilated and very much engorged with blood. Microscopically, in severe cases the capillaries and veins throughout the lobes and interstitium were engorged with blood (Fig. 4) while in moderate cases congestion was prominent in certain lobes and in milder forms it was confined to parts of a lobe.

4.4.1.2 Haemorrhage

Nineteen cases (12.5 per cent) revealed haemorrhages of varying degrees. The affected pancreas showed petechiae or echymosis (Fig. 5). Five per cent presented extensive haemorrhages with diffuse collections of erythrocytes displacing the parenchyma. Infact the extravasated blood was seen occupying the entire area and the acinar tissue appeared as irregular islands (Fig. 6). In almost all cases the haemorrhage was seen in certain localized regions affecting a few lobules. Only in two cases the entire pancreas was affected which showed massive haemorrhage. The severely affected regions showed necrosis and atrophy of acinar pancreas. In milder cases erythrocytes were seen scattered between the acinar cells.

4.4.1.3 Oedema

Oedema was noticed in eight cases (11 per cent). Grossly there was no appreciable change. Microscopically, homogeneous fluid staining pink was seen in the widened interstitial and interlobular spaces. The acinar cells were displaced and compressed resulting in stenosis of the acinar lumen.

4.4.1.4 Lymphangiectasis

Severe lymph stasis in the parenchyma was observed in a pancreas. Microscopically lymph vessels were conspicuous with stasis of lymph in them, which appeared as pink stained fluid (Fig. 7). All the blood vessels were also engorged with blood.

4.4.2 Degenerative Changes.

Degenerative changes were further classified into vacuolar degeneration and fatty infiltration.

4.4.2.1 Vacuolar Degeneration

This was recorded in 11 cases (15.27 per cent). Grossly, the areas of vacuolar degeneration could be distinguished only in a few cases as pale or greyish white spots. Histologically, the cytoplasms of pancreatic acinar cells were vacuolated. The cytoplasm was condensed into feathery strands between vacuoles (Fig. 8). Isolated acinar cells with pyknotic nuclei were scattered through out the parenchyma. Usually vacuolar degeneration was found localized to a particular region of the pancreas especially the acinar cells in the periphery of the lobule.

4.4.2.2 Stromal Lipomatosis

Nine cases (12.5 per cent) showed fatty infiltration. Stromal fatty infiltration was extensive in two per cent cases while five per cent showed moderate infiltration. In extensive conditions the pancreas appeared to be covered by a smooth glistening adipose tissue yellowish in colour (Fig. 9). The organ was easy to incise and in certain areas the parenchyma appeared virtually replaced by adipose tissue. Microscopically, fatty infiltration was seen both in the interstitium and also within the interacinar areas. It was predominant in the interstitial

connective tissue. In severe cases the acinar parenchyma was replaced by fat vacuoles (Fig. 10). At some places fat cells coalesced and formed fat cysts (Fig.11).

4.4.3 Necrosis

Eleven cases (15.2 per cent) revealed pancreatic necrosis. Grossly, the necrotic areas appeared as greyish white patches or spots diffusely distributed in the parenchyma. In cases where necrosis was observed in association with massive haemorrhage a dark red zone could be detected around the lesion. Microscopically, there was loss of normal architecture and the cellular cytoplasm appeared homogenous and eosinophilic. The nuclei of necrotic acinar cells were in varying stages of karyorrhexis and karyolysis. The normal contour of cells could not be seen and cell outlines had disappeared. In certain lobes the acinar tissue appeared completely coagulated and the periphery of which showed mild infiltration with inflammatory cells (Fig.12). Necrosis usually accompanied vascular disturbances and hydropic degeneration. Necrosis associated with massive haemorrhages was noticed in three cases (Fig.13). Islands of unaffected acinar cells in varying stages of atrophy could be seen between the necrotic zones.

4.4.4 Atrophic Changes

Acinar atrophy was observed in 17 cases (23.6 per cent). Gross changes were not discernible in these cases. The atrophied cells were smaller in size than normal acinar cells and seen surrounded by proliferating fibrous tissue (Fig.14). The interlobular and intercalated ducts appeared prominent (Fig. 15). There was a reduction in zymogen granules and the cytoplasm showed increased basophilia. Disorganisation of the lobules and acini appearing as small islands of cells amidst proliferating connective tissue were also observed. In some cases atrophy was noticed in areas adjacent to regions of haemonecrosis (Fig.16).

4.4.5 Hypoplasia

Pancreatic hypoplasia was noticed in three cases (4.2 per cent). Hypoplasia was mostly confined to focal areas affecting two or three lobules. This was identified only on histopathological examination. Hypoplasia affecting the entire pancreas was noticed in a Spitz. Grossly the affected pancreas was smaller in size and strand like (Fig.17). Microscopically, the acinar cells appeared smaller in size with scanty cytoplasm, which was basophilic. A pyknotic nucleus occupied the whole cell. Zymogen granules were absent. Cells were dissociated, individually separate and there was no acinar or glandular arrangement. Delicate connective tissue strands separated the extremely smaller cells into groups (Fig.18). The duct system was prominent.

4.4.6 Acinar Cell Hypertrophy.

This was observed in five pancreases (6.9 per cent). This could be detected only histologically. The hypertrophied acinar cells were present as small groups clearly demarcated from the surrounding parenchyma by their bigger size, more zymogen granules making the apex of cells more eosinophilic (Fig. 19).

4.4.7 Ductular Changes

4.4.7.1 Periductular Fibrosis

Twenty cases (27.7 per cent) revealed fibrosis of the duct wall. Of these fibrosis was severe in seven cases, moderate in six and mild in the rest. Histologically, there was dense fibro-collagenous tissue surrounding the duct causing thickening of the duct wall (Fig. 20). The lumen of the duct was reduced and the lining epithelial cells were prominent. The acinar cells adjoining the duct usually showed atrophic changes.

4.4.7.2 Periductular Fibrosis and Inflammation

Two out of 100 pancreases screened showed periductular inflammation on histological examination. The microscopic picture was ductular fibrosis with infiltration of neutrophils in one and mononuclear cells in the other (Fig. 21).

4.4.7.3 Ductular Epithelial Hyperplasia

Epithelial proliferation was noticed in 13 (18.05 per cent) pancreas screened. The lining epithelial cells were hyperplastic and the proliferating cells formed papillary projections into the lumen (Fig. 22).

4.4.7.4 Squamous Metaplasia

Squamous metaplasia of ductular epithelium was recorded in two cases. The normal cuboidal to columnar epithelium of the duct had undergone metaplasia to squamous epithelium. In a German shepherd the proliferation and metaplasia of the ductular epithelium had resulted in ductular obstruction and stasis of the pancreatic secretions (Fig. 23).

4.4.7.5 Ductular Adenoma

Adenomatous proliferation of pancreatic duct was noticed in an eight-year-old German shepherd. Grossly the pancreas was hard and difficult to incise. Histologically, there was very great proliferation of the main pancreatic duct. The duct wall was lined by many layers of cells, which were cuboidal to columnar with clear cytoplasm and uniform vesicular nuclei. The proliferating cells were also found filling the entire lumen (Fig. 24 and 25). The proliferation, which was localised in the interlobular area was seen extending into the adjacent lobules replacing and disrupting the acinar parenchyma.

4.4.8 Pigments in Pancreas

4.4.8.1 Haemosiderosis

Out of 100 pancreas included in the study, six (8.3 per cent) showed haemosiderosis. Haemosiderin pigments were seen deposited as coarse granular golden yellow pigments in the interlobular spaces and between the exocrine cells (Fig. 26). Pigments stained blue with Pearl's stain.

4.4.8.2 A case of pigmentation on the serosal surface of the pancreas was observed during the study. The pigment appeared as pinpoint black deposits to black patches (Fig. 27) with moderate extension into the parenchyma. Diffuse petechiae and engorgement of vessels were also observed. The pigment was seen as blackish deposits of varying size in the interacinar and interstitial areas of the pancreatic parenchyma (Fig. 28). Haemorrhage with mild haemosiderosis and degeneration of acinar cells were observed. The pigment could be stained by neither the Pearls stain nor the Von Kossa.

4.4.9 Proliferative Changes

4.4.9.1 Fibrosis

Eighteen (25 per cent) cases revealed fibrous tissue proliferation in the parenchyma. Grossly, the pancreas was firm in consistency in severe cases and in mild cases no changes were noticed. Histologically, the proliferating fibrous tissue extended out irregularly from the interstitium into the adjacent parenchyma (Fig. 29). In some cases the acinar cells got entrapped within the proliferating fibrous tissue causing atrophy of these cells. The adjacent acinar cells were hyperplastic and hypertrophic.

4.4.9.2 Nodular Hyperplasia of Acinar Cells

Nodular hyperplasia was noticed in four (5.5 per cent) pancreas examined. On gross examination nodular hyperplasia appeared as greyish white, focal, circumscribed, raised, smooth nodules of two millimetre diameter, which were hard in consistency than the adjacent parenchyma. In the remaining cases no gross lesions were seen. Microscopically, circumscribed focal aggregates of hyperplastic acinar cells that were separated from the adjacent acinar cells by very thin band of fibrocollagenous tissue could be seen (Fig. 30). Hyperplastic cells were larger than normal acinar cells with eosinophilic cytoplasm. One or more nodules were seen within a lobule.

4.4.9.3 Blood Vessel Proliferation

Grossly, a blood cyst of five-millimetre diameter was seen noticed in a German shepherd. Histologically, proliferating blood vessels with increased blood vascular space was observed. Vascular spaces were completely filled with blood (Fig. 31). The normal acinar parenchyma was distorted due to the distended and proliferating vessels.

4.4.10 Inflammatory Changes

About seven per cent of cases revealed inflammatory changes. These were classified into acute necrotizing pancreatitis, suppurative pancreatitis, chronic pancreatitis and parasitic pancreatitis.

4.4.10.1 Acute Necrotizing Pancreatitis

Acute necrotizing pancreatitis was observed in two cases. Histologically, there was necrosis of the acinar cells and diffuse areas of the acinar parenchyma were replaced by infiltrating neutrophils (Fig. 32 and 33). The proliferating

fibrous tissue was noticed encircling groups of acinar cells. Adjacent fat was necrotic and infiltrated by neutrophils (Fig. 34). Saponification of fat was seen in a few areas.

The second was acute pancreatic fat necrosis. Grossly, the pancreatic lobulations appeared conspicuous with the fat white and opaque (Fig. 35). Microscopically, the peripancreatic adipose tissue revealed necrosis, saponification and infiltration with neutrophils (Fig. 36). The adjacent acinar tissue appeared normal except in areas were inflammation had proceeded into the parenchyma. The interstitial connective tissue septum was thickened. Separation of interstitial connective tissue, lysis of fibres and aggregates of neutrophils circumscribed by connective tissue were also observed in this case (Fig. 37)

4.4.10.2 Suppurative Pancreatitis

A single case of suppurative pancreatitis was recorded during the study in a Doberman. Grossly the affected pancreas was very much distorted. It was whitish and firmer in consistency. The normal lobulated appearance of pancreas was lost and some areas were reduced to small strands (Fig. 38). Microscopically, a focal area of coagulative necrosis of pancreatic parenchyma with extensive infiltration of neutrophils surrounded by fibrous tissue was noticed (Fig. 39 and 40). The adjacent parenchyma appeared unaffected. There was thickening of the interlobular connective tissue.

4.4.10.3 Chronic Pancreatitis

This was observed in three of the cases. The affected pancreas was of increased firmness with accentuation of lobular pattern. Histologically, there was periacinar and periductular fibro-collagenous tissue proliferation along with diffuse infiltration of mononuclear cells (Fig. 41 and 42). In a severe case

pseudolobulation and hyperplasia of acinar parenchyma was visible (Fig. 43). In all the three cases the islet cells showed hyalinisation (Fig. 54)

4.4.10.4 Parasitic Pancreatitis

In this case, grossly the pancreas had miliary whitish spots on the surface. Histopathologically, the inflammation was seen in the acini adjacent to the pancreatic duct. A portion of the parasite was seen in the centre of the lesion encircled by aggregates of mononuclear cells and eosinophils (Fig. 44 and 45). The acinar tissue surrounding the nodule appeared normal. The duct revealed periductular fibrosis, ductular epithelial proliferation, degeneration and desquamation (Fig. 46).

4.4.11 Pancreatic Abscess

Pancreatic abscess was observed in a Dalmatian. Grossly, there was an increase in the size of the pancreas. The abscesses were seen as cream to yellow small masses of five-millimetre diameter with a friable consistency along with petechial and ecchymotic haemorrhages (Fig. 47). On histopathology the masses consisted of areas of central necrotic zone with calcification and caseation surrounded by infiltrating cells, predominantly neutrophils (Fig. 48). Fibrous tissue proliferation and encapsulation was seen around the abscess. Acinar cells surrounding the abscess were atrophic.

4.4.12 Islet Cell Changes

Islet cell changes were seen in 32 (44 per cent) pancreases screened. This included degeneration and depletion in eleven cases, hyperplasia in seven and hyalinisation in four.

4.4.12.1 Congestion and Haemorrhage

Fourteen cases showed congestion of islets, the capillaries of which were engorged with blood (Fig. 49). Haemorrhage was seen in islets in four cases. Islet cells were displaced by the accumulating erythrocytes.

4.4.12.1 Degeneration and Depletion

Degeneration of islets was noticed in eleven cases. The changes were mild in most cases. Two cases, there was severe loss of islet cells in association with haemonecrosis of the pancreatic parenchyma. In moderate cases the degenerated islets showed decrease in cellularity of the islets and cellular clumping. Vacuolar change of islets was noticed in a seven-year-old Pug. The cells had distended clear cytoplasm with vesicular nucleus with indistinctive borders and pyknotic nuclei (Fig. 50).

4.4.12.2 Hyperplasia

Islet cell hyperplasia was recorded in seven cases screened. None of the cases revealed any gross lesion. In four of the five cases of hyperplasia there was increase in the size of islet zone with increase in the number of the cellular components (Fig. 51). In one of the cases hyperplasia was confined to a single islet where the cells appeared crowded and the zone had a nodular appearance (Fig. 52). Gomoris' chromium haematoxylin phloxin stained sections revealed an increase in alpha cells in one case (Fig. 53), beta cells in two cases and a proportionate increase in all the cells types in the others. The alpha cells stained red and beta cells stained blue to purple.

4.4.12.3 Hyalinisation

Four pancreases revealed hyaline changes in islet. Affected islets appeared homogenous pink with decreased cellularity (Fig. 54).

4.4.13 Adenocarcinoma

A single case of adenocarcinoma of exocrine pancreas was recorded in a two and a half year old German shepherd. Grossly, nodular sessile greyish white growths of varying size were seen distributed throughout the pancreas, duodenum and some parts of the mesentery. The size of the masses ranged from millet sized to five centimetres in diameter (Fig. 55). Some of the tumour masses were firm in consistency and some were friable. Incised masses appeared solid and had a greenish yellow colour. Metastases to other organs were not seen. Histologically, the tumour was identified as a well-differentiated adenocarcinoma of pancreas. It was composed of cells with a rather small, round dark-staining nucleus and moderate amount of eosinophilic cytoplasm arranged as small distinct acini with lumen (Fig. 56). Hyperchromatic cells, forming distorted glandular arrangements and sheets were seen in the interacinar connective tissue (Fig. 57). The cytoplasm lacked zymogen granules. In some areas typical acinar areas alternated with trabecular and solid formations. The peripancreatic fat remained intact and there was no evidence of tumour necrosis. Masses of tumour cells could also be seen invading the duodenal villous epithelium, sub mucosa and muscular layer (Fig. 58 and 59).

4.5 CONCURRENT POST MORTEM LESIONS

The most prominent post mortem finding associated with cases having pancreatic disorders is given in table 5. In eighteen cases cardiopulmonary lesions accompanied the vascular changes in pancreas. The cardiac lesions included cardiac hypertrophy, cardiac dilatation, myocarditis, myocardial necrosis

and coronary thrombosis. Pneumonia, pulmonary congestion and oedema were the most common pulmonary lesions. Gastrointestinal disorders mainly gastroenteritis were seen in 11 cases with pancreatic vascular lesions. In two cases with spleenic torsion and splenomegaly, massive haemorrhage and necrosis were noticed in the pancreas.

Eight cases with atrophic changes, 11 cases with ductular changes and 14 cases with proliferative changes at necropsy had revealed hepatorenal disorders such as hepatosis, hepatomegaly, hepatitis, perihepatitis, cirrhosis, renal infarction, renal calculi, acute and chronic nephritis. Severe hypoplasia of pancreas was observed in a case with thyroid tumour. In nine of the cases with degenerative changes hepatorenal disorder was noticed especially hepatosis while five out of the ten cases of necrosis of pancreas, severe cardiopulmonary disorders such as, traumatic cardiac failure, coronary thrombosis and pneumonia were observed.

Out of the 11 cases of degenerative changes in islets, seven were in cases with hepatorenal disorders. Hyperplasia of islets in four out of the seven cases was observed along with gastrointestinal disorders like gastroenteritis.

There were two cases of acute pancreatitis. In one case the associated post mortem findings were cardiac hypertrophy, pulmonary collapse, hepatomegaly with distended gall bladder, chronic interstitial nephritis and congestion and oedema of brain. Cirrhosis, chronic nephritis and cardiac dilatation were the extra pancreatic lesions observed in the other case.

The three cases of chronic pancreatitis were accompanied by ascites, cardiac hypertrophy, pneumonia, hepatitis, nephritis and haemorrhagic enteritis.

Suppurative pancreatitis was noticed in a case with ascites, cardiac hypertrophy and cirrhosis. Parasitic pancreatitis was accidentally detected in a case with severe Ancylostomiasis.

The post mortem lesions observed in cases of adenocarcinoma was icterus, liver cirrhosis, cardiac hypertrophy, tumour masses on intestinal wall and parts of mesentery.

Table.1 Age wise distribution of lesions in the pancreas

Age group	Number of animals	Number with pancreatic lesions	Per cent
<1 year	18	10	55.55%
1-3 years	34	27	79.44%
3-5years	26	20	76.93%
>5years	22	15	68.18%
	100	72	

Table.2 Relationship of pancreatic weight and length to body weight based on age.

Age (years)	Number of animals	Total Body weight (Kg)	Average body weight (g)	Pancreas		Average Pancreas		Pancreas weight (g)/ body weight (kg)
				Weight (g)	Length (cm)	Weight (g)	Length (cm)	
<1	18	85.7	4.76	298.06	317.9	16.55	17.66	3.47
1-3	34	516	15.17	1210.64	494.2	35.07	14.53	2.3
3-5	26	403.6	15.52	794.92	556.8	30.57	21.41	1.9
>5	22	358.1	16.27	754.31	501.2	34.28	22.78	2.1

Table.3 Breed wise distribution of lesions in the pancreas

Breed	Total	Number of pancreas with lesions	Per cent
Non Descript	20	13	65%
German shepherd	27	25	92%
Others	53	34	64%
Total	100	72	

Table 4.Average pancreas weight and body weight based on breed

Breed	**Average body weight (Kg)**	**Average weight of Pancreas (g)**
German Shepherd	33.68	28
None Descript	23.29	93.75
Doberman	40.46	18.43
Labrador	30.02	15.9
Spitz	16.56	7.37
Crossbred	20.21	4.57
Dachshund	27.8	11.52
Dalmatian	31.58	12.56
Rottweiler	30.02	12.1
Great Dane	59.83	39
Boxer	47.37	25.75

Table.5 Pancreatic pathology - general post mortem findings

Pancreatic pathology	General post mortem finding			
	Cardio pulmonary	Hepato renal	Gastro intestinal	Others
Vascular changes	18	8	11	4
Atrophic changes	2	8	3	1
Ductular changes	4	17	6	-
Degenerative changes 1. Vacuolar 2. Fatty change	 3 2	 5 4	 3 1	 1 1
Necrosis	5	2	2	1
Proliferative changes 1.Acinar hyperplasia 2.Fibrous tissue proliferation	 1 3	 4 10	 2 1	 1 2
Inflammatory changes 1.Supprative 2.Chronic 4. Acute pancreatitis 5.Parasitic pancreatitis	 1 1 1	 1 2 1	 1 2 1 1	
Pancreatic Abscess	1	1	1	
Islet cell Changes 1.Hyperplasia 2.Degenerative 3.Hyalinisation	 1 2 -	 2 7 2	 4 1 -	 - 1 2

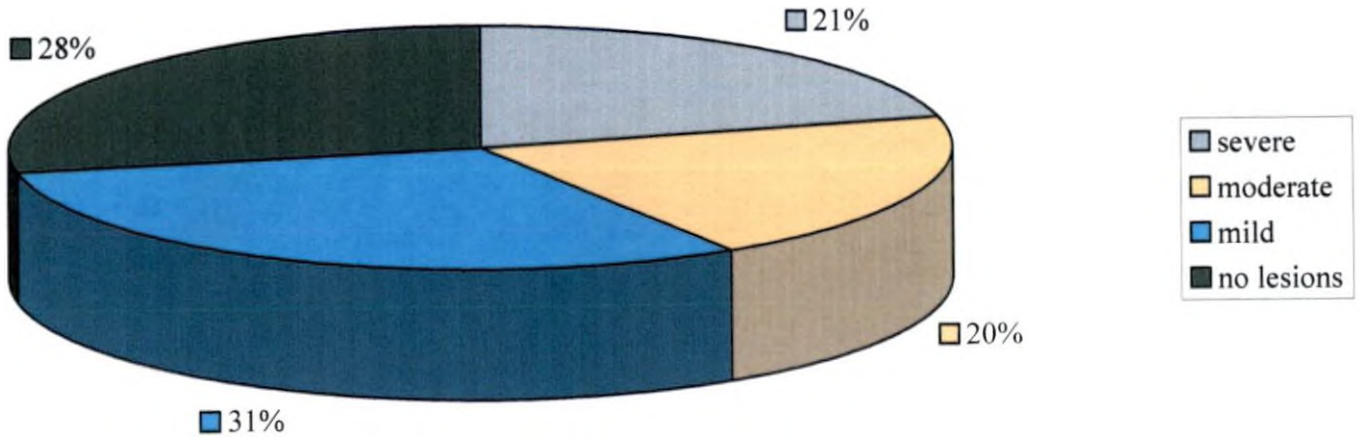
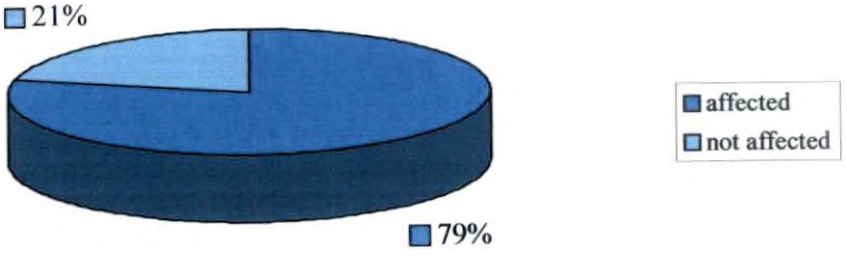
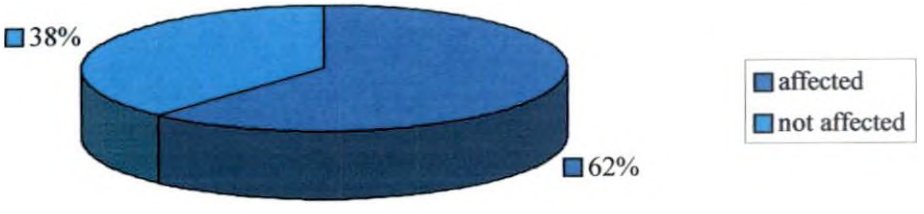


Fig.1. Prevalence and nature of pancreatic disorders in canines



Females



Males

Fig.2 Comparison between prevalence of pancreatic disorders among males and females

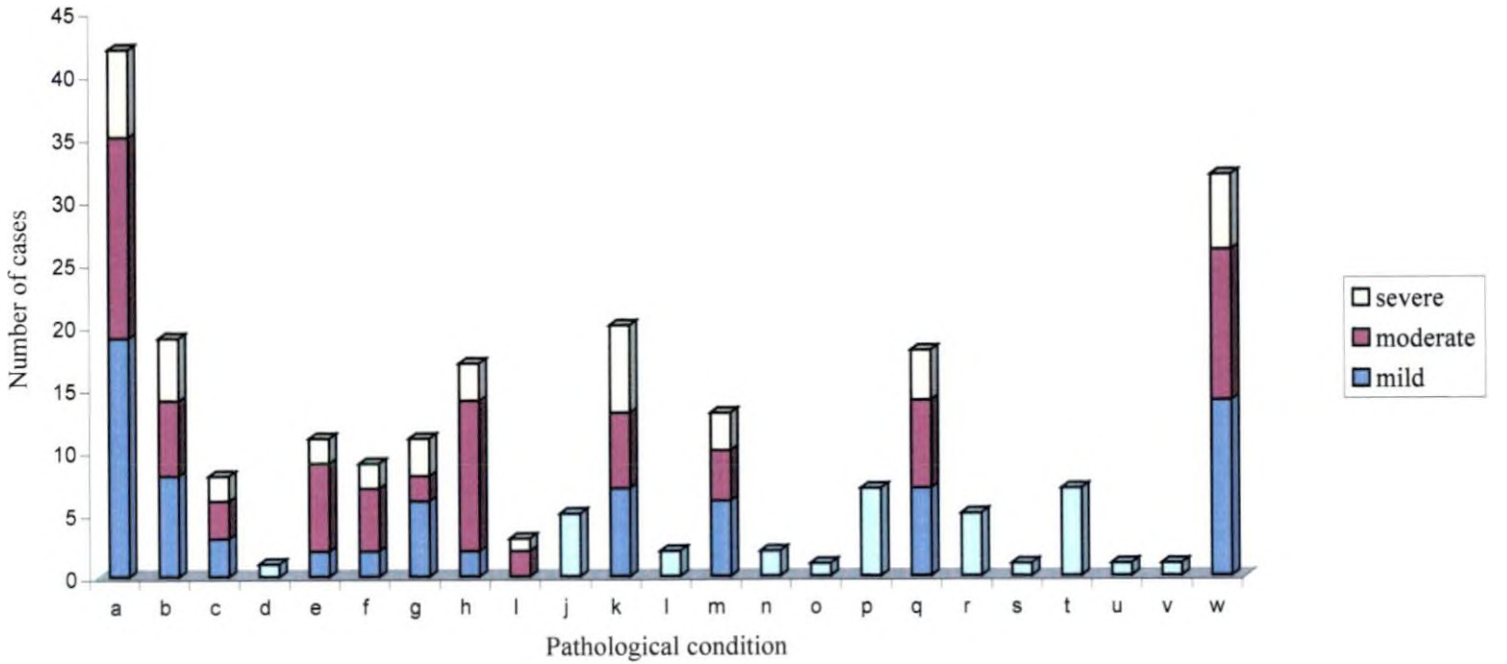


Fig.3 Classification and nature of pancreatic disorders in canines

a. Congestion
b. Haemorrhage
c. Oedema
d. Lymphangiectasis
e. Vacuolar degeneration
f. Stromal lipomatosis
g. Necrosis
h. Atrophy
i. Hypoplasia
j. Acinar cell hypertrophy
k. Periductular fibrosis
l. Periductular inflammation
m. Ductular epithelial proliferation
n. Squamous metaplasia of duct epithelium
o. Ductular adenoma
p. Pigmentation
q. Fibrosis
r. Nodular hyperplasia
s. Blood vessel proliferation
t. Pancreatitis
u. Pancreatic abscess
v. Adenocarcinoma
w. Islet changes

Discussion

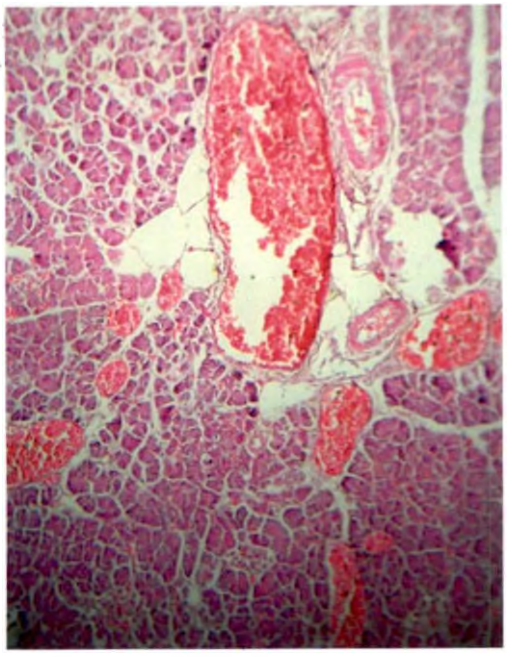


Fig. 4

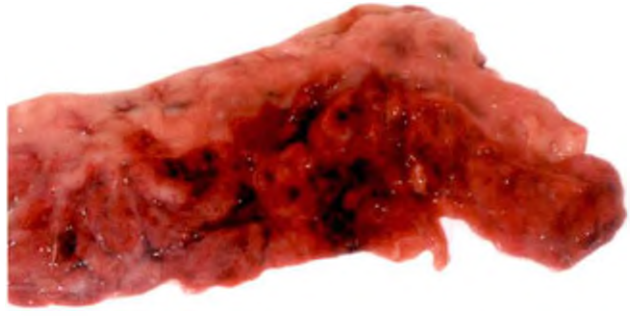


Fig. 5

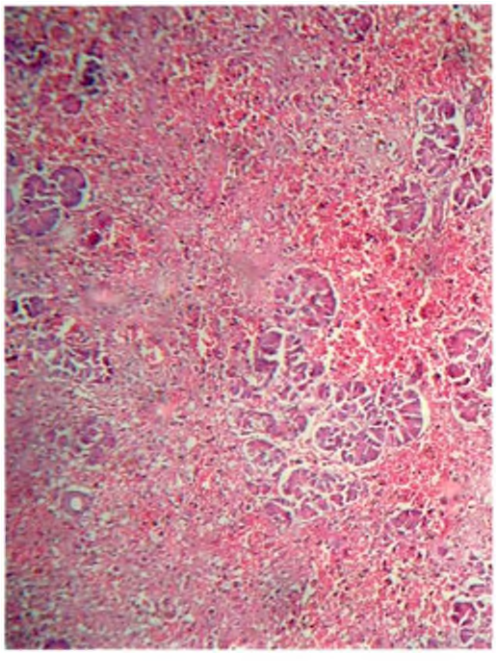


Fig. 6

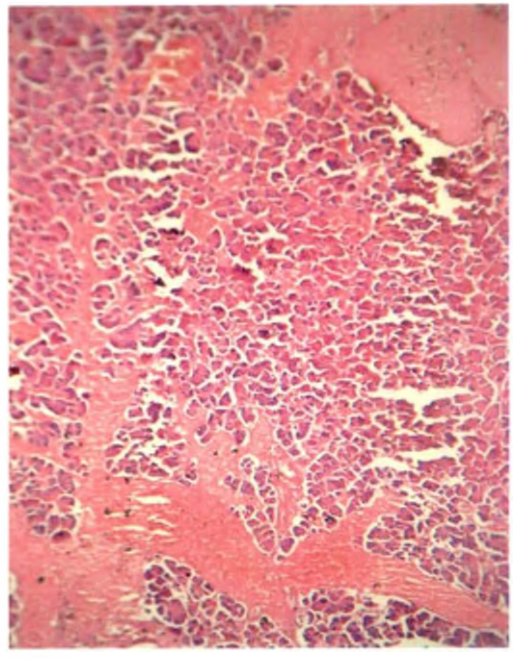


Fig. 7

Figure - 4. Congestion of pancreas: engorged blood vessels filled with blood - H&E x 100.

Figure - 5. Haemorrhage in the pancreas.

Figure - 6. Haemorrhage: extravasated blood replacing the parenchyma, acinar tissue seen as irregular islands - H&E x 100.

Figure - 7. Lymphangiectasis: lymph vessels conspicuous with stasis of lymph - H&E x 100.

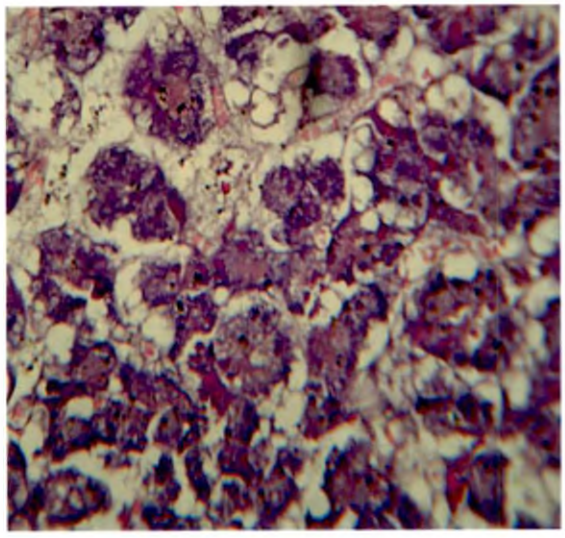


Fig. 8

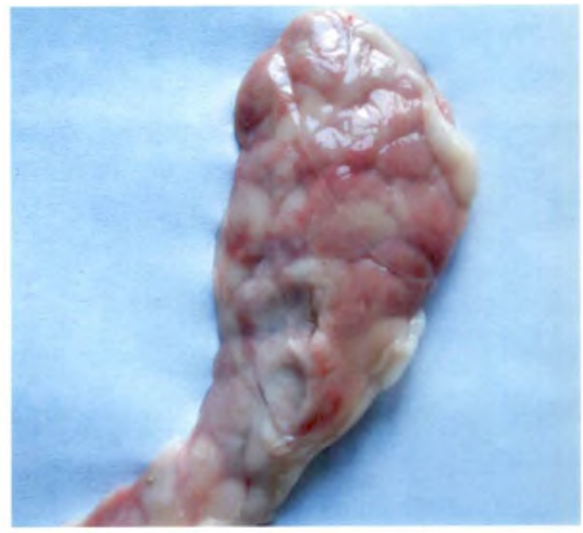


Fig. 9

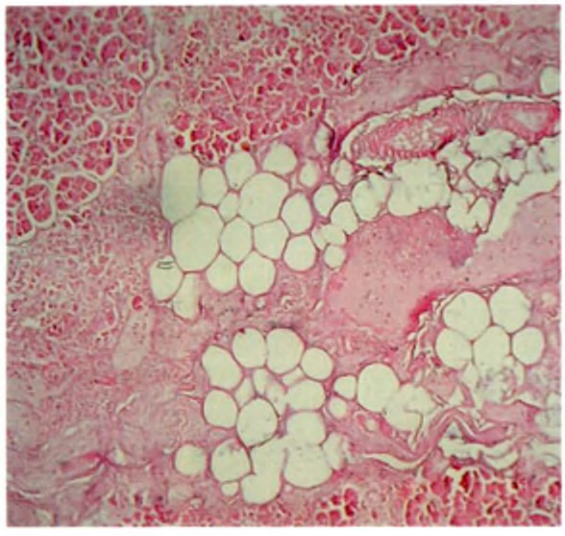


Fig. 10

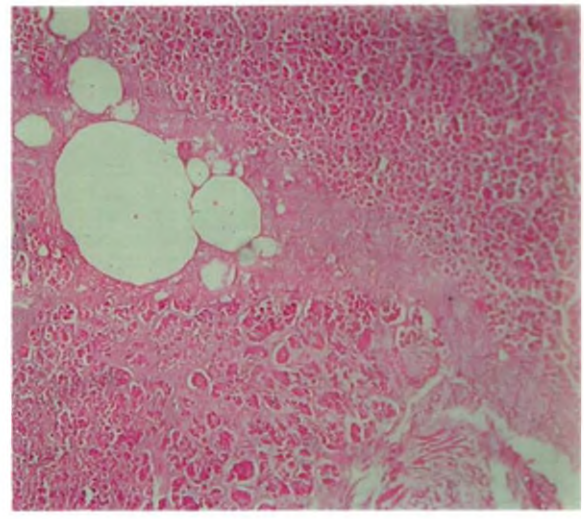


Fig. 11

Figure - 8.
Vacuolar degeneration : cytoplasmic vacuolation of pancreatic acinar cells - H&E x 400.

Figure - 9.
Stromal lipomatosis: glistening adipose tissue covering the pancreas.

Figure - 10.
Stromal lipomatosis: fat vacuoles replacing the parenchyma - H&E x 100.

Figure - 11.
Fat cyst: fat vacuoles coalaescing to form fat cyst - H&E x 100.

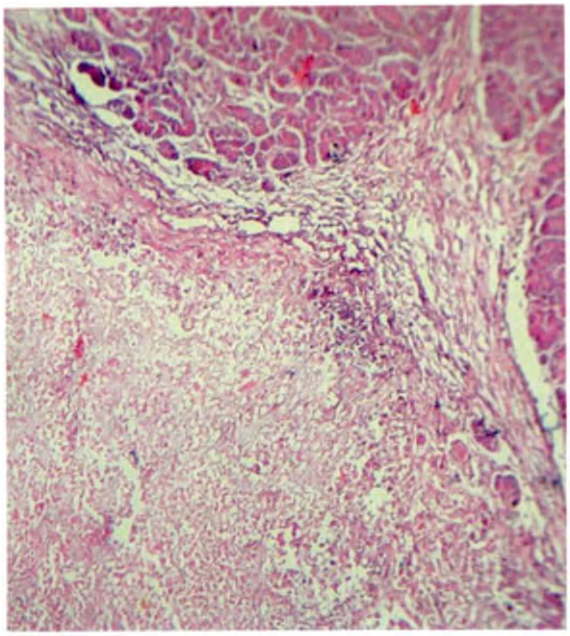


Fig. 12

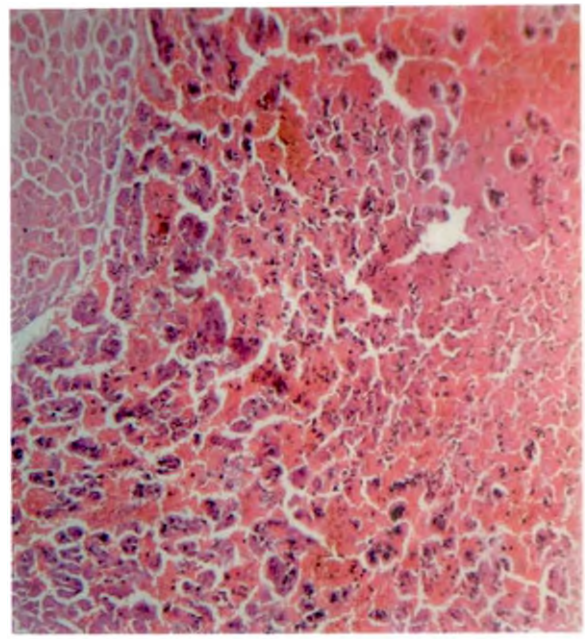


Fig. 13

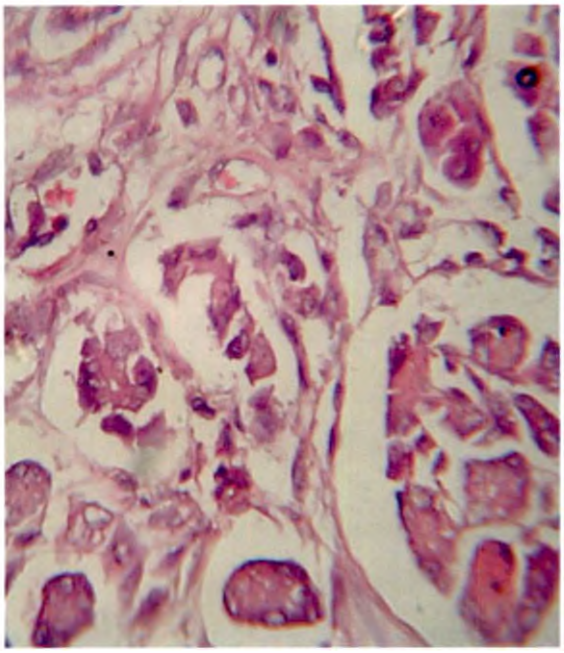


Fig. 14

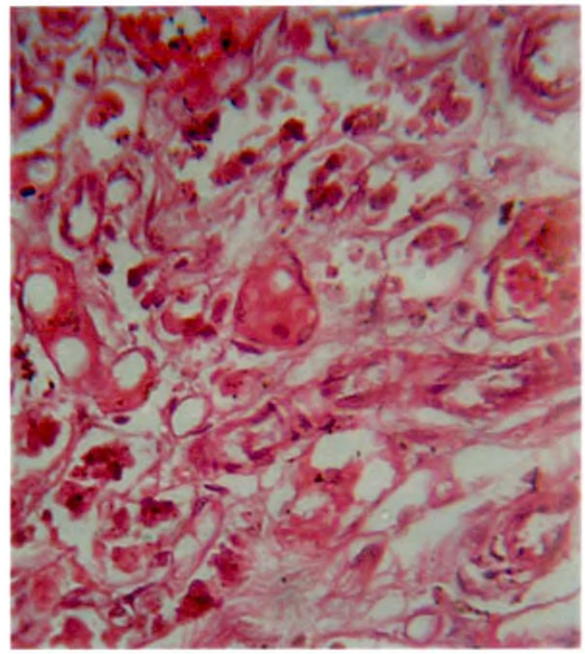


Fig. 15

Figure - 12.
Pancreatic necrosis: coagulation of parenchyma and mild inflammatory cell infiltration - H&E x 100.

Figure - 13.
Haemonecrosis: massive haemorrhage and necrosis - H&E x 100.

Figure - 14.
Pancreatic atrophy: atrophic acinar tissue surrounded by proliferating fibrous tissue - H&E x 400.

Figure - 15.
Atrophy: ducts appearing prominent - H&E x 400.

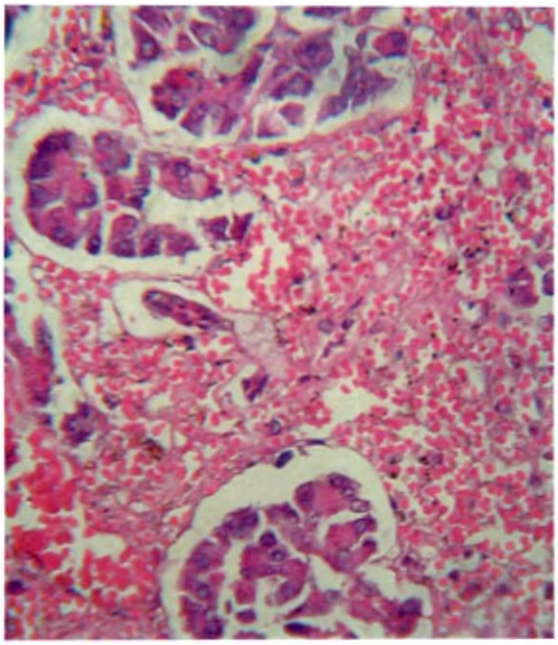


Fig. 16

Fig. 17

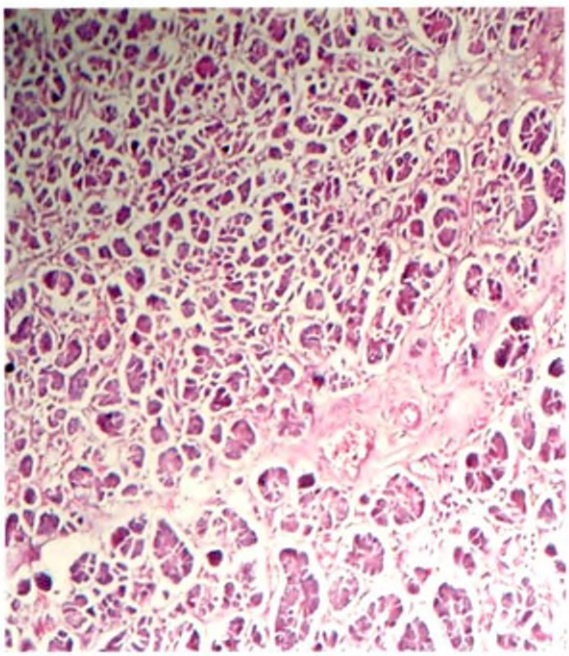


Fig. 18

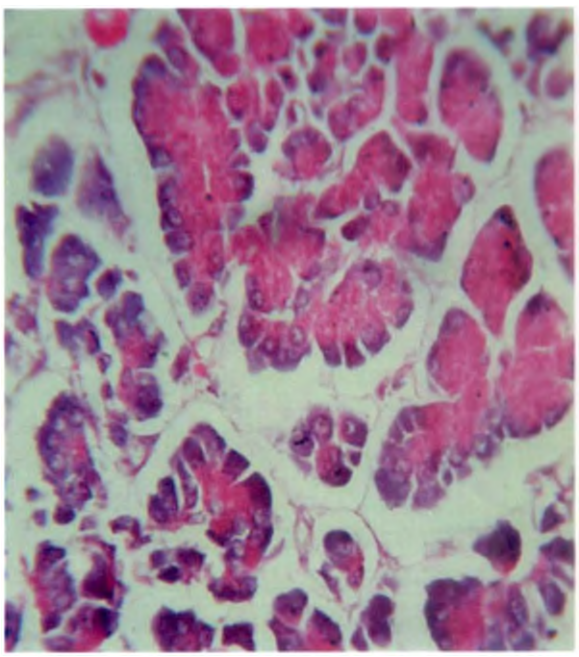


Fig. 19

Figure - 16.
Atrophy with haemonecrosis - H&E x 400.

Figure - 17.
Hypoplastic pancreas.

Figure - 18.
Hypoplastic pancreas: very small acinar cells appearing dissociated and separated by narrow strands of fibrous connective tissue - H&E x 100.

Figure - 19.
Acinar cell hypertrophy: bigger acinar cells with highly eosinophilic cytoplasm - H&E x 400.

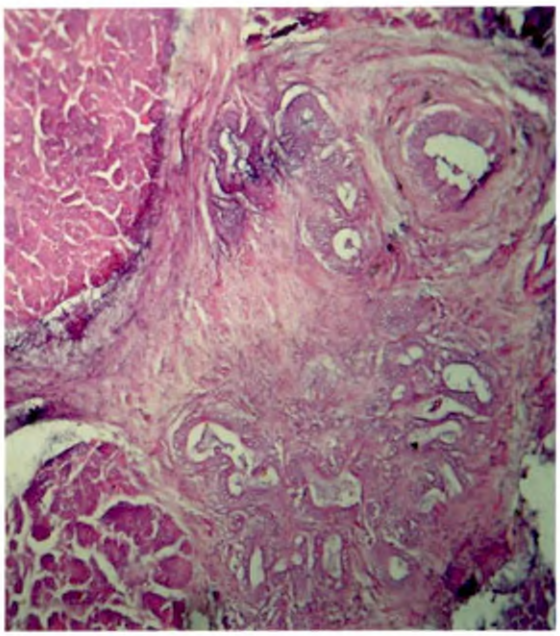


Fig. 20

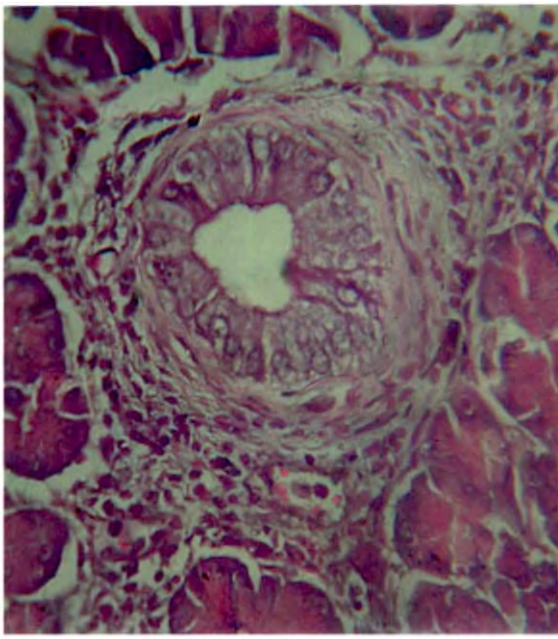


Fig. 21

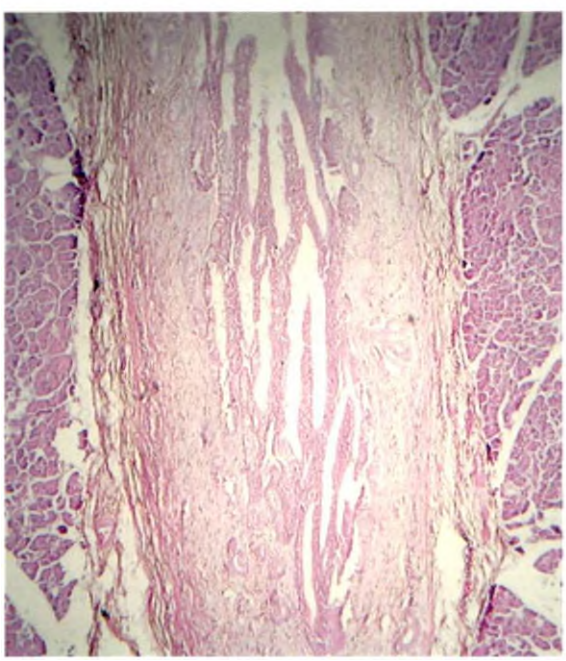


Fig. 22

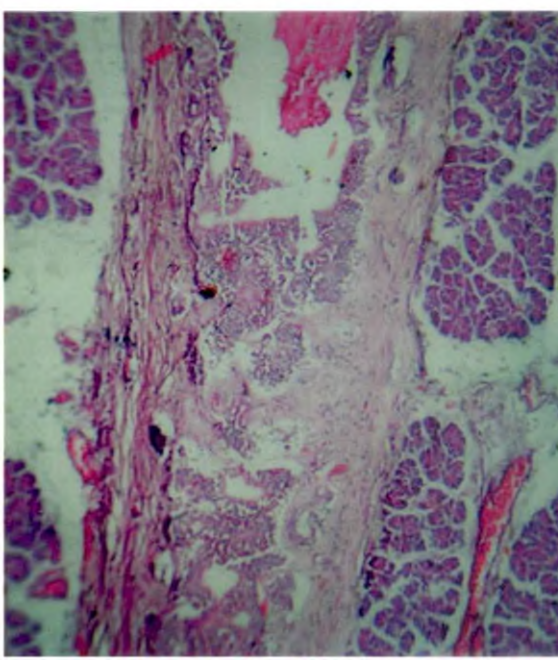


Fig. 23

Figure - 20.

Pancreas, periductular fibrosis: dense fibrocollagenous tissue around duct wall - H&E x 100.

Figure - 21.

Periductular fibrosis and inflammation - H&E x 400.

Figure - 22.

Ductular epithelial hyperplasia: hyperplastic cells forming papillary projections - H&E x 100.

Figure - 23.

Squamous metaplasia: ductular epithelium - H&E x 100.

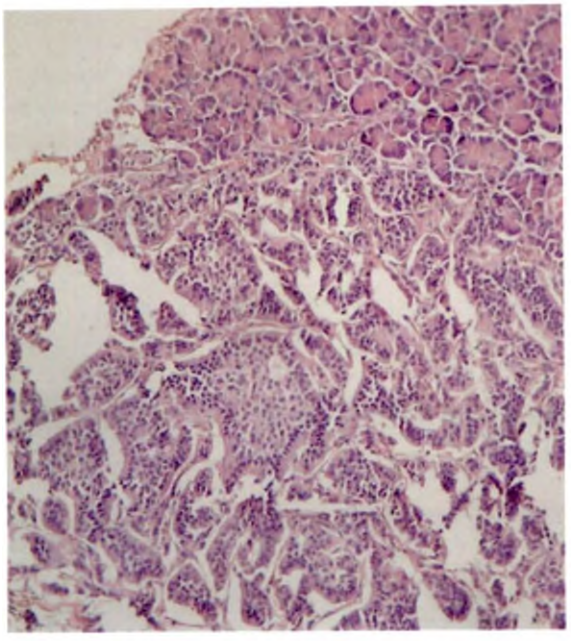


Fig. 24

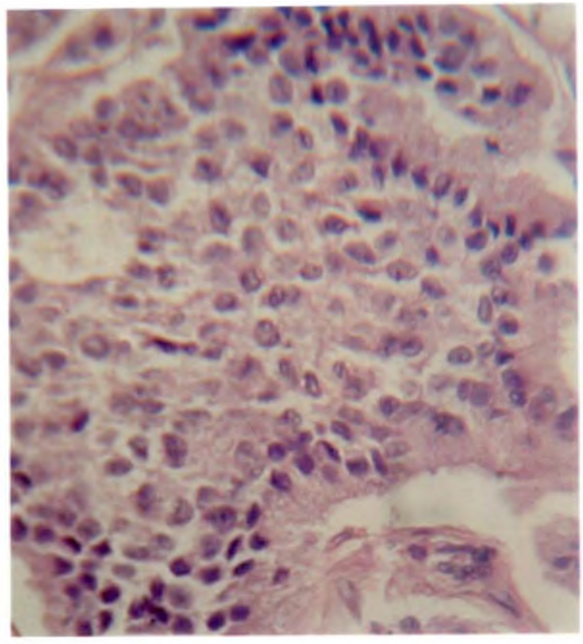


Fig. 25

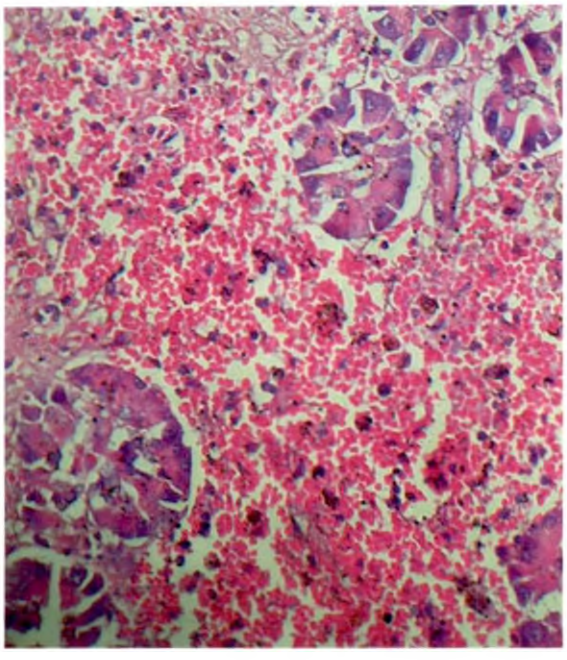


Fig. 26

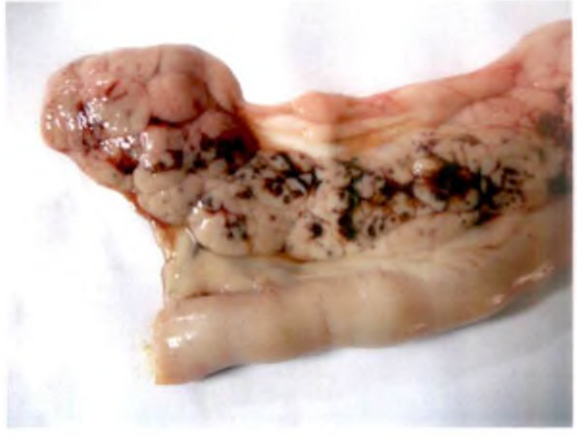


Fig. 27

Figure - 24.

Pancreas, ductular adenoma: proliferation of duct and wall lined by many layers of cells - H&E x 100.

Figure - 25.

Ductular adenoma: cells with clear cytoplasm and uniform vesicular nuclei - H&E x 400.

Figure - 26.

Haemosiderosis - H&E x 250.

Figure - 27.

Black pigments on the serosal surface of pancreas.

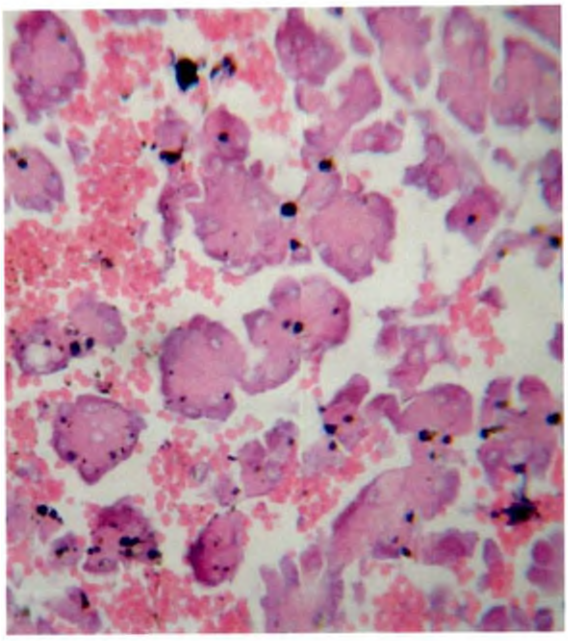


Fig. 28

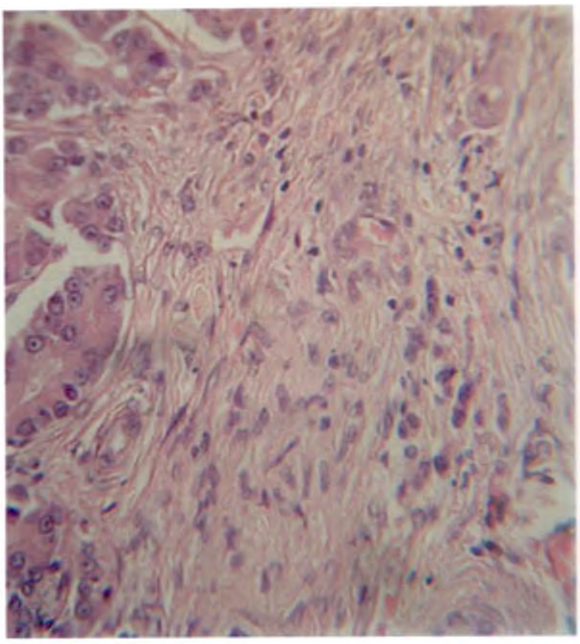


Fig. 29

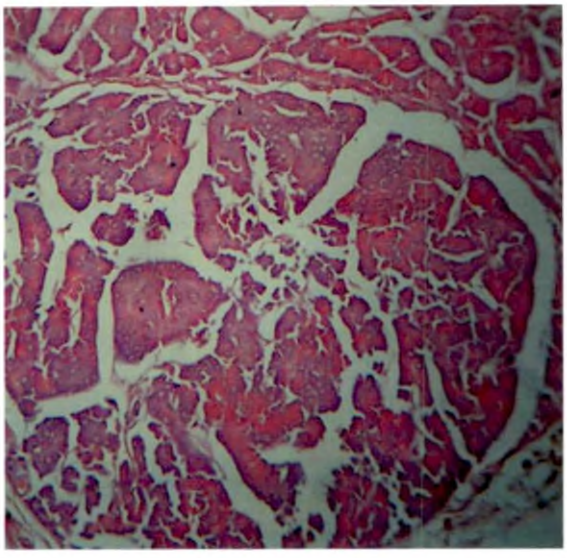


Fig. 30

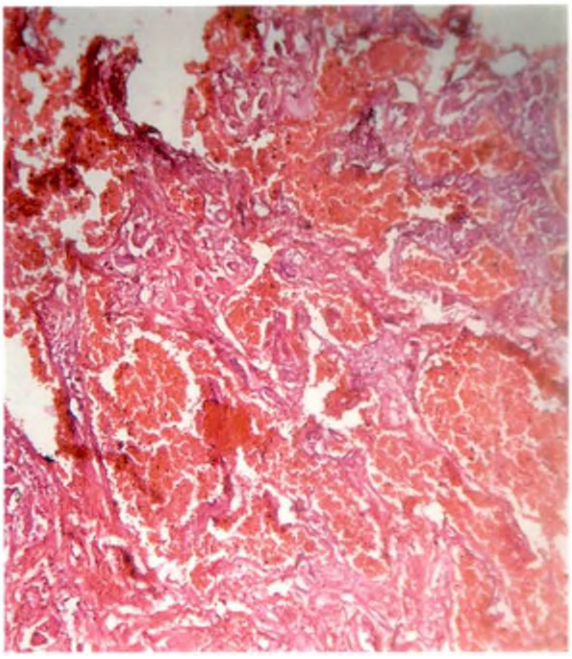


Fig. 31

Figure - 28.
Pancreatic haemorrhage: mild haemosiderosis and black pigments in the parenchyma - H&E x 400.

Figure - 29.
Fibrosis: proliferating fibrous tissue extending from interstitium into the adjacent parenchyma - H&E x 400.

Figure - 30.
Nodular hyperplasia of acinar parnchyma: focal aggregates of hyperplastic acinar cells - H&E x 100.

Figure - 31.
Pancreatic parenchyma, blood vessel proliferation: proliferating blood vessels filled with blood - H&E x 100.

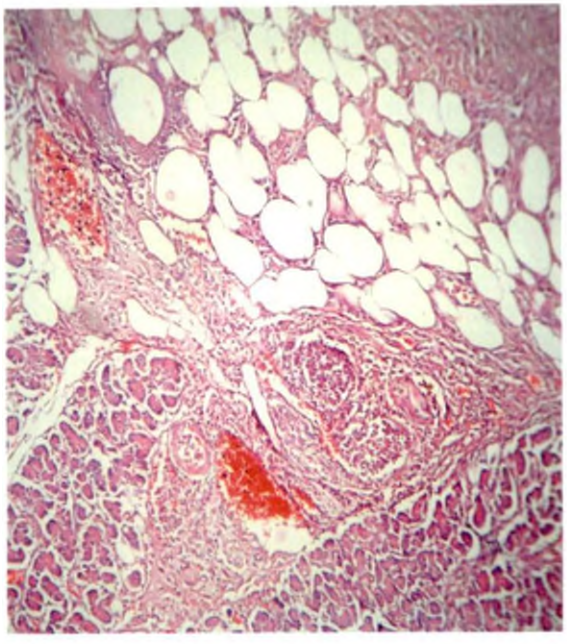


Fig. 32

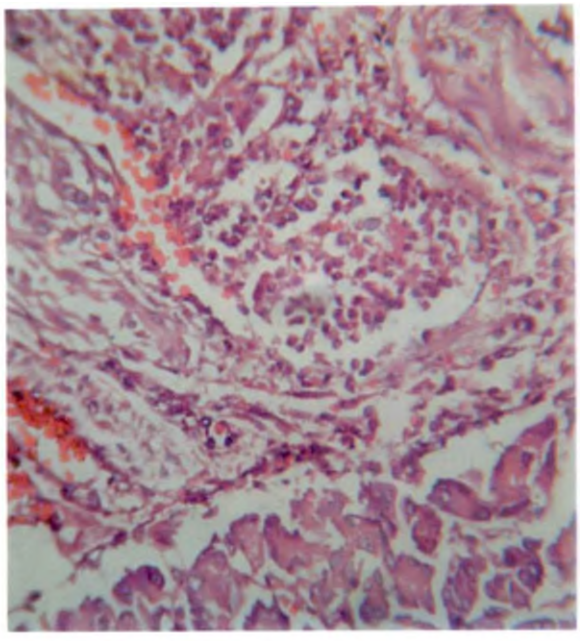


Fig. 33

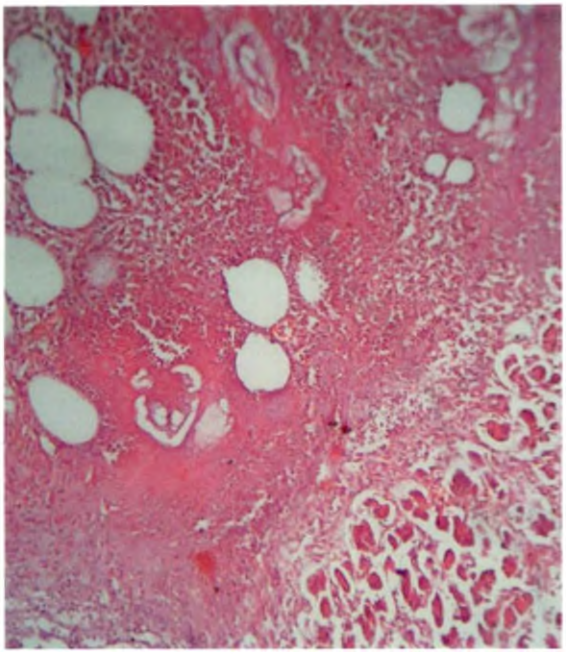


Fig. 34

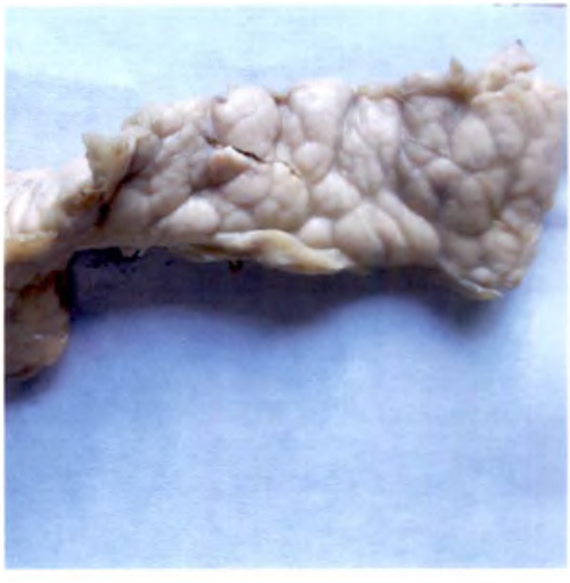


Fig. 35

Figure - 32.
Acute necrotizing pancreatitis: necrosis of acinar cells and infiltration of neutrophils - H&E x 100.

Figure - 33.
Acute necrotizing pancreatitis: necrosis of acinar cells and infiltration of neutrophils - H&E x 400

Figure - 34.
Acute necrotizing pancreatitis: fat necrosis and infiltration of neutrophils - H&E x 100.

Figure - 35.
Pancreatic fat necrosis: conspicuous pancreatic lobulations with fat white and opaque.

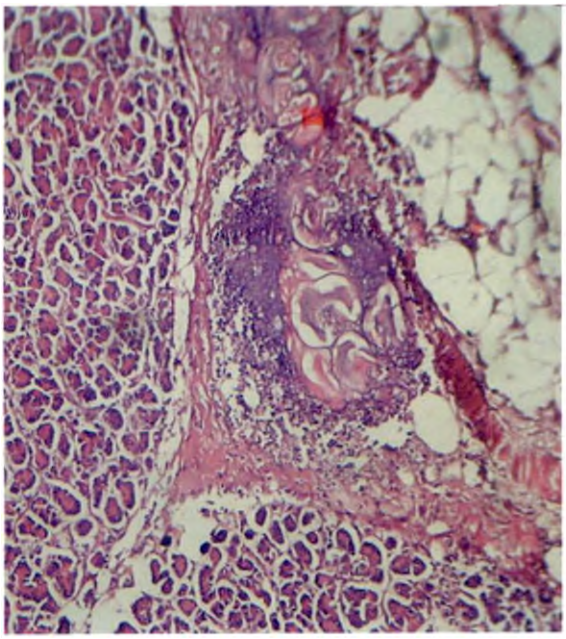


Fig. 36

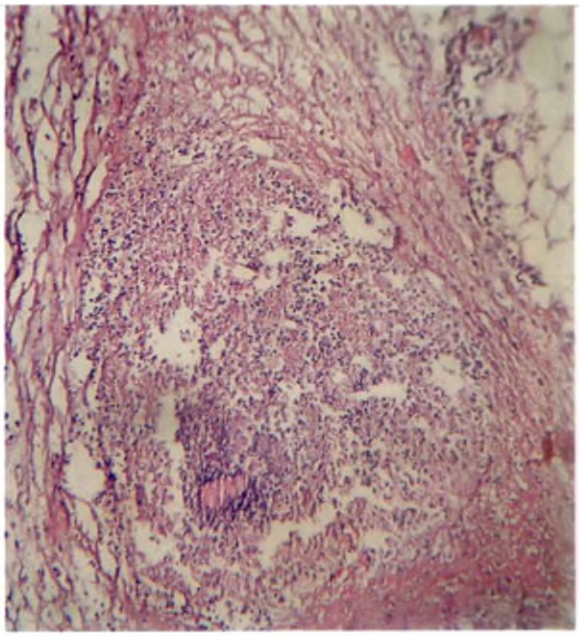


Fig. 37

Fig. 38

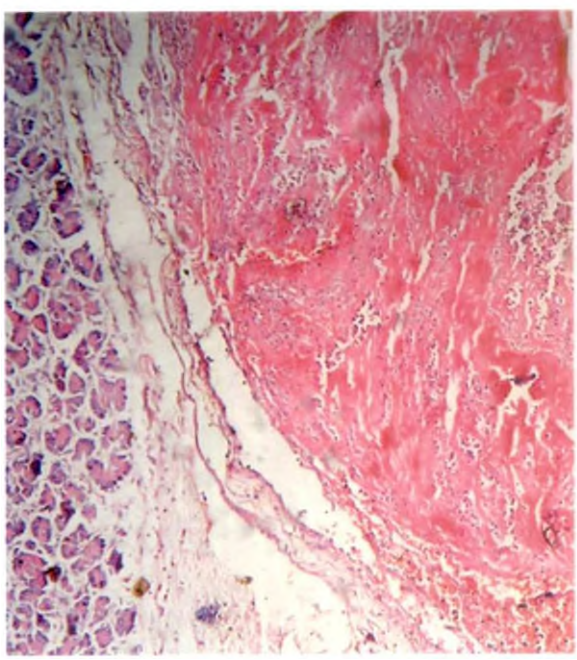


Fig. 39

Figure - 36.
Pancreatic fat necrosis: peripancreatic adipose tissue necrosis and infiltration of neutrophils - H&E x 100.

Figure - 37.
Pancreatic fat necrosis: neutrophil acculmulation in the connective tissue - H&E x 100.

Figure - 38.
Suppurative pancreatitis: loss of normal lobulated appearance.

Figure - 39.
Suppurative pancreatitis: coagulative necrosis with infiltration of neutrophils surrounded by fibrous tissue - H&E x 100.

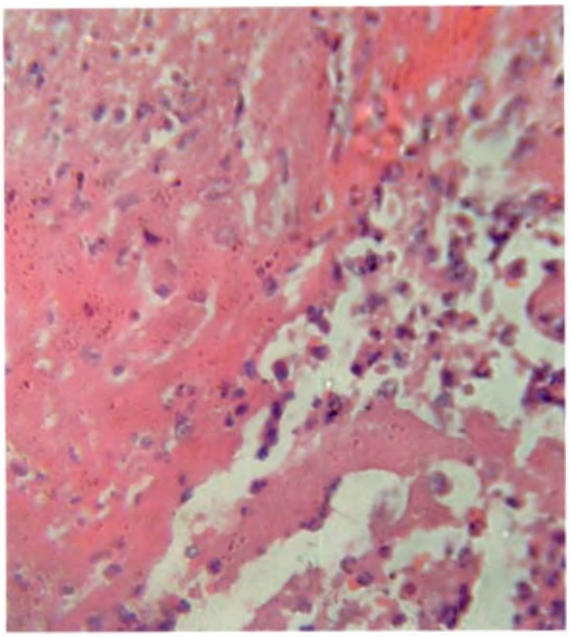


Fig. 40

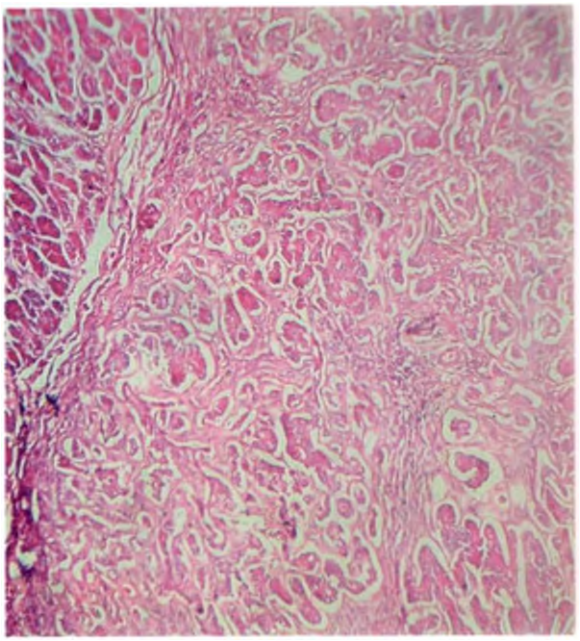


Fig. 41

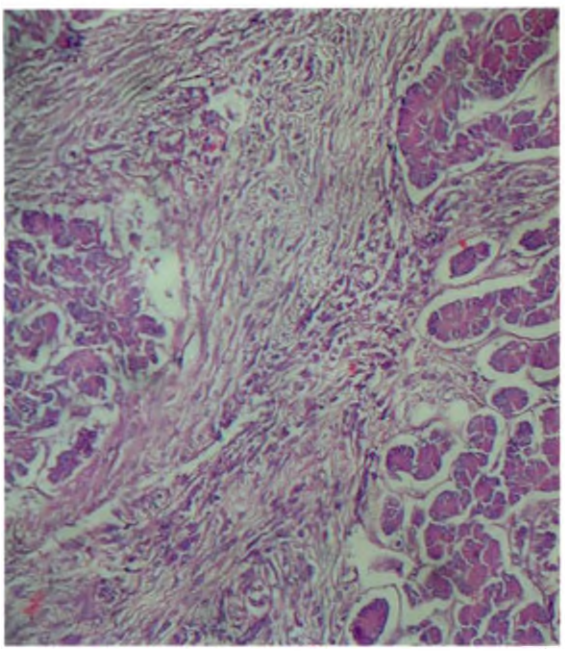


Fig. 42

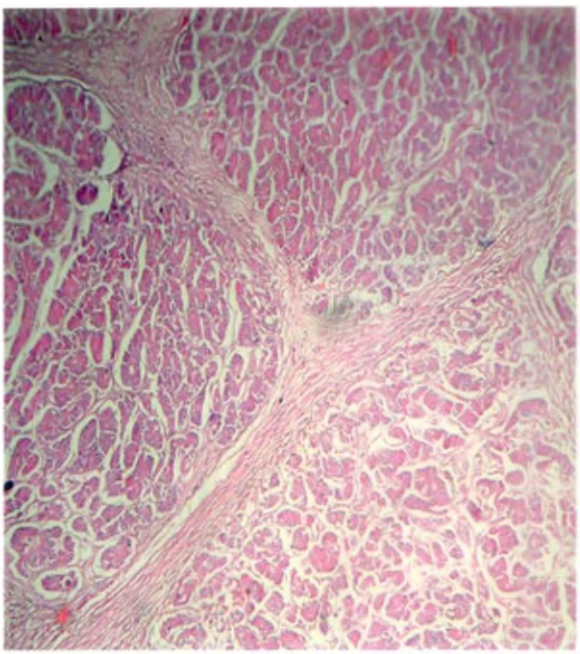


Fig. 43

Figure - 40.
Suppurative pancreatitis: coagulative necrosis with infiltration of neutrophils - H&E x 400.

Figure - 41.
Chronic pancreatitis: periacinar fibrosis and mononuclear cell infiltration - H&E x 100.

Figure - 42.
Chronic pancreatitis: periacinar fibrosis and mononuclear cell infiltration - H&E x 250.

Figure - 43.
Chronic pancreatitis: pseudolobulation of pancreatic parenchyma - H&E x 100.

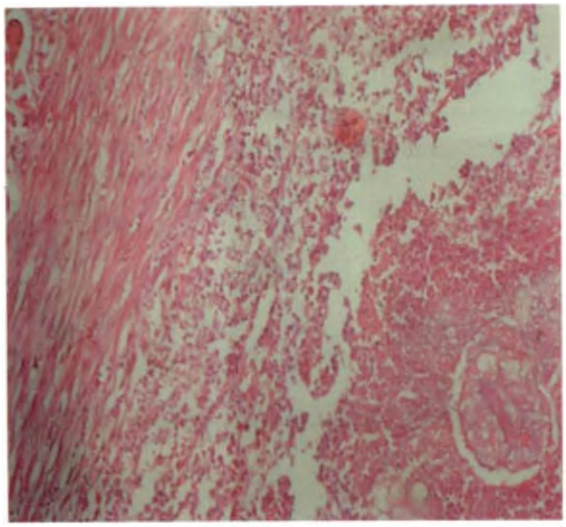


Fig. 48

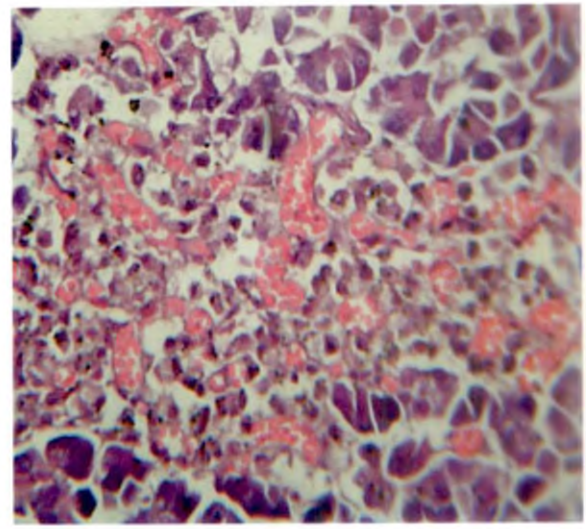


Fig. 49

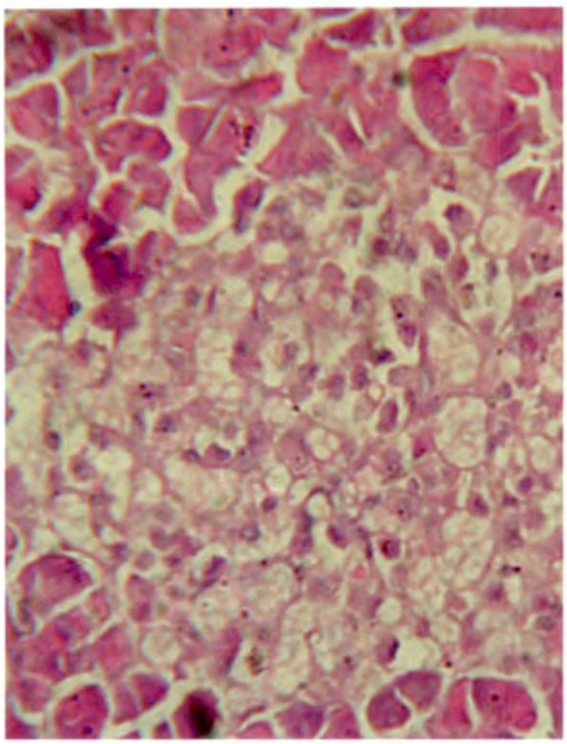


Fig. 50

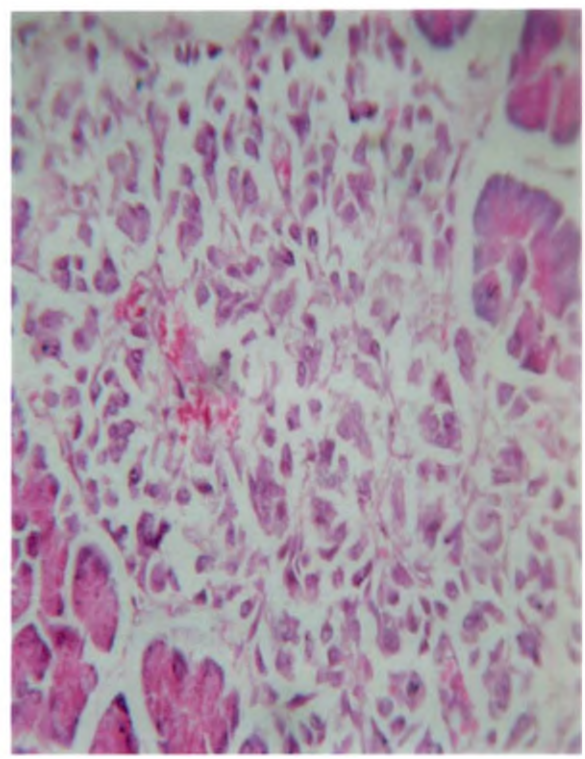


Fig. 51

Figure - 48.
Pancreatic abscess: central necrotic zone with caseation and calcification surrounded by neutrophils and fibrous tissue - H&E x 250.

Figure - 49.
Congestion of islet of Langerhans - H&E x 400.

Figure - 50.
Islet of Langerhans: Vacuolar degeneration - H&E x 400.

Figure - 51.
Islet hyperplasia: increase in islet zone and cellular components - H&E x 400.

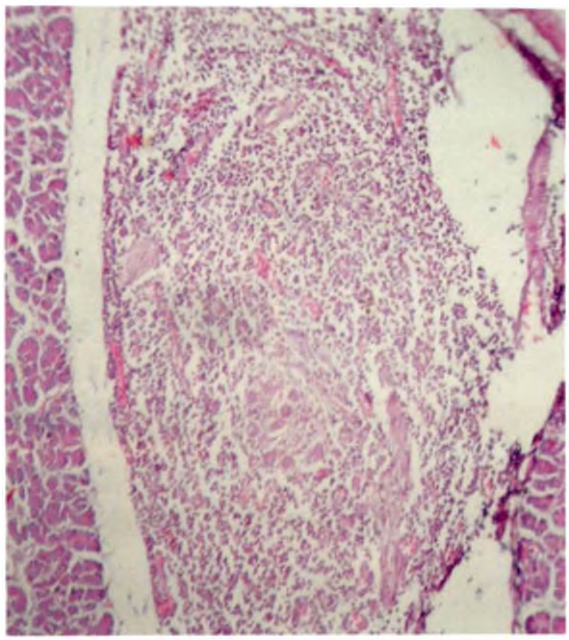


Fig. 52

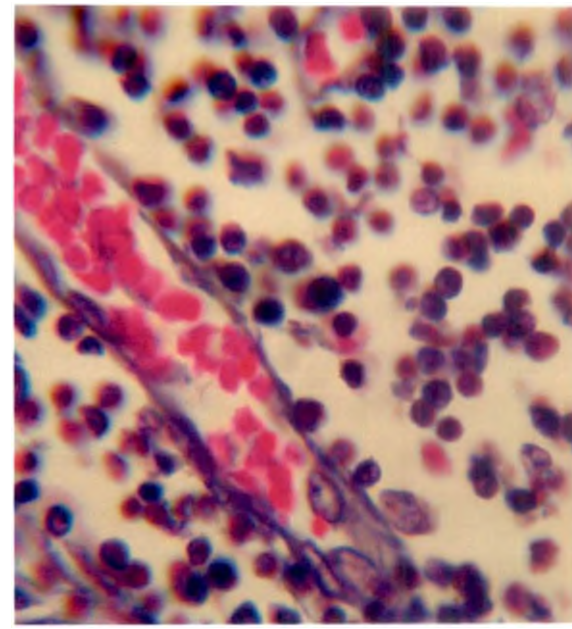


Fig. 53

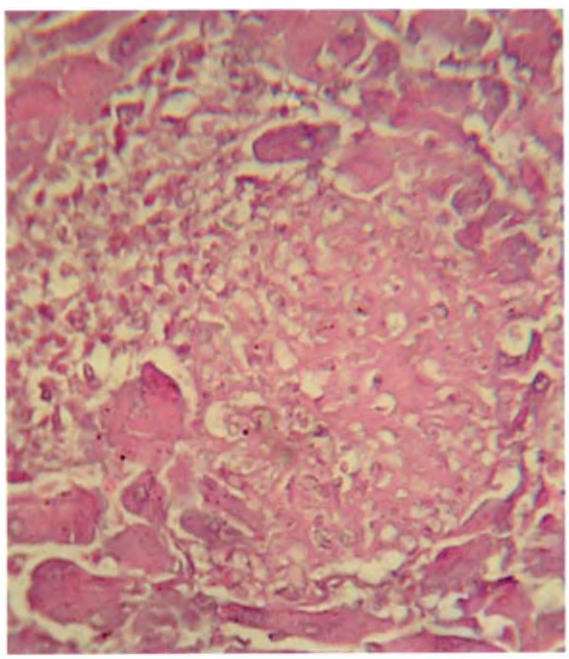


Fig. 54

Fig. 55

Figure - 52.
Nodular hyperplasia of islet - H&E x 100.

Figure - 53.
Islet of Langerhans: hyperplasia, alpha cells appearing red and beta cells purple - Gomoris' chromium haematoxylin phloxin x 1000.

Figure - 54.
Hyalinisation of islet of Langerhans - H&E x 400.

Figure - 55.
Adenocarcinoma of pancreas: tumour masses of varying size on the pancreas, duodenum and mesentry

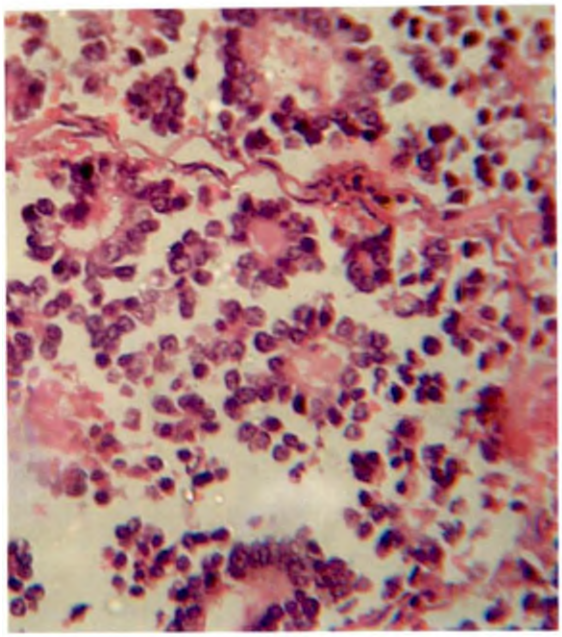


Fig. 56

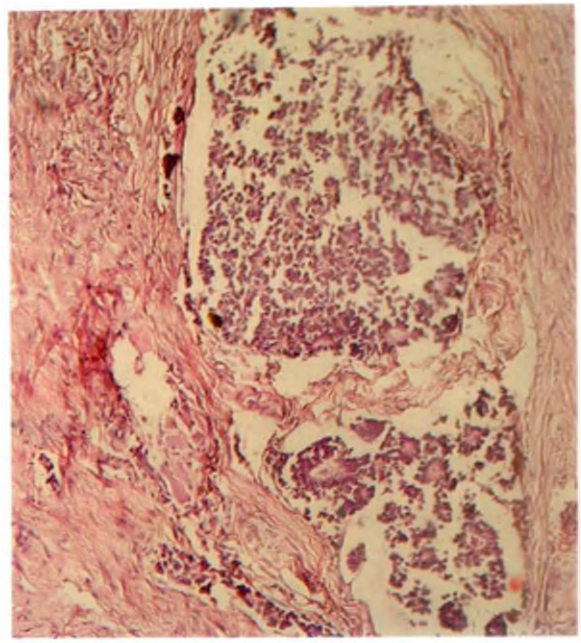


Fig. 57

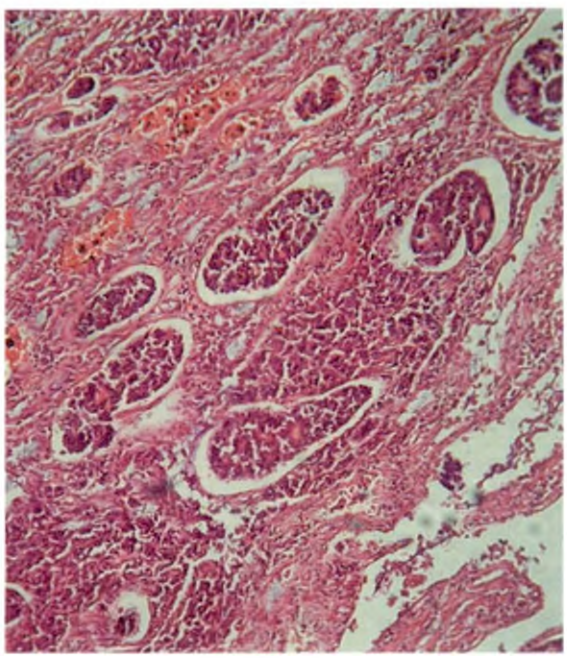


Fig. 58

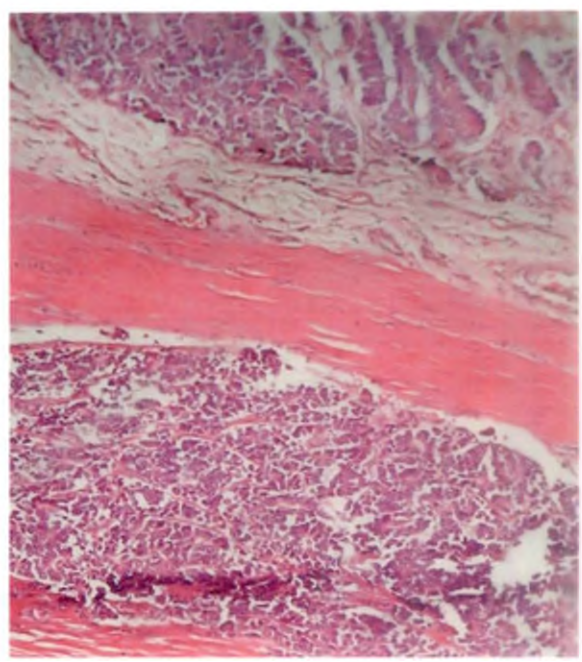


Fig. 59

Figure - 56.

Adenocarcinoma of pancreas: cells with small round dark staining nuclei and moderate amount of eosinophilic cytoplasm arranged as small distinct acini with lumen - H&E x 400.

Figure - 57.

Adenocarcinoma of pancreas: hyperchromatic cells forming distorted glandular arrangements in interacinar connective tissue - H&E x 100.

Figure - 58.

Adenocarcinoma of pancreas: clumps of neoplstic cells in the duodenal mucosa - H&E x 100.

Figure - 59.

Adenocarcinoma of pancreas: neoplastic cells in the duodenal muscular layer x 100.

5. DISCUSSION

The present investigation was undertaken to evaluate the prevalence and nature of pathological conditions of pancreas in canines. Special attention was given to classify various pancreatic disorders based on gross and histopathological lesions and to correlate them with the general post mortem findings. The study made it abundantly clear that the disorders of the pancreas in canines are more than what is generally expected.

The systematic gross and histopathological examination revealed pancreatic lesions of varying forms and degrees to the tune of 72 per cent. Of these 40 per cent showed severe to moderate lesions and 32 per cent mild lesions.

The influence of age, breed and sex on the pancreatic pathology was studied. It was found that dogs of age groups between one to five years were more affected than dogs of greater than five or less than one year of age. It was seen that majority of the cases presented with pancreatic atrophy and pancreatitis were in the age group of one and a half to six years. The age prime for the occurrence of pancreatic acinar atrophy has been reported to be six to eight months by Westermack *et al.* (1989). No age predisposition was reported by Williams (2000) and Shridhar and Yathiraj (2004) as they observed pancreatic atrophy in all age groups. Strombeck and Guilford (1991) has reported pancreatitis as a disease of middle-aged dogs in contrast to observations made by Cook *et al.* (1990), Hess *et al.* (1999) and Williams (2000). They observed pancreatitis in aged dogs.

Among the breeds the disorders were found high in German shepherd followed by non-descripts, which indicated the breed as the predisposing factor for pancreatic disorders. Westermarck *et al.* (1989), Williams (2000) and Shridhar and Yathiraj (2004) reported high prevalence of pancreatic acinar

atrophy in German shepherd. A difference in the susceptibility of breeds to pancreatitis was observed by various authors. Strombeck and Guilford (1991) observed this in Dachshund, Cook *et al.* (1990) in terriers and Hess *et al.* (1999) in Yorkshire terriers. The breeds presented with pancreatitis in this study were German shepherds, Labrador retriever, Lasapso, Great dane and Dalmatian. Three German shepherds and one each of others had pancreatitis.

A gender bias towards females was noticed in the present study. The prevalence among females was found to be 79 per cent whereas in males it was only 62 per cent. Of the seven cases of pancreatitis observed during the study five were in females. This was in agreement with the reports of Strombeck and Guilford (1991) that there was a higher incidence of pancreatitis among females. However Hess *et al.* (1999) have reported an increased prevalence among male and neutered female dogs.

The relative weight of pancreas to the body weight was found to be 0.2 per cent, in this study which was similar to that reported by Strombeck and Guilford (1991). The length of the pancreas was found to increase proportionately with age except in the age group between 1-3 years.

Lesions in the pancreas showed variation from lobe to lobe ranging from degeneration to inflammation and in some cases all lobes were affected in a uniform manner. Jubb (1993) suggested that the circulatory arrangements and complex interplay of hormones might influence the common pathological changes and distribution of pancreatic disorders.

Among the various types of histopathological lesions encountered in pancreas, vascular changes like congestion and haemorrhage were the predominant ones. In many cases, other internal organs also revealed congestion and haemorrhage suggesting a systemic involvement. The probable causes could have been an infection or toxin induced damage to vascular endothelium. In two

of the cases where severe vascular changes were seen leptospirosis was suspected considering the accompanying lesions like icterus, anemia and haemoglobinuria along with hepatic and renal lesions on post mortem. The case was later confirmed by dot ELISA. Massive haemorrhage in the pancreas and sudden death in dogs has been reported in canine distemper (Thomson, 1984). In eighteen cases cardiac and pulmonary lesions accompanied vascular lesions in pancreas. Pneumonia and cardiac decompensation can result stasis of blood and congestion of various organs (Thomson, 1984). In long standing cases of chronic venous stasis or haemorrhage, haemosiderosis was noticed in the parenchyma. A strong relation was noticed between the vascular changes in the pancreas and gastrointestinal lesions like haemorrhagic gastroenteritis and gastrointestinal ulcer. The pancreas being intimately related with the gastrointestinal system any alteration occurring in them would reflect on the pancreas and secondary lesions are produced. Another significant finding noticed was massive haemorrhage and total destruction of pancreas in a case of splenic torsion and splenomegaly.

Oedema was observed in 11 per cent of the cases. Varying degrees of congestion noticed in the parenchyma indicated circulatory disturbances as the cause. This could also be a local manifestation of a general disease.

Greatly distended lymph vessels and stasis of lymph was noticed in a few cases. This lesion was confined to certain lobes only. Hypertrophy of pancreatic acinar cells in focal areas and periductular fibrosis away from such lesions point to the obstruction of lymph flow at some point along the course and stasis.

Pancreatitis was one of the common disorders noticed. The etiology of naturally occurring canine pancreatitis is considered obscure and is often complex and multifactorial (Jubb, 1993). In human beings, a variety of factors like autodigestive destruction, ductular obstruction due to parasitic infection, toxic and nutritional factors have been identified (Kloppel and Heitz, 1984). Autodigestion due to reflux regurgitation of duodenal contents into the main pancreatic duct and

consequent ductal inflammation, leakage and activation of enzymes in the pancreatic parenchyma has been suggested as a cause in dogs by Hendrick (1980). Regurgitation of bile through ampulla of vater has also been pointed out as a possible factor. This destroys the phospholipids of the cell membrane leading to inflammatory response in the tissue. The possibility of the afore said factors causing pancreatitis in dogs is more as gastrointestinal disorders leading to stasis of contents, torsion, ingestion of foreign bodies causing obstruction and helminthiasis are relatively common. Parasitism becomes a problem when proper deworming regimes are not followed. In one of the cases, histopathological examination revealed a parasitic nodule in the acini wherein the parasitic larvae was seen surrounded by great aggregates of eosinophils and mononuclear cells. The case was diagnosed with heavy ancylostomiasis at autopsy and therefore it was inferred that the parasite might have migrated through the ducts to acini and caused pancreatitis. Jubb (1993) reported that the parasites could pass from the duodenum into the pancreatic duct through the ampulla of vater. Anderson *et al.* (1987) have reported a case of *Eurytrema procyonis* infection in the pancreas of a cat.

Bacterial and viral infection can be an etiological factor in precipitating pancreatitis particularly viruses with epitheliotropic properties like canine parvo and canine distemper virus (Jubb, 1993). Seong and Seo (1996) observed pancreatitis in a dog with canine distemper. Infectious etiology like viral, bacterial, mycoplasmal and parasitic has been suggested by Williams (2000) as well as Strombeck and Guilford (1991). Focal suppurative pancreatitis was observed in a case. The etiology of this could not be identified as no isolation was attempted. It appears to be secondary as hepatomegaly and gastroenteritis were the concurrent lesions observed in this case. Bacterial translocation from the intestinal tract and secondary pancreatic infection might be a possible pathogenesis. It is worth mentioning here that in a case with leptospirosis, multiple abscesses were seen in the parenchyma.

Four cases of trauma causing extensive damage to pancreas and pancreatitis were noticed in this study. Feldman *et al.* (1981) and Strombeck and Guilford (1991) had recognized abdominal trauma as cause of acute pancreatitis.

The importance of nutritional imbalances in the pathogenesis of chronic pancreatitis was stated by Steer *et al.* (1995) and Williams (2000). This points to the importance of proper diet management. The exact etiology of the three cases of chronic pancreatitis could not be ascertained. The possible role of diet in the pathogenesis of these cases cannot be ruled out.

Pancreatitis is not being diagnosed clinically in veterinary practice and therefore cases of these go unnoticed and undiagnosed, leading to poor digestability and intestinal malabsorption. This retards the growth and reproductive performance of canines. It is therefore advisable to evaluate the pancreatic function too in clinical cases of gastrointestinal disorders.

Degenerative changes such as vacuolar degeneration, fatty change and degeneration with necrosis were recorded in the pancreas in various severities. The vacuolar changes as well as necrosis were seen mostly in the periphery of the lobule. This pattern was similar to the one described by Jubb (1993) who stated a role for hypoperfusion or reperfusion in the pathogenesis as the periphery of the lobule is the periphery of the circulatory fields. In many cases of vacuolar degeneration and necrosis the pancreas revealed passive congestion, which could have been the cause of hypoxia and consequent degenerative changes. A variety of local and systemic diseases have been incriminated as the cause of acinar cell degeneration by MacLachalan and Cullen (2001). In this study severe pancreatic necrosis was observed in a dog diagnosed with leptospirosis. Two cases with pancreatic necrosis had the history of prolonged corticosteroid therapy. Jubb (1993) while stating the pathogenesis of pancreatic necrosis as obscure has named few risk factors such as prolonged corticosteroid therapy, surgical manipulation of pancreas and feeding diets high in fat and low in protein.

Fatty infiltration was seen in nine cases. The infiltration was prominent in the interstitium and in certain cases it extended into the parenchyma. This could be attributed to part of general obesity as the animals had excess fat deposition in the omentum, mesentry and even the kidneys were seen embedded within fat.

Seventeen cases revealed atrophic changes. Acinar atrophy due to protein calorie malnutrition has been described in Kwashiorkor in human children (Kloppel and Heitz, 1984). Jubb (1993) and Williams (2000) observed that toxicities, deficiency of essential amino acids and trace minerals like copper, zinc and selenium would cause pancreatic atrophy. The possible role of these factors in the causation of the changes observed could not be ascertained and controlled experiments have to be carried out in canines to find out the role of deficiencies of essential amino acid and trace minerals as the cause of pancreatic atrophy. Churg and Richter (1971) reported atrophy of acinar tissue, following ligation of the duct. However in this study pancreatic acinar atrophy was not observed in cases with duct obstruction.

Duct showed pathological alteration in 23 cases, which consisted of periductular fibrosis and inflammation, hyperplasia of the ductular epithelium, squamous metaplasia and adenoma. Ductular fibrosis and inflammation and hyperplasia of epithelium were noticed in cases with chronic pancreatitis. The pancreatic duct in parasitic pancreatitis too showed severe periductular fibrosis, epithelial hyperplasia, degeneration and desquamation. These findings were in concordance with those reported by Steer *et al.* (1995) and Princy (2000) in chronic pancreatitis, by Kelly *et al.* (1975) in interstitial pancreatitis and by Suda and Miyano (1985) in bile pancreatitis.

A case of ductular adenoma was observed which consisted of cells of low columnar to cuboidal in nature with a clear cytoplasm. Adenomas of ductular

origins are considered to be extremely rare (Jubb 1993). MacLachlan and Cullen (2001) have suggested a difficulty in differentiating adenomas from hyperplasia.

Nodular hyperplasia of the acinar epithelium was recorded in four cases. Three of the animals with this condition were above five years of age. It would appear, as a compensatory mechanism for the declining cellular activity in senility. The condition has been reported as a relatively common finding in aged animals by Jubb (1993). The other animal was young and the hyperplasia was seen along with pancreatitis. Duffel (1975) has reported nodular hyperplasia in pancreatitis. Gastrointestinal and hepatorenal lesions were observed at autopsy in cases with acinar cell hyperplasia. One or two hyperplastic nodules could be seen in certain lobules. The nature and distribution of lesion and associated gastrointestinal and hepatorenal lesions indicated acinar hyperplasia as compensatory with phase of a deteriorating digestive and absorptive process. Pancreas is directly involved in the digestive and absorptive processes and also for the normal gastointestinal homeostasis. It is also possible that hepatorenal disorders could result in sedimenting of various toxic substances in the body system augmenting the aging process and resulting in degenerative changes in some cells while surviving cells try to compensate for those lost.

Pancreatic exocrine adenocarcinoma was noticed in a two and a half year old German shepherd. Histologically, the tumour was well differentiated with hyperchromatic small round cells having eosinophilic cytoplasm forming distorted glandular arrangement or compact acinar pattern. The peripancreatic fat remained intact and there was no evidence of tumour necrosis. Metastasis was there into the different layers of duodenum where the tumour cells appeared individually separate or in clusters and replacing the villus epithelial cells. Xu (1985) has reported exocrine adenocarcinoma of small tubular pattern in a nine-year-old male Fox terrier and he gave similar histological changes. Jubb (1993) reported that pancreatic adenocarcinomas are rare and is seen usually in older animals. In man necrosis is an important feature of pancreatic acinar neoplasms and is associated

with disseminated fat necrosis caused by lipase released by the neoplastic cells (Alcantara *et al.*, 1984).

Thirty two cases of the animals examined had lesions in the islets of Langerhans. Lesions included congestion, haemorrhage, degeneration, and hyalinisation. Hyalinisation was observed in association with both chronic and suppurative pancreatitis. Scant numbers of atypically small islets with extensive cytoplasmic vacuolation and cellular fragmentation observed in the islets in degeneration were certainly high. Both these changes could have caused an endocrine insufficiency resulting in diabetes. However, it could not be ascertained whether these animals had clinical diabetes mellitus. These observation made clearly points to the need for undertaking routine laboratory tests to detect diabetes in dogs. Nelson (2000) reported an incidence of diabetes in dogs as one in 100 to one in 500. Cotton *et al.* (1971) reported diabetes mellitus in dogs with acute and chronic pancreatitis.

Islet cell hyperplasia was noticed in a few cases. It was a consistent finding in cases with chronic pancreatitis. Hyperplasia could also be noticed in parasitic pancreatitis and pancreatic necrosis. A possible pathogenesis might include compensatory hyperplasia due to decreased production of endocrine hormones by islet cells. Proliferation of pancreatic endocrine tissue is a poorly defined phenomenon in animals. A similar condition has been reported by Brunnert *et al.* (1990) in an aged spider monkey. In human beings hyperplastic islets has been associated with disorders like Zollinger-Ellison syndrome, hyperinsulinaemic hypoglycemia in infants and in multiple endocrine neoplasia (Jaffe *et al.*, 1980). In one of the cases nodular hyperplasia of the islet was observed and in this case there was no associated acinar or duct lesions. On special staining the alpha cells were found to be predominant as compared to beta cells.

The systemic investigation undertaken has made it possible to categorise and catalogue the various pancreatic disorders encountered and proved that

disorders of the pancreas are more common than expected. The higher incidence of various categories of lesions encountered in dogs in this study point to the need for regular monitoring of pancreatic function and inclusion of a few important tests in the routine battery of clinical diagnostic evaluations. Further, correlation of the pancreatic lesions with the general post mortem findings has brought to light the fact that many gastrointestinal disorders have concurrent pancreatic lesions and almost all chronic disorders of hepatorenal system, pancreatic changes to the same severity are seen. The pancreas is neither considered in the treatment regime of these cases nor given the commensurate share of attention given to hepatorenal system in clinical practice. The study has therefore been fruitful in highlighting the importance of an organ practically ignored in all clinical examinations and an understanding of documented typical abnormalities affecting pancreas in dogs would definitely help to improve veterinarian's ability to diagnose and treat the diseases in a timely manner.

Summary

6. SUMMARY

An investigation was undertaken to assess the prevalence and pathology of pancreatic disorders in canines. Special attention was given to classify various pancreatic disorders based on gross and histopathological lesions and to correlate them with the general post mortem findings.

The study on one hundred samples of pancreases revealed a prevalence of pancreatic disorders in canines to the tune of 72 per cent making it abundantly clear that the disorders of the pancreas in canines are more than what is generally expected.

It was found that the dogs between one to five years were the most commonly affected. Among the different breeds of dogs, German shepherds were the most susceptible to pancreatic disorders. Females were found to be more susceptible for pancreatic disorders.

The weight of pancreas remained approximately 0.2 per cent of the body weight in animals above one year of age. There was an increase in the length of the pancreas associated with advancing age.

Gross pathological changes were subtle and not very distinguishable except in cases like pancreatic abscess and adenocarcinomas. The histopathological lesions observed were classified as vascular changes, degenerative changes, atrophic changes, ductular changes, inflammatory changes, pigmentation, proliferative changes and neoplastic changes. The vascular changes included congestion (42), haemorrhage (19), oedema (8) and lymphangiectasis (1) and degenerative changes were, vacuolar degeneration (19) and stromal fatty infiltration (9). Atrophic changes were recorded in 17, pancreatic necrosis in 11, hypoplasia in three, pancreatitis in seven, haemosiderosis in six and abscess and adenocarcinoma in one case each. The proliferative changes consisted of fibrosis (18), nodular hyperplasia (4) and blood vessel proliferation (1). The ductular

changes included fibrosis (20), fibrosis with inflammation (2), ductular epithelial proliferation (13), squamous metaplasia (2) and ductular adenoma (1). Islet changes were seen in 32 per cent of cases.

Among the various types of histopathological lesion encountered in pancreas, vascular changes like congestion and haemorrhage were the predominant ones. This could have been due to an infection, toxin or hypoxia induced damage to vascular endothelium.

Pancreatitis was one of the common disorders noticed. This included acute, suppurative, chronic and parasitic pancreatitis. The etiological factors suggested were autodigestive destruction, ductular obstruction as in parasitic infection, reflux regurgitation of duodenal contents, regurgitation of bile, bacterial and viral infection, trauma and nutritional imbalances. In the present study the etiology could be traced as parasitic in one case. The other etiologies suspected were infection and trauma. But the exact etiology of all cases could not be ascertained.

Nodular hyperplasia of acinar epithelial cells was seen in four per cent of cases. This could be explained as a compensatory change in declining cellular activity in senility. Pancreatic atrophy was documented in seventeen percent of cases, of which three per cent revealed severe atrophy. The role of nutritional deficiencies, ischemia and infections in these have been described. Degenerative changes like vacuolar degeneration, fatty change and necrosis were recorded in pancreas in various severities and the importance of these in leading to digestive disorders have been pointed out. The vacuolar changes as well as necrosis were seen mostly in the periphery of the lobule suggesting a role for hypoperfusion and possibly reperfusion in the pathogenesis.

In a case, parasitic nodule was detected histopathologically in the parenchyma. A portion of the parasite was seen in the centre of the lesion

encircled by aggregates of mononuclear cells and eosinophils. It was inferred to be ancylostome larvae considering the severe ancylostomiasis detected at autopsy. Proliferation of blood vessels was noticed in a case, the probable etiopathogenesis could not be determined. A case of adenocarcinoma was encountered in pancreas during the course of this study.

Islet changes were seen in 32 cases. The degenerative lesions observed showed high incidence. Hyalinisation was seen along with pancreatitis. However, it could not be ascertained whether these animals had clinical diabetes mellitus. Islet cell hyperplasia was seen in association with other pathologies of pancreas. This can be considered as mechanism to compensate the reduced level of hormones. Based on these observations the need for undertaking routine laboratory tests to detect diabetes has been pointed out.

Efforts were made to compare the general postmortem changes with the disorders encountered in pancreas. The correlation study has brought into light the fact that many gastrointestinal disorders have concurrent pancreatic lesions and related pancreatic changes of the same severity are seen in almost all cases of chronic hepatorenal system disorders. The study has thus been fruitful in highlighting the importance of pancreas; an organ practically ignored by clinician in gastrointestinal and hepatorenal problems. The observations made in the investigation clearly emphasises the need for regular monitoring of pancreatic function and ensuring the organ commensurate share of attention as given to other organs in clinical practice.

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PATHOLOGY OF PANCREATIC DISORDERS IN CANINES

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ABSTRACT

The present investigation was undertaken to evaluate the prevalence and nature of pathological conditions of the canine pancreas and to correlate these with the general post mortem lesions. A detailed systematic examination of 100 carcasses brought for autopsy during the period of investigation was conducted and the gross and histopathological lesions were studied in detail, classified and documented. The study has revealed the high prevalence of pancreatic disorders in canines to the tune of 72 per cent. It was found that the dogs between one to five years were the most commonly affected. Among the different breeds German shepherds were found to be the most susceptible to pancreatic disorders. Females were found to show a predisposition for pancreatic disorders. The weight and length of the pancreas was found to increase with age. Out of the 72 per cent cases, the pancreatic lesions were severe in 21 per cent of the cases, moderate in 20 per cent and mild in 31 per cent. The specific conditions encountered were pancreatitis, parasitic infection, abscessation, blood vessel proliferation, ductular adenoma, adenocarcinoma of acinar pancreas, duct obstruction due to squamous metaplasia and islet cell hyperplasia and hyalinisation. The other pathological conditions included atrophy, hypoplasia, vacuolar degeneration, lipomatosis, ductular changes like fibrosis, hyperplasia, congestion, haemorrhage, oedema, lymph stasis and islet changes like degeneration and necrosis. Correlation of the pancreatic lesions with general postmortem findings has brought into light the fact that many gastrointestinal disorders had concurrent pancreatic lesions and almost all cases of chronic hepatorenal system disorders, related pancreatic changes of the same severity were seen.