PREVALENCE AND PATHOLOGY OF PANCREATIC DISORDERS IN CATTLE

By
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THESIS

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2000

DECLARATION

I hereby declare that the thesis entitled **"PREVALENCE AND PATHOLOGY OF PANCREATIC DISORDERS IN CATTLE"** 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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CERTIFICATE

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

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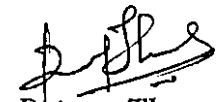

Princy Thomas

DEDICATED

TO MY

BELOVED PARENTS AND HUSBAND

CONTENTS

Chapter no.	Title	Page no.
1.	INTRODUCTION	1
2.	REVIEW OF LITERATURE	6
3.	MATERIALS AND METHODS	29
4.	RESULTS	33
5.	DISCUSSION	59
6.	SUMMARY	79
	REFERENCES	84

LIST OF GRAPHS

Figure No.	Title	Page No.
1	Degree and nature of pancreatic disorders in cattle	34
2	Distribution of various lesions in the pancreas	35

LIST OF FIGURES

Fig. No.	Title	Page No.
1	Pancreas: Petechial Haemorrhages on the surface of Pancreas	47
2	Pancreas: Haemorrhage in the parenchyma. Haemosiderin pigments can be seen as yellowish brown granules	47
3	Pancreas: Fat deposits on the surface of the pancreas	48
4	Pancreas: Fat Necrosis. Fat vacuoles replacing the acinar parenchyma. Fat vacuoles are seen as empty spherical to oval spaces	48
5	Pancreas: The fat vacuoles stained red and acinar parenchyma stained blue.	49
6	Pancreas: Fibrous tissue encircling the hyperplastic nodule	49
7	. Pancreas: Atrophy of the pancreatic acini	50
8	Pancreas: Chronic pancreatitis- Fibrosis and infiltration with lymphocytes and macrophages	50
9	Pancreas: Periductular pancreatitis- fibrosis and infiltration with lymphocytes and macrophages in the periductular zone	51
10	Pancreas: Fluctuating mass in the pancreas	51
11	Pancreas: Pseudocyst- cystic spaces amidst the parenchyma of the organ	52
12	Pancreas: Interlobular fibrosis seen as thick bands of collagenous tissue	52
13	Pancreas: Fibrosis of the duct wall	53
14	Pancreas: Ductular epithelial proliferation	53
15	Pancreas: Papillary projection of the ductular epithelium.	54
16	Pancreas: Hyperplasia of the islet cells- dense collections of islet cells in multicentric foci.	54
17	Pancreas: Pancreatic tumour- Lymphosarcoma- Circumsribed greyish white nodular mass embedded in the parenchyma.	55
18	Pancreas: Metastatic lymphosarcoma in the pancreas- Invasion of neoplastic cells into the pancreatic parenchyma	55

19	Pancreas: Adenomatous proliferation of the pancreatic duct	56
20	Pancreas Adenoma: Higher magnification	56
21	Pancreas: Parasite seen inside the vein. Fibrosis along with inflammatory cells can be appreciated in the wall of the vessel	57
22	Pancreas: Parasite seen inside the dilated pancreatic veins. No reaction is seen in the surrounding parenchyma	57
23	The pancreoliths stained blue with haematoxylin are seen inside the dilated pancreatic duct.	58
24	Pancreas: Calculi seen inside the pancreatic duct stained red.	58

INTRODUCTION

1. INTRODUCTION

Pancreas as an exocrine and endocrine gland plays a significant role in the maintenance of normal metabolic homeostasis in the animal and human system. The exocrine part of the pancreas is concerned with secretion of a variety of enzymes, which are important in the digestion of lipids, proteins and carbohydrates. The endocrine part consists of islet cells which liberate the hormones that are mainly responsible for regulation of blood sugar level. The duct system of the pancreas is responsible for secreting electrolytes which helps to maintain the pH of the intestinal contents within a range that is most favourable for enzymatic activity.

Even though the history of veterinary science in India dates back to ancient times, only a few records reportedly have been made till now on pancreatic diseases, especially in cattle. Even the scientific literature of the modern era reveals only very few references to the diseases of the pancreas in cattle. The reason may be that there are large reserves of both acinar tissue and islet cells in the organ, so that metabolic disturbances do not become manifested

until a large portion of the organ or the islets of Langerhans are destroyed. Moreover, the pancreas is tucked away with the duodenum in the upper abdomen where it is not readily accessible to the clinicians. For this reason, pancreatic diseases that do not cause pain or disability may progress silently for long periods.

It is pertinent to point out that the symptomatology in pancreatic disorders are vague, clinically poorly defined, lacking specificity and therefore, diseases of the pancreas certainly need laboratory tests for diagnosis. Besides this, clinical diagnostic tests to detect pancreatic diseases are not systematically conducted in most of the veterinary hospitals and disorders of the pancreas are bound to miss the attention of the clinician, even though they may exist.

Based on the work done in the other species, it could be surmised that the incidence of the diseases of the pancreas like acute and chronic pancreatitis, carcinomas of the pancreas, fibrosis, hypoplasia, nodular hyperplasia, exocrine pancreatic insufficiency and diabetes are relatively common. Infection, injury,

nutritional factors and genetic factors can be responsible for the diseases. Some diseases can be prevented, others can be controlled, but these could be accomplished only if there is adequate knowledge about the disease process. So far no systematic investigation on pancreatic pathology in cattle has been undertaken.

In the case of human beings, extensive studies have been made and a variety of disorders have been described. The incidence of diabetes mellitus is on the increase every year in human beings. Throughout the world, about 30 million people suffer from diabetes mellitus. Mc Millan and Geevarghese (1979) reported that excessive consumption of dietary cyanide could lead to diabetes mellitus in man. Tapioca, an unconventional feed ingredient which consists of thiocyanate is used extensively in the state. So, the chances of diabetes in cattle are high in the state of Kerala. Moreover, in Kerala ruminal acidosis is a very common disorder in ruminants, especially cattle. Ivanov (1974) stated that diabetes mellitus could occur as a consequence of chronic recurrent acidosis. The clinical signs in such cases are poor appetite, low milk yield and progressive emaciation along with

hyperglycemia and glycosuria. Clinical cases with similar signs are commonly encountered, but these symptoms are not viewed against the background of diabetes mellitus due to lack of awareness about this disease.

In the case of animals, particularly cattle, investigations on pancreatic disorders are very few. Although a few isolated reports on pancreatic diseases in cattle are available in the literature, information are sparse and pathological features encountered in this organ are poorly defined. Man and animals share the same environment and the feed ingredients are exposed to a variety of agrochemicals and other pollutants which can be injurious to pancreatic cells. Therefore, the possibility of subclinical or clinical disorders of the pancreas are certainly high. The pancreatic dysfunction can cause reduced feed consumption, growth rate and production leading to severe economic losses. Although it is the largest gland in the body next to the liver, it is given the least importance both clinically and in postmortem examinations. Systematic studies will provide us a better understanding about the disease conditions affecting the pancreas. If the pancreatic disorders

are identified, diagnostic tests can be developed, curative and preventive measures can be suggested and economic losses can be prevented.

Therefore, it is imperative that earnest efforts should be made to delineate the disease problems associated with pancreas, so that a plan of action can be chalked out to prevent and control the pancreatic diseases. The investigations on the pancreatic disorders in cattle, which had been a neglected field, has therefore, great relevance.

REVIEW OF LITERATURE

2. REVIEW OF LITERATURE

2.1. General

The pancreas was first mentioned as a separate organ by Heterophilus of Chalkidon in the first half of the third century BC and the term pancreas was introduced by Rufus of Ephesus.

Georg Wirsung (1642) recorded the structure of the major pancreatic duct in man.

Graaf (1641- 1673) experimentally demonstrated the external secretion of the pancreas in the dog with a temporary fistula.

Cawley (1788) associated diabetes with pancreas and Langerhans (1869) discovered the endocrine pancreas (Kloppel and Heitz, 1984).

2.2. Histology

Sengar and Singh (1971) stated that the lobes and lobules of the exocrine portion of the pancreas in ruminants are separated by connective tissue, while the acini are separated by reticular cells. According to them, the islets of Langerhans are relatively less

scattered than in other animals and are separated from the exocrine acini by a membrane. These cells are relatively small and lie in compact masses.

Kern and Ferner (1971) described the ultrastructure of the acinar cells. There was extensive rough endoplasmic reticulum surrounding the nucleus in the basal part of the cell and a large number of zymogen granules in the apical cytoplasm.

Malik and Prakash (1972) reported that the general histology of the pancreas was similar in the ox and buffalo and the histology agreed with that described for various animals.

The islets of Langerhans were spherical in outline and relatively small in the ox whereas in the buffaloes they were irregular in outline and larger (Malik and Prakash, 1972).

Pancreas is one of the largest extra intestinal digestive glands consisting of an exocrine and endocrine portion. The exocrine pancreas is surrounded by a capsule of dense irregular connective tissue from which originate trabeculae which subdivide the

compound tubuloacinar gland into lobes and lobules. The individual lobule is composed of acini which are formed by a single layer of pyramidal cells with a broad base resting on a basal lamina. The cell nucleus was generally located at the base of the cell and cytoplasm contained zymogen granules. A characteristic feature of the exocrine pancreas is the origin of the intercalated ducts in the lumen of the acini. The endocrine pancreas consisted of islets cells containing different cell types like A, B, C, D, F.

The sympathetic nerves to the pancreas were derived from the celiac plexus and the parasympathetic nerves regulated the secretory activity (Kloppel and Heitz, 1984).

2.3. Function

Banting and Best (1921) isolated insulin from the pancreatic islets of dogs.

Frier *et al.* (1976) observed that in Insulin dependent diabetes, there was a low pancreatic amylase output.

Henderson *et al.* (1981) stated that the exocrine and endocrine parts of the pancreas are not only anatomically related but functionally also.

Williams *et al.* (1981) demonstrated the existence of distinct insulin receptors on the pancreatic acinar cells.

Kloppel and Heitz (1984) stated that the major function of the exocrine pancreas involved the secretion of digestive enzymatic fluid and electrolytes and thereby played a decisive role in the breakdown of food.

2.4. Prevalence of diseases

Pellegrini and Braca (1971) reported eight cases of functional beta cell insulinomas in cattle in a five-year study conducted at the Pisa abattoir.

Velling (1975) examined the eviscerated pancreas of cattle at slaughter houses and found that 0.19 per cent of animals less than four and 0.82 per cent of animals above four years old were having pancreolithiasis and the condition was more frequent in females.

Baba *et al.* (1979) observed lesions in 225 pancreas in a series of 696 cattle aged 18 months to 12 years. Of these, 68 showed nodular proliferation grossly and microscopically.

Khater *et al.*(1980) made studies on the pancreatic function in 100 cattle and 105 buffaloes in an abattoir and found that all specimens were normal.

Bossaert *et al.* (1989) investigated *Eurytrema coelomaticum* infection in bovines in an abattoir in South Brazil and found that two and a half per cent of the 200 pancreas examined were infected.

Kelley *et al.* (1996) based on a retrospective study of pancreatic tumours in slaughter cattle reported 16 primary tumours, out of which there were 11 islet cell tumours, three pancreatic exocrine carcinomas, one neurofibroma and one neurofibrosarcoma. Other lesions observed by them included nodular hyperplasia (15), exocrine acinar atrophy and fibrosis (1), pancreatitis (1), peripancreatic fibrosis (2), pancreatic steatosis (1) and pancreatic haemorrhage (1).

2.5. Pathological conditions of the exocrine pancreas

2.5.1. Ectopic pancreas

Shimada *et al.* (1998) reported a case of biliary cirrhosis secondary to obstruction of the common bile duct by ectopic pancreas in a cow.

2.5.2. Nodular hyperplasia

Baba *et al* (1979) reported nodular proliferation in the pancreas of cattle. Macroscopically, there were defined whitish grey to yellowish nodules with bacon like consistency. Microscopically, they were made up of hyperplastic acini with many cells with giant nuclei and hypertrophic nucleoli.

2.5.3. Fat necrosis

Motoi *et al.* (1984) observed clinico-chemical changes of cows affected with fat necrosis and stated that fat necrosis was caused by a disorder of the endocrine function of the pancreas.

2.5.4. Amyloidosis

Yano *et al.* (1981) suggested that the pp-congo red staining procedure was more useful for differentiating insular amyloid from secondary

systemic amyloid which have different composition and pathogenesis.

2.5.5. Haemochromatosis

House (1994) reported a case of haemochromatosis in the pancreas of a three year old salers cow. Grossly, the pancreas was bright orange in colour. Histological examination of the pancreas revealed intracytoplasmic iron accumulation in the exocrine pancreas.

2.5.6. Pancreatic cyst

Stevenson (1972) observed pancreatic cysts in 16 out of 62 lambs. Approximately, two to three cysts of 3 mm were present in each.

2.5.7. Degenerative and inflammatory conditions

Dzhurov and Jourov (1975) observed inflammatory and degenerative changes in the pancreas of fattening calves with ruminal acidosis.

Jolly and Thompson (1978) reported severe vacuolation of exocrine epithelial cells in the pancreas associated with mannosidosis in a calf.

Zharov *et al.* (1987) found degenerative and reactive changes in the pancreas of cows with metabolic disorders with evidence of disorders of oxidation and reduction in acinar and insular cells.

Taniyama *et al.* (1995) observed necrotic islets and a reduction in number of pancreatic islets in cattle with persistent Bovine viral diarrhoea virus (BVDV) infection. Lesions in residual islets revealed hydropic degeneration and decreased number of secretory granules which were similar to those caused by IDDM (Insulin dependent diabetes mellitus) in man.

2.5.8. Infectious conditions

2.5.8.1. Viral infections

Deeb *et al.*(1987) observed degeneration and necrosis of pancreatic acinar tissue in calves experimentally infected with Foot and mouth disease virus. Elevated amylase and lipase activities and decreased glucose levels were found in the serum of these calves.

Ye *et al.* (1997) reported based on Electron microscopic study reported that the 139H scrapie agent produced pancreatic islet changes. They observed

cytoplasmic vacuolation, damage and disruption of the cytoplasmic organelles and rupture of cytoplasmic organelles in the beta cells in these animals infected with 139H scrapie agent. He suggested that scrapie *prion protein PrpSc* acted as a neurotoxicant which altered the hypothalamic neuroendocrine regulation of the pancreas.

Taniyama *et al.* (1999) immunohistochemically demonstrated Bovine viral diarrhoea viral antigen in the pancreatic islets of cattle with Insulin dependent diabetes mellitus. They suggested that autoimmune IDDM was due to persistent BVDV infection, resulting in gradual destruction of the islet beta cells.

2.5.8.2. Parasitic infections

Ashizawa *et al.* (1971) compared the lesions in the pancreas of goats infected with *Eurytrema pancreaticum* with those found in cattle.

Campos *et al.* (1974) reported that there was significant positive correlation between the number of parasites (*Eurytrema pancreaticum)* and the weight of the pancreas. The weight of infected pancreas ranged

from 91.8g to 659.7g. For normal glands the range was 81.5 to 83.7 g. The number of parasites found in the individual gland ranged from 2 to 3915.

Hussein and Haroun (1977) reported a case of fascioliasis in which lesions were found in the pancreas.

Lawrence (1978) stated that lesions in the pancreas were produced by eggs of *Schistosoma matheei.*

Shien *et al.* (1979) studied pathological changes of the pancreas of cattle and goats naturally infected with *Eurytrema pancreaticum.* There was hyperplasia and fibrosis of the pancreatic duct and atrophy of the glandular cells of the pancreas.

Harada *et al.* (1980) reported *Eurytrema* infection in dairy cattle. Clinicopathological evaluation revealed increase in the cholesterol and glucose values, decrease in amylase values and this was associated with cirrhosis of the pancreas.

Kono *et al.* (1980) made pathological studies on cattle heavily infected with *Eurytrema coelomaticum.*

Observations revealed pancreatic cirrhosis, thickening of surrounding connective tissue, atrophy of the pancreatic lobules, papillary hyperplasia of the pancreatic duct mucosa, peripheral fibrosis, atrophy and disappearance of pancreatic cells.

Sakamoto *et al.* (1980) suggested that film test of faeces and glucose tolerance test could be adopted for diagnosis and prognosis of pancreatic function in cattle infected with *Eurytrema coelomaticum.*

Kono *et al.* (1981) studied the pathological changes in the pancreas of cattle infected with *Eurytrema coelomaticum* after anthelmintic treatment with special reference to globule leukocytes.

Nikalaenka (1981) reported reduced lipase activity in the serum, pancreas, bile and duodenum of calves experimentally infected with liorchiasis (paramphistomiasis).

Pereira *et al* (1988) studied the microscopic changes of cattle pancreas parasitized by *Eurytrema coelomaticum.*

Bossaert *et al.* (1989) screened *Eurytrema coelomaticum* infection in bovines at slaughter. The lesions were mainly subacute periductular pancreatitis and the accompanying alterations in the adjacent parenchyma.

2.5.8.3. Mycotic infection

Histopathological examination of slaughtered breeding bull with *Candida guilliermondii* infection revealed mycotic infection in the pancreas along with other organs (Sutka and Meszaros, 1978).

2.5.9. Toxic conditions affecting pancreas

Allen *et al.* (1983) studied the natural occurrences of zinc toxicity in sheep and calves and reported that pancreas was the only organ consistently affected and that the degenerative lesions were restricted to exocrine portion of the organ.

Fell *et al.*(1985) observed defects in the acinar basement membrane, splitting and disorganisation of acini, cellular atrophy and dissociation and stromal proliferation in the pancreas of cattle deficient in copper.

Galitzer *et al.* (1986) reported marked degranulation of the pancreatic acinar cells in cattle with experimental monensin toxicosis.

Ladukar *et al.* (1990) studied the morphology of the pancreas and biochemical changes in untreated and alloxan treated buffalo calves. The alloxan treated calves showed hyperglycaemia with glycosuria and ketonuria. A dose level of 70 mg/kg body weight was found to be lethal to buffalo calves.

Panciera *et al.* (1992) studied the pathological changes in experimentally induced Hairy Vetch poisoning in cattle. Microscopic examination revealed typical cellular infiltration in the pancreas along with other organs.

Smith and Embling (1993) stated that the early pancreatic lesions in the sheep with zinc toxicity involved necrosis of the pancreatic duct epithelium, periductular inflammation and intralobular fat necrosis followed by oedema, lobular cystic changes, atrophy, fibrosis and ductular hyperplasia.

Saunders *et al.* (2000) reported lymphocytic to lymphogranulomatous inflammation of the pancreas in citrus pulp toxicity in dairy cattle.

2.5.10. Pancreolithiasis

Verine (1970)reviewed 196 cases of bovine pancreatic lithiasis based on case histories and post-mortem reports and observed that it was a benign condition mainly of old cows. Of the 59 affected carcasses, 49 were in good condition. Some animals had shown intermittent diarrhoea with a butyric acid smell. The condition could not be diagnosed clinically.

Braca *et al.* (1974) reported pancreatic lithiasis in cattle.

Velling (1975) reported a case of bovine pancreolithiasis. Major histopathological lesions were dilatation, ulceration or proliferation of the mucosa and fibrosis of the lamina propria and submucosa of the ducts. The shape, size and texture of the stones were variable but all were composed mainly of calcium carbonate.

Collins and Dromey (1976) reported pancreatic lithiasis in a short horn cow. The calculi were confined to the ducts of the pancreas which were hypertrophied.

Moore and Verine (1987) investigated on pancreatic calcification and stone formation. They reported that pancreatic stones are observed in both humans and cattle and that they contained approximately 95 per cent Calcium carbonate.

De Caro *et al.* (1988) reported that Calcium carbonate was the major component of stone in humans, ox, rat, dog, swine and monkey.

Groom (1994) has reported a case of pancreolithiasis in a cow.

2.6. Pathological conditions of the endocrine pancreas

2.6.1. Diabetes mellitus

Ivanov (1974) stated that recurrent subacute or chronic ruminal acidosis caused lesions in the pancreas leading to diabetes syndrome in cattle.

Hamana (1979) reported diabetes mellitus in a heifer.

Taniyama *et al.* (1993) carried out pathomorphological studies on bovine diabetes mellitus. Postmortem examination showed two animals with atrophy of the pancreas. Microscopically there was atrophy and reduced numbers of pancreatic islets accompanied by interlobular and interacinar fibrosis and compensatory enlargement of some of the remaining islets. Lymphocytes were observed commonly within and around atrophic islets and occasionally within and around enlarged islets.

Doherty *et al.* (1988) studied diabetes mellitus associated with lymphocytic pancreatitis in a cow.

Hasegawa *et al.* (1999) reported a case of diabetes mellitus in Japanese black cattle. The histopathological findings in the pancreas revealed insulinitis with infiltration of macromolecular cells.

Taniyama *et al.* (1999) made a study on the histopathological lesions of the endocrine and exocrine pancreas in cattle with Insulin dependent

diabetes mellitus (IDDM). The most characteristic lesions of the pancreas in IDDM was a decrease in the size and number of pancreatic islets, interlobular and interacinar fibrosis, mild lymphocytic insulinitis and vacuolation of a few islets. In acute IDDM, there was vacuolation of the cytoplasm of islet cells. The pathological observations suggested that beta cells were being destroyed by an inflammatory process, which selectively affected the pancreatic islets. Lymphocytic insulinitis and anti-bovine immunoreactive islets were thought to be the most significant changes in determining the etiology and pathogenesis of bovine IDDM and suggested their role in anti-islet autoimmunity in the form of diabetes.

Tajima *et al.* (1999) studied the possible causes of diabetes mellitus in cattle with Bovine viral diarrhoea virus. The results suggested that IDDM associated with BVDV infection was not a direct effect of BVDV on islet cells, but rather might be an autoimmune disease induced by autoantibodies against islet cells.

Taniyama *et al.* (1999) made immunohistochemical detection of the enzyme glutamic acid decarboxylase

and hormones of the islets of Langerhans in spontaneous Insulin dependent diabetes mellitus in cattle. The most characteristic changes were atrophy and decreased number of pancreatic islets, enlarged islets with vacuolated beta cells and lymphocytic islet adenitis. These findings suggested that islet cells in cattle with IDDM lose their insulin synthesis function and their ability to regulate hormonal secretion of alpha and delta cells.

2.7. Tumours

Mannocchio *et al.* (1974) conducted electron microscopic study of adenocarcinoma of beta cells of the pancreatic islets in cattle and found that nodules consisted of sheets or clumps of epithelial cells of varying sizes.

Liu (1984) reported pancreatic adeno and squamous cell carcinoma in six cattle.

Mughetti *et al.* (1985) reported in a cow, a beta islet cell adenocarcinoma metastasis to the liver.

Tontis *et al.* (1986) reported adenocarcinoma of the exocrine pancreas in two cows.

Kelley *et al.* (1996) based on a retrospective study, reported 16 primary tumours out of which there were 11 islet cell tumours, three pancreatic exocrine carcinomas, one neurofibroma and one neurofibrosarcoma. Other lesions observed by them included nodular hyperplasia (15), exocrine acinar atrophy and fibrosis (1), pancreatitis (1), peripancreatic fibrosis (2), pancreatic steatosis (1) and pancreatic haemorrhage (1).

2.8. Diagnosis

2.8.1. In humans

Olsen (1974) reported diminished plasma calcium, magnesium and oxygen tension along with respiratory as well as metabolic acidosis in acute pancreatitis in humans.

Gyr (1975) commented that serum amylase was frequently, but not always elevated during the course of acute pancreatitis. However, lipase was not excreted in urine.

Read *et al.* (1976) reported that there was no correlation between the magnitude of the increase of

the enzyme activity and severity or prognosis of the disease.

Frier *et al.* (1976) observed that Insulin dependent diabetes, often showed a low pancreatic amylase output.

Gyr (1977) observed elevated serum values for haemoglobin, haematocrit, white blood cell count, blood glucose, urea, serum creatinine, bilirubin, serum lipids, alkaline phosphatase, transaminases, lactate dehydrogenase and methaemalbumin in acute pancreatitis.

Brooks (1980) stated that increase in serum amylase levels were not specific for pancreatitis whereas, he observed an increase in serum trypsin in patients with pancreatic diseases.

Haffter and Gyr (1981) reported that measurement of urinary amylase was a more sensitive test. They also reported that serum lipase was elevated in acute pancreatitis and appeared to be slightly more specific but not a more sensitive diagnostic criteria.

2.8.2. In cattle

Moulton and Sollod (1976) studied clinical, serologic and pathologic changes in calves with experimentally induced *Trypanosoma brucei* infection. They found mononuclear cell infiltration, eosinophils and oedema in pancreas along with other organs.

Mostaghni and Ivoghli (1977) reported diabetes mellitus in bovines. Diagnosis was made on the basis of clinical laboratory and histopathological findings. All animals showed a febrile debilitation and polydypsia. Hyperglycaemia was present with a quantitative reduction in the amount of pancreatic islet tissue.

Papkova *et al.* (1986) found, by a specific immunological method that changes in blood sugars and autoantibodies reflected definite stages and inter organ localization of pathological processes in the pancreas of cattle.

Kholod *et al.* (1988) reported increased concentrations of serum and urine amylase in cattle with chronic or acute pancreatitis.

Kholod *et al.* (1988) observed that the activities of alpha amylase, gama glutaryl transferase, alanine amino transferase and aldolase were high in cattle with pancreatic syndrome in comparison with healthy cows.

Kreikemeier *et al.* (1990) reported that pancreatic weight and alpha amylase activity were influenced greatly by diet composition and feed intake by calves.

Belem *et al.* (1992) reported that the film test was not reliable in the detection of Eurytrema infection in cattle.

2.8.3. In other species

Boari *et al.* (1994) reported that serum trypsin like immunoreactivity might be a useful diagnostic aid in identifying exocrine pancreatic insufficiency in puppies.

Archer *et al.* (1997) made evaluation of three pancreas specific protein assays trypsin-like immunoreactivity (TLI), pancreas specific protein (PASP) and glycoprotein for use in the diagnosis of

canine pancreatitis and concluded that the sensitivity of these assays were not sufficient to distinguish between healthy dogs and those with pancreatitis.

Braun *et al.* (1997) reported TLI (trypsin like immunoreactivity) as a most useful test in the measurement of plasma or serum trypsinogen and its concentration was lowered below 5µg per litre in exocrine pancreatic insufficiency.

Mulas *et al.* (1997) reported immunohistochemical detection of high levels of hog cholera virus antigen in paraffin embedded tissues of pancreas.

MATERIALS AND METHODS

3. MATERIALS AND METHODS

The present study was conducted at the Centre of Excellence in Veterinary Pathology, College of Veterinary and Animal Sciences, Mannuthy, to investigate the prevalence and pathological disorders of pancreas in cattle.

3.1. Sample collection

One hundred samples of pancreas collected at random from the cattle slaughtered at the Meat technology unit, College of Veterinary and Animal Sciences, Mannuthy, as well as Municipal slaughter house and also from the carcasses brought for autopsy to the Centre of Excellence in Pathology, Mannuthy were used for the study. In order to make an assessment of the clinical pancreatic disorders in cattle blood (15- 20 ml) was collected from the jugular vein for serological studies and urine (five milliliter) was collected from the urinary bladder of the animal at the time of slaughter.

3.2. Serum studies

Blood collected from the animals was left in the test tube for half an hour at room temperature. A part of the serum was separated and used for the estimation of glucose. Then the test tube with the remaining serum was kept at 4°C for six hours for retraction of clot. Then the serum was separated and stored at -20°C in sterile vials until used for serum amylase estimation.

a) Serum glucose

Serum glucose was estimated using the glucose kit* which followed the GOD POD method.

b) Serum amylase

Estimation of serum amylase was done two weeks after collection by kinetic method using EPS-G_7 as the reagent. It was done according to the procedure given in the manual of Merck's Company India Ltd. (1989).

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* E-MERCK- India. Ltd., Raigad, Maharashtra

c) Urine analysis

Urine samples collected was tested for the presence of sugar using Benedict's reagent on the day of collection (Sastri, 1983).

3.3. Gross examination

The pancreas was dissected out completely. The organ was examined in detail for any gross changes like congestion, haemorrhage, fat necrosis and abnormalities of shape and size. The organ was palpated and multiple incisions were made to detect the presence of any pancreatic cyst, tumour or calculi.

3.4. Histopathology

Representative samples of tissues from different areas of the pancreas were collected and preserved in 10 per cent neutral buffered formalin and Bouin's fixative. The tissues collected were processed, after proper fixation by routine paraffin embedding techniques (Sheehan and Hrapchak, 1980). Sections were cut at 3-5 microns and stained with Haematoxylin and Eosin

(Bancroft and Cook, 1984) for evaluation of the histological changes. Duplicate sections were stained using Gomoris' chromium haematoxylin phloxine for studying the changes in the islet cells, wherever necessary. Frozen sections of the pancreas were stained for fat with oil-Red-o (Luna, 1968). Sections suspected for pancreatic calculi were stained for calcium with Alizarin red and those for haemosiderin pigments were stained with Pearls' stain (Luna, 1968).

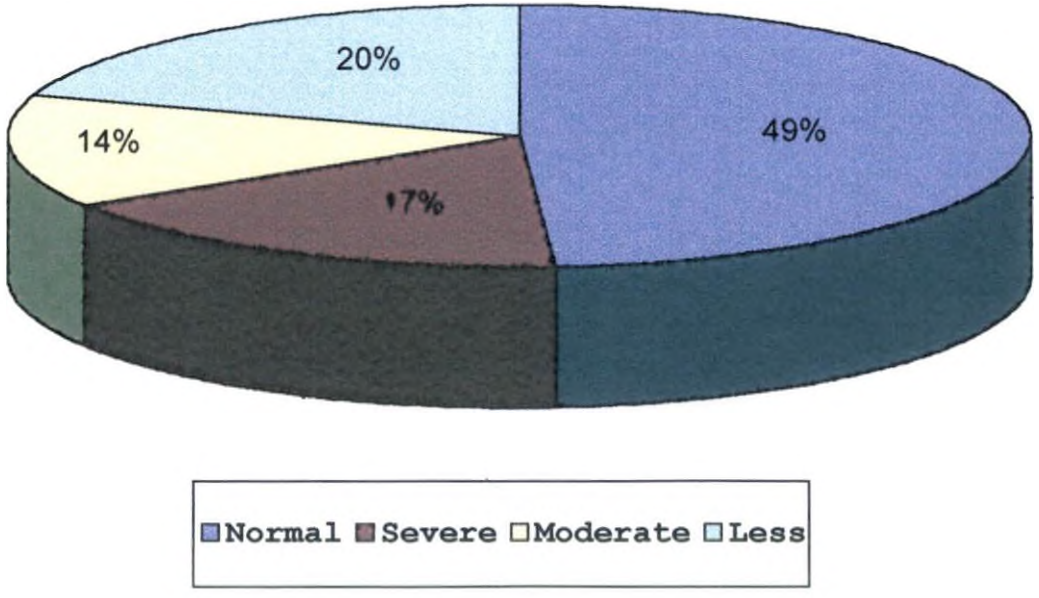
RESULTS

4. RESULTS

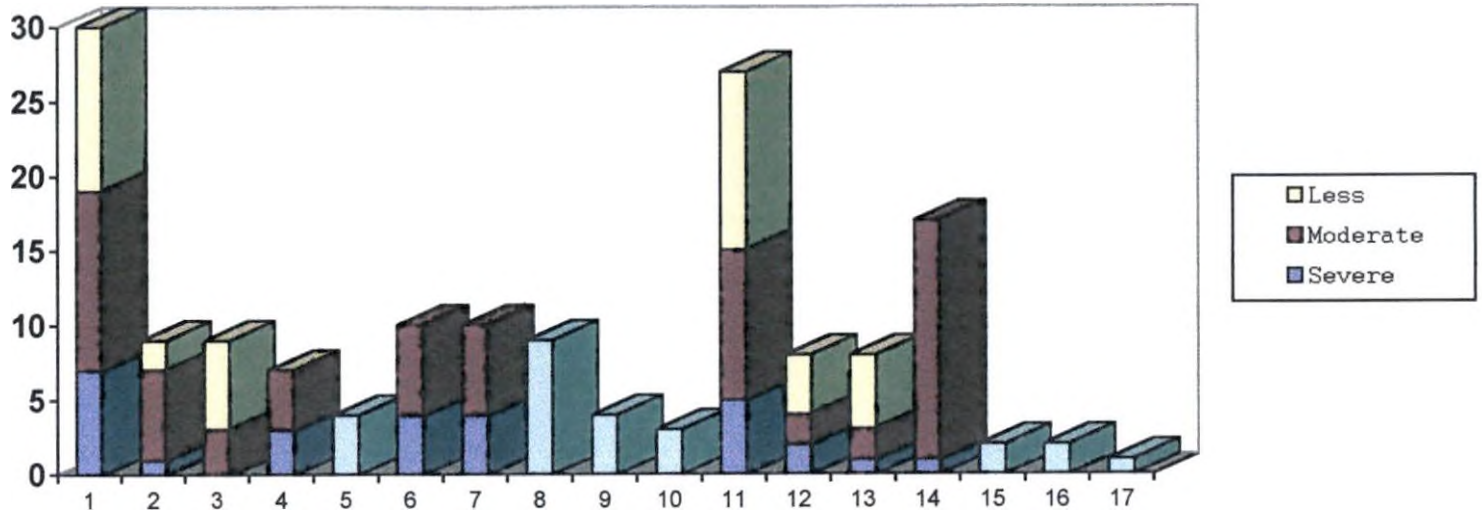
4.1. Prevalence

Out of the 100 pancreas screened during the period from May 1999 to June 2000 from the Meat Technology Unit, College of Veterinary and Animal Sciences, Mannuthy as well as the Municipal slaughter house, Thrissur and also from the carcasses brought for autopsy in the Centre of Excellence in Pathology, 51 per cent of the pancreas revealed pathological changes. Among these, 17 per cent had prominent lesions consisting of pancreatic tumour (2), parasite in the pancreas (2), chronic pancreatitis (4), atrophy of the pancreas (4), fat necrosis (3), islet cell hyperplasia (1) and pancreolith (1). Of the remaining, 14 per cent revealed moderate lesions and 20 per cent revealed mild changes in the pancreas (Graph 1). This included congestion, haemorrhage, oedema, degeneration, pseudocyst in the acinar parenchyma, ductular changes like fibrosis, hyperplasia and dilatation of the ducts and islet changes like degeneration and necrosis (Graph 2).

Graph 1. Degree and nature of pancreatic disorders in cattle.



Graph 2. Distribution of various lesions in the pancreas



1. Congestion
2. Haemorrhage
3. Oedema
4. Fatty change
5. Nodular hyperplasia
6. Atrophy
7. Chronic pancreatitis
8. Pseudocysts
9. Fibrosis
10. Haemosiderosis
11. Fibrosis of duct wall
12. Ductular epithelial proliferation
13. Dilatation of pancreatic duct
14. Islet changes
15. Tumors
16. Parasites
17. Calculi

4.2. Pathological disorders

4.2.1. Vascular changes

4.2.1.1. Congestion

Out of the 100 pancreas screened, 30 had congestion of varying degree. Of this seven per cent had severe congestion whereas 12 per cent had moderate congestion and 11 per cent revealed mild congestion.

The organ was slightly enlarged and dark brown. Grossly the veins in particular were dilated and seen very much engorged with blood. Microscopically, the veins and capillaries throughout the parenchyma were distended with blood. The surrounding parenchyma was slightly compressed.

4.2.1.2. Haemorrhage

Isolated foci of haemorrhages were recorded in nine per cent of cases. Multifocal severe haemorrhage was observed in pancreas. Six per cent revealed moderate haemorrhage and two per cent showed mild haemorrhage. Petechial haemorrhages were seen in two instances (Fig. 1). Microscopically, erythrocytes were seen scattered in between the acinar cells or

focal or diffuse collection of erythrocytes were seen displacing the parenchyma (Fig. 2).

4.2.1.3. Oedema

Oedema was recorded in nine per cent of the cases. It varied from moderate (three per cent) to mild oedema (six per cent). The condition was not appreciable grossly. Microscopically the interstitial and inter lobular spaces contained homogenous fluid stained faintly pink with eosin. The acinar cells were displaced and compressed. The capillaries were engorged.

4.2.2. Fatty change (stromal fat infiltration)

Fatty change was recorded in seven per cent of the cases. Out of these, three per cent showed extensive fatty changes in the parenchyma and four per cent showed moderate fatty change. In those cases which showed severe fatty change, the condition was visible grossly. The smooth glistening adipose tissue covered the organ and at certain places infiltrated into the parenchyma. The pancreas appeared enlarged as if it had been replaced by adipose tissue. When the organ was incised, droplets of fat could be seen on the blade of the knife (Fig. 3). Microscopically, it

was seen that most of the acinar parenchyma was replaced with fat vacuoles. The fat cells were spherical to oval and at places coalesced to form fatty cysts. The acinar cells were compressed and they were seen as compressed bands of cells encircled by fatty tissue (Fig. 4). The globules of fat stained red with oil red-o (Fig. 5).

4.2.3. Nodular hyperplasia

Four per cent of the pancreas examined, revealed nodular hyperplasia. On gross examination greyish white, focal, circumscribed, raised, smooth nodules of two millimeter diameter which were hard in consistency were seen in the parenchyma of the pancreas. Microscopically, circumscribed focal aggregates of hyperplastic acinar cells which were separated from the adjacent acinar cells were seen. These foci were encircled by a thin band of fibrocollagenous tissue (Fig. 6).

4.2.4. Atrophy

Out of the 100 pancreas screened four per cent of the pancreas had extensive areas of atrophy, and six per cent showed moderate atrophy. The condition was identified only on histopathological examination.

Grossly, there was no visible alteration in the structure of the organ. Histologically, the acinar cells were smaller in size, the cytoplasm was scant, and the whole cell was occupied by a pyknotic nucleus (Fig. 7).

4.2.5. Inflammation

4.2.5.1. Chronic pancreatitis

Out of the 100 pancreas screened, ten per cent showed chronic pancreatitis. Out of these, five per cent revealed severe changes and another five per cent had mild to moderate pancreatitis. Grossly, the pancreas revealed no recognisable changes. Histologically, there was dense fibro-collagenous tissue around the duct. The cuffing of the fibro-collagenous tissue around the duct caused narrowing of the lumen. Amidst these, there was severe diffuse infiltration of mononuclear cells. In a few cases the surrounding tissue revealed oedema. In all these cases there was engorgement of capillaries in the surrounding zone. There was also focal areas of fibrosis and inflammatory cells in between the acinar parenchyma (Fig. 8). The inflammatory cells were mostly lymphocytes and mononuclear cells (Fig. 9).

4.2.6. Pseudo cysts

Cystic spaces were observed in nine per cent of the cases. The condition was identified grossly in two cases. On palpation it was felt as raised, fluid filled, fluctuating mass on the surface of the organ. Three to four cysts could be palpated in one pancreas of which one was big with a diameter of one centimeter size (Fig. 10). Others were two to three millimeter in diameter. On histological examination, multiple pseudo cysts of varying sizes without an epithelial lining were seen. The surrounding parenchyma was compressed. The cyst wall consisted of fibro-collagenous tissue and the lumen contained pale pink stained material(Fig. 11).

4.2.7. Fibrosis

Fibro-collagenous bands were seen amidst the acinar tissue in four per cent of the cases. Interlobular fibrosis characterised by thick bands of collagenous tissue was seen in five per cent of the cases (Fig. 12). None of these conditions could be identified on gross examination.

4.2.8. Haemosiderosis

Out of the 100 pancreas studied, a three per cent showed haemosiderosis. Haemosiderin pigments were seen deposited as coarse granular golden yellow pigments in the interlobular spaces and in between the exocrine cells(Fig. 2). Pigments stained blue with Pearl's stain, confirming that these were haemosiderin pigments.

4.2.9. Ductular changes of the pancreas

4.2.9.1. Fibrosis of the duct wall

Twenty per cent of the cases revealed fibrosis of the duct wall, of these only five per cent showed severe fibrosis of the duct wall. Ten per cent showed moderate fibrosis and 12 per cent revealed mild fibrosis of the duct. Histologically, there was dense fibro-collagenous tissue surrounding the duct. The lumen of the duct was very much narrowed and the lining epithelial cells were prominent (Fig. 13).

4.2.9.2. Ductular epithelial proliferation

Eight per cent of the cases revealed ductular epithelial proliferation. Of these two per cent had severe, two per cent revealed moderate and another four per cent had mild epithelial proliferation (Fig.

14). The lining epithelial cells were hyperplastic, hypertrophic and hyperchromatic. The cells were thrown into small papillary projections into the lumen (Fig. 15).

4.2.9.3. Dilatation of the pancreatic duct.

There was ductular proliferation in eight per cent of the cases and out of these one pancreas revealed dilatation of the duct along with ductular hyperplasia. Two per cent of the cases had moderate changes and rest five per cent revealed mild to moderate dilatation of the duct. Lumen of the ducts were dilated and were seen lined with flattened epithelial cells.

4.2.10. Islet cell changes in the pancreas

Out of the 100 pancreas screened by histological examination, clumping of the islet cells were seen in seven per cent and necrosis in four per cent of the pancreas examined. But these changes were only mild. Islet cells of the pancreas in two cases revealed increased number of beta cells in many of the islets, whereas alpha cells were normally distributed in them. This was demonstrated by special staining with Gomori's chromium haematoxylin phloxine stain. The

beta cells were normal in size but numerically out numbered the alpha cells. There was a crowding effect of beta cells in the islets. In another two cases, there was an increase in the alpha cells and the beta cells were less in number. In one instance, there was islet cell hyperplasia. The condition could not be recognised grossly. Microscopically the islet cells were more in number. They were arranged as anastomosing cords or as solid clumps. They were not separated from the normal pancreatic acini and in certain areas small groups of acini were seen in between the islet clumps. Examination of the exocrine pancreas did not reveal any changes (Fig. 16).

4.2.11. Tumour

4.2.11.1. Metastatic lymphosarcoma in the pancreas

A metastatic focus of lymphosarcoma was seen in the pancreas of a cow as an incidental finding at slaughter. It was a generalised case of lymphosarcoma involving all lymphoid organs. There were metastatic lesions in most of the organs including the pancreas. On gross examination, there was nodular enlargement of the pancreas and on palpation there was a circumscribed nodule which was hard in consistency and firmly embedded in the parenchyma. On incision the

parenchyma revealed a circumscribed greyish white nodular mass about four to five centimeter in diameter (Fig. 17). Histological examination of the enlarged mass revealed the presence of large number of densely packed lymphocytes and lymphoblasts invading and infiltrating the pancreatic tissue. The lymphocytes were spherical to oval with very prominent enlarged basophilic nucleus and very scant cytoplasm. It was diagnosed as a case of metastatic lymphosarcoma in the pancreas (Fig. 18).

4.2.11.2. Cystadenoma

A case of cystadenoma was found during the histopathological screening of one of the samples of the pancreas. Grossly, there was no appreciable change in the pancreas. On histopathological examination, cystic spaces of varying sizes lined with cuboidal cells were seen. In certain areas, papillary projections into the lumen were seen. The nuclei were round and vesicular with prominent nucleoli (Fig.s 19 and 20).

4.2.11.3. Parasites in the pancreas

Two pancreas out of 100 screened, had the presence of parasites within the pancreatic vessels.

Grossly, the pancreas appeared normal. The presence of the parasite was an incidental finding during histopathological examination. In one case, there was severe inflammatory reaction along with dense fibrosis surrounding the vessel (Fig. 21), whereas in the other case there was no reaction around the vessel (Fig. 22). The parenchyma surrounding the vessel appeared normal in both the cases. Based on the location and morphological features on histological examination, the parasites were identified as Schistosoma species. Speciation could not be done as live parasites were not available.

4.2.11.4. Pancreatic calculi

While incising one of the specimens collected from the slaughter house, a grittiness was felt. On palpating the area small pancreatic stones of different shapes varying from grain like particles to needle like stones were seen within the duct and also with in the parenchyma of the organ. Microscopically, the stones were seen in the duct as blue irregular masses stained with haematoxylin. There was severe fibrosis around the ducts and the surrounding tissue (Fig. 23). The presence of the calculi was confirmed by staining with Alizarin- red for calcium (Fig. 24).

4.3. Biochemical tests

Estimation of serum amylase, glucose and urine glucose was done for those cases collected from the slaughter house. The serum glucose and urine glucose were estimated to screen the presence of diabetes. Serum amylase was estimated to identify the clinico-pathological changes in pancreatic disorders.

4.3.1. Urine and serum glucose

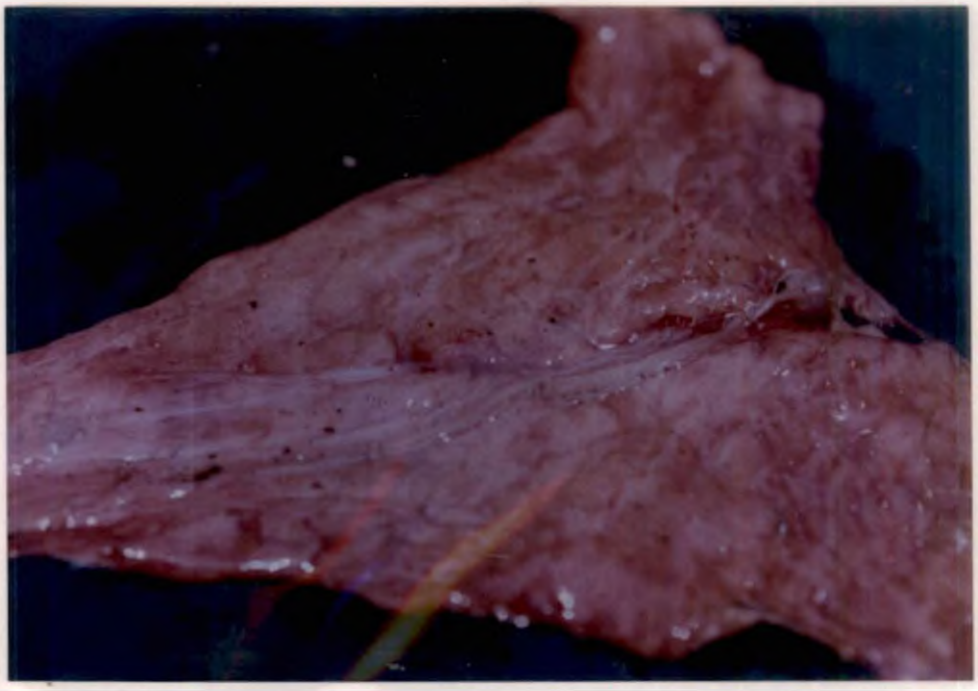
Urine glucose was found positive in eight cases out of the 84 samples tested. But only in three of these cases, the serum glucose level was above the renal threshold. Among these three cases none showed islet changes. The histological findings in these cases were pseudocyst formation, inflammation, atrophy and fatty infiltration.

4.3.2. Serum amylase

Serum amylase value was seen high in 18 cases. Out of these eight cases showed no lesions grossly or histopathologically. In the rest of the ten cases, the histological lesions included fat necrosis (2), inflammation (2), congestion, haemorrhage and oedema (2), fibrosis (2) and fatty change and pseudocyst (1).

Fig. 1. Pancreas: Petechial Haemorrhages on the surface of Pancreas.

Fig. 2. Pancreas: Haemorrhage in the parenchyma. Haemosiderin pigments can be seen as yellowish brown granules (H&Ex 160).



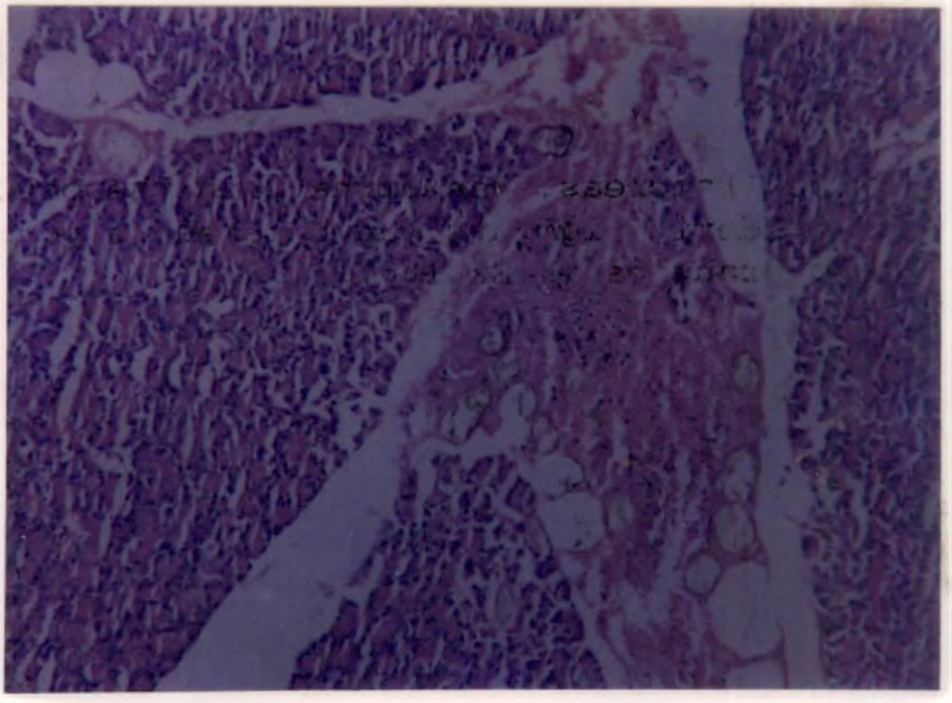
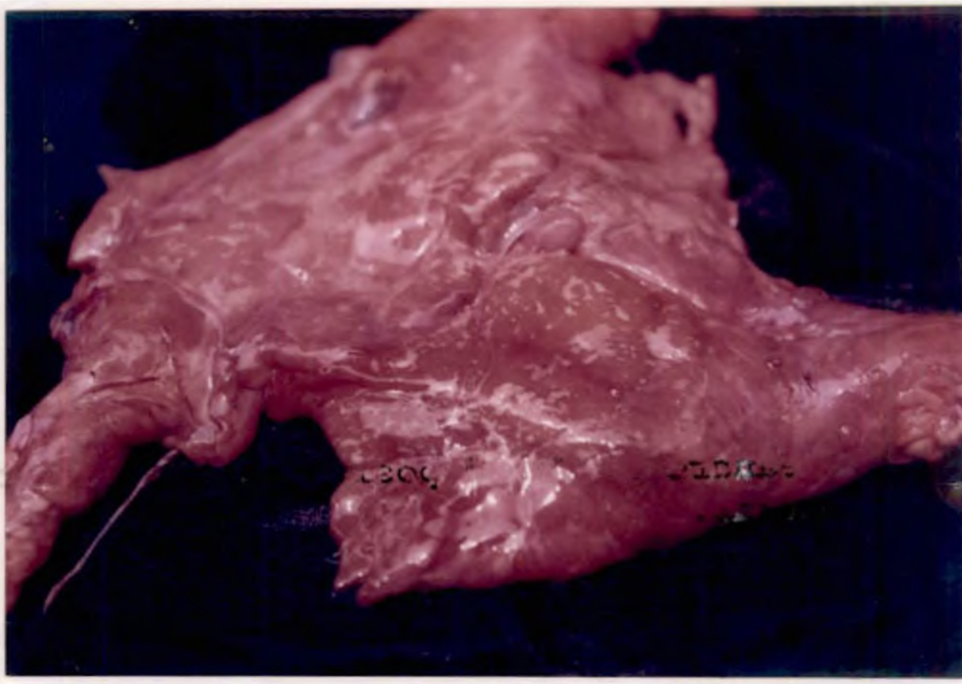


Fig. 3. Pancreas: Fat deposits on the surface of the pancreas.

Fig. 4. Pancreas: Increase in fat cells in the stromal connective tissue. Fat vacuoles replacing the acinar parenchyma. Fat vacuoles are seen as empty spherical to oval spaces (H&E x 60)



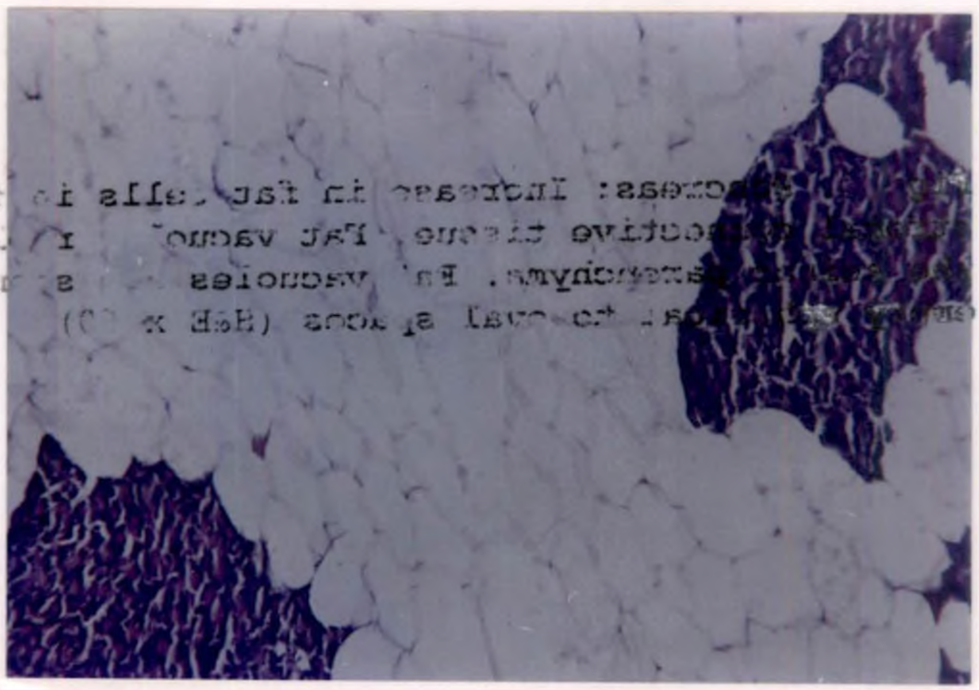
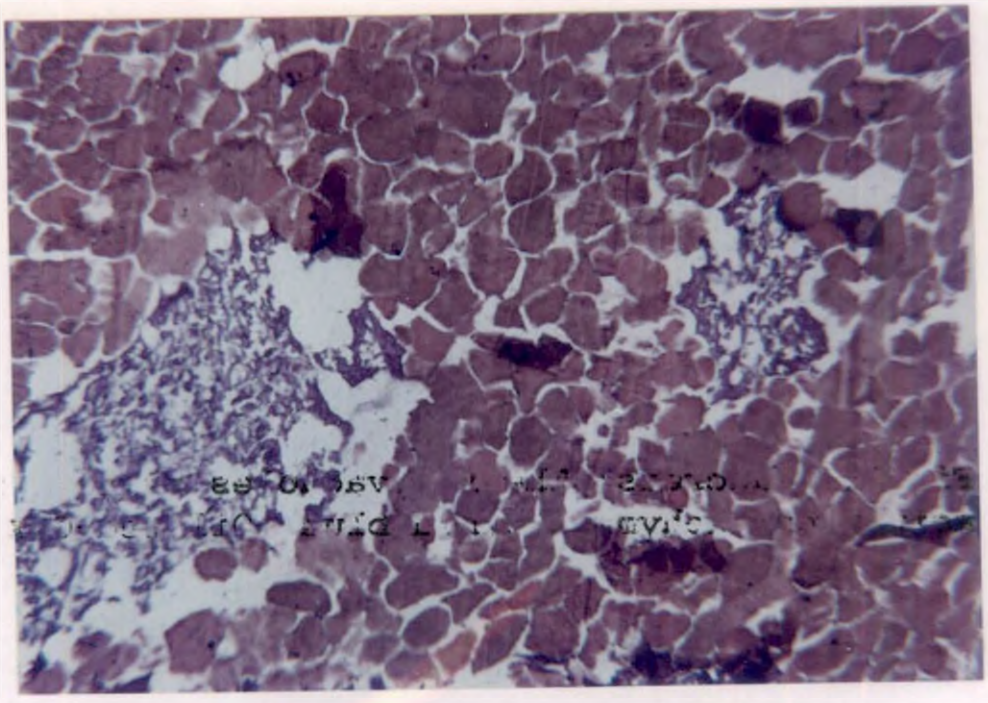


Fig. 5. Pancreas: The fat vacuoles stained red and acinar parenchyma stained blue. Oil red-O x 60

Fig. 6. Pancreas: Fibrous tissue encircling the hyperplastic nodule (H&Ex 160)



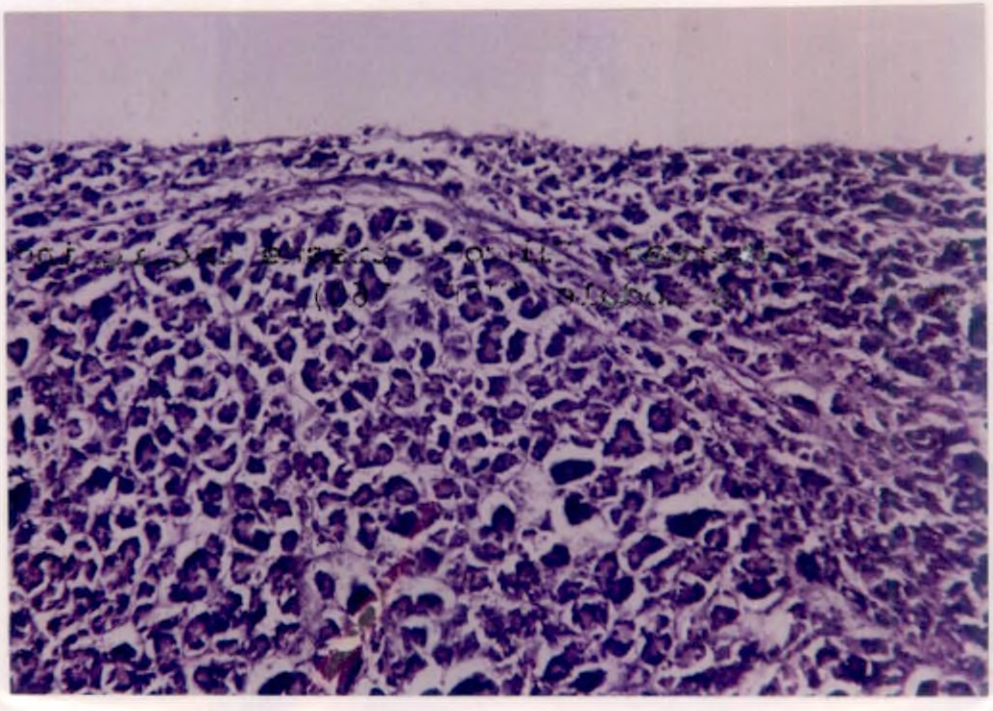
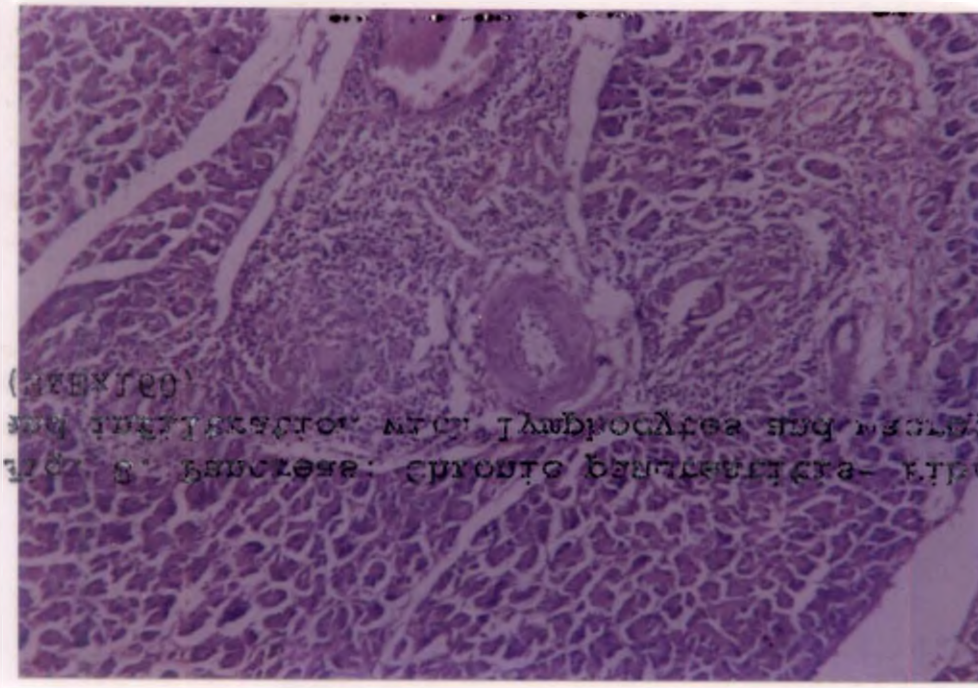


Fig. 7. Pancreas: Atrophy of the pancreatic acini (H&Ex160)

Fig. 8. Pancreas: Chronic pancreatitis- Fibrosis and infiltration with lymphocytes and macrophages. (H&Ex160)



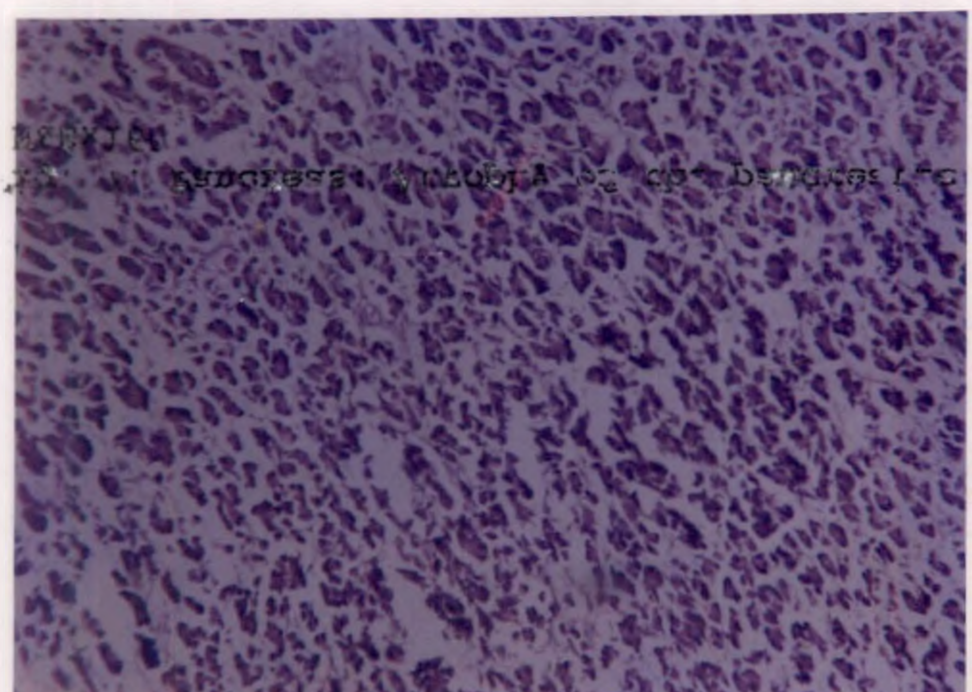
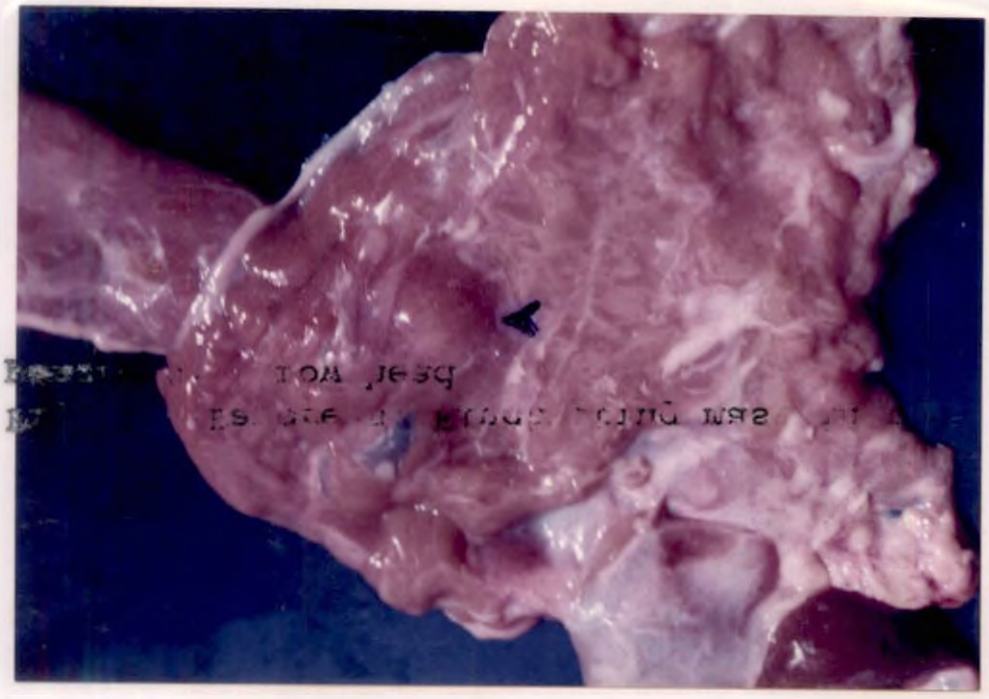


Fig. 9. Pancreas: Periductular pancreatitis-fibrosis and infiltration with lymphocytes and macrophages in the periductular zone. (H&Ex 160)

Fig. 10. Pancreas: Fluctuating mass in the pancreas- arrow head



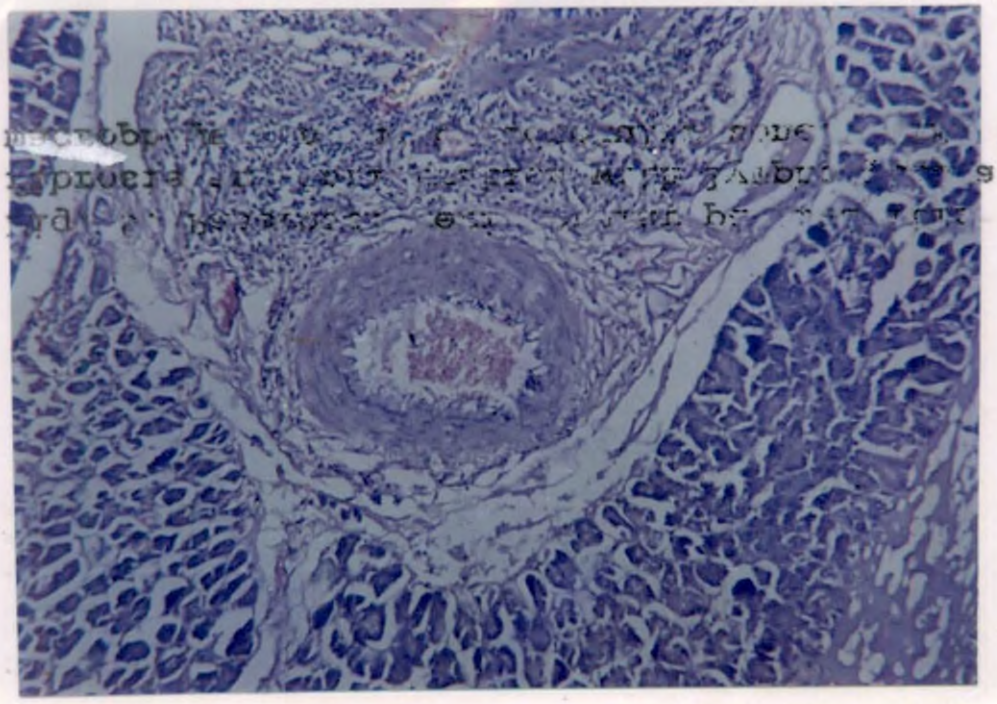
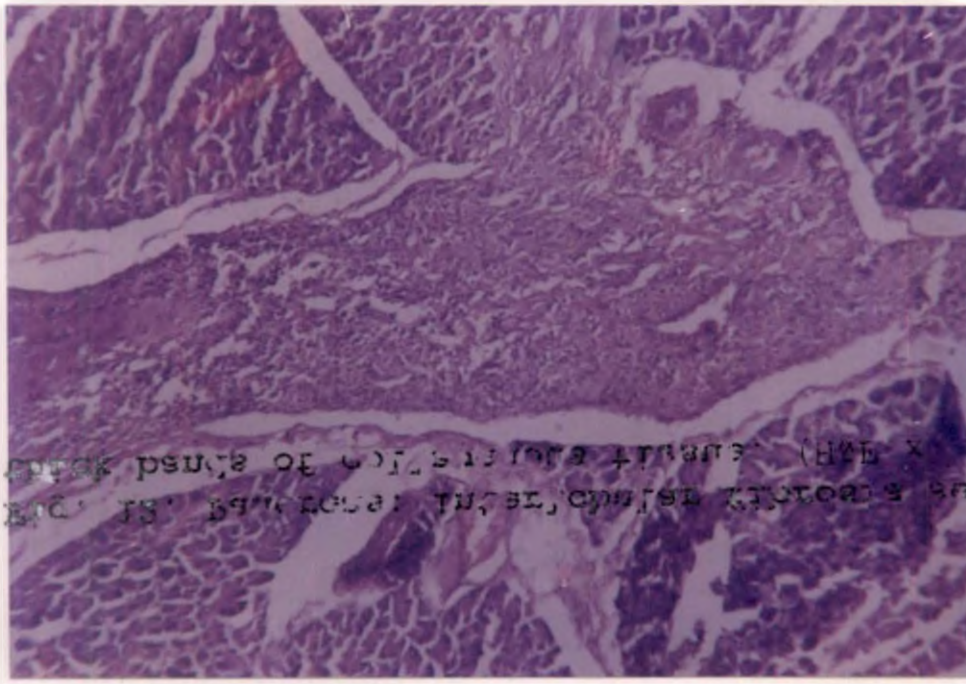


Fig. 11. Pancreas: Pseudocyst- cystic spaces amidst the parenchyma of the organ (H&E x 160)

Fig. 12. Pancreas: Interlobular fibrosis seen as thick bands of collagenous tissue. (H&E x 160)



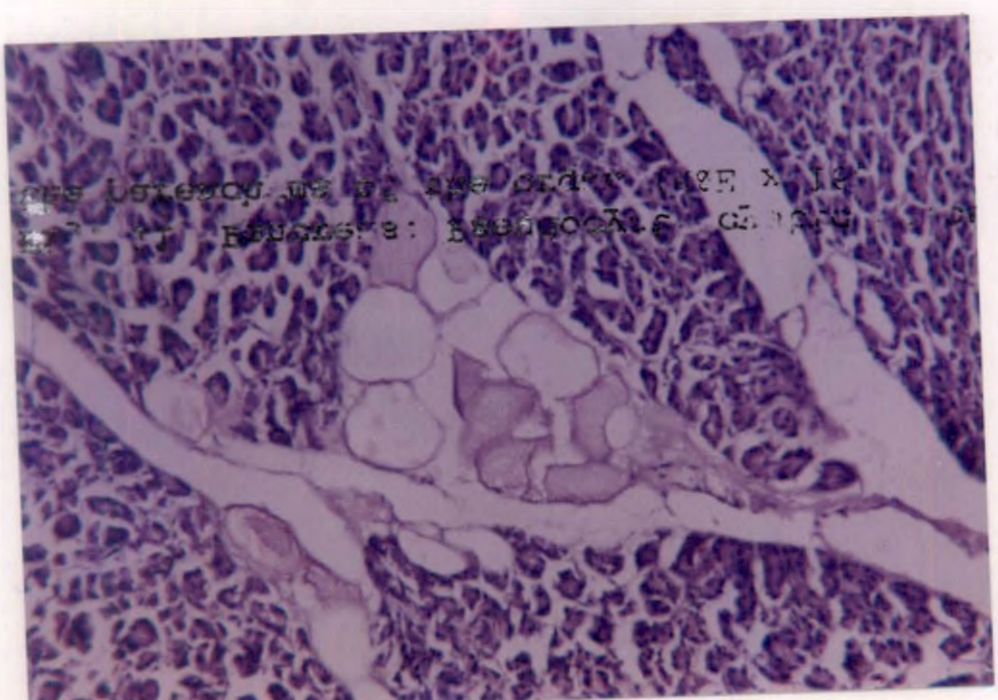
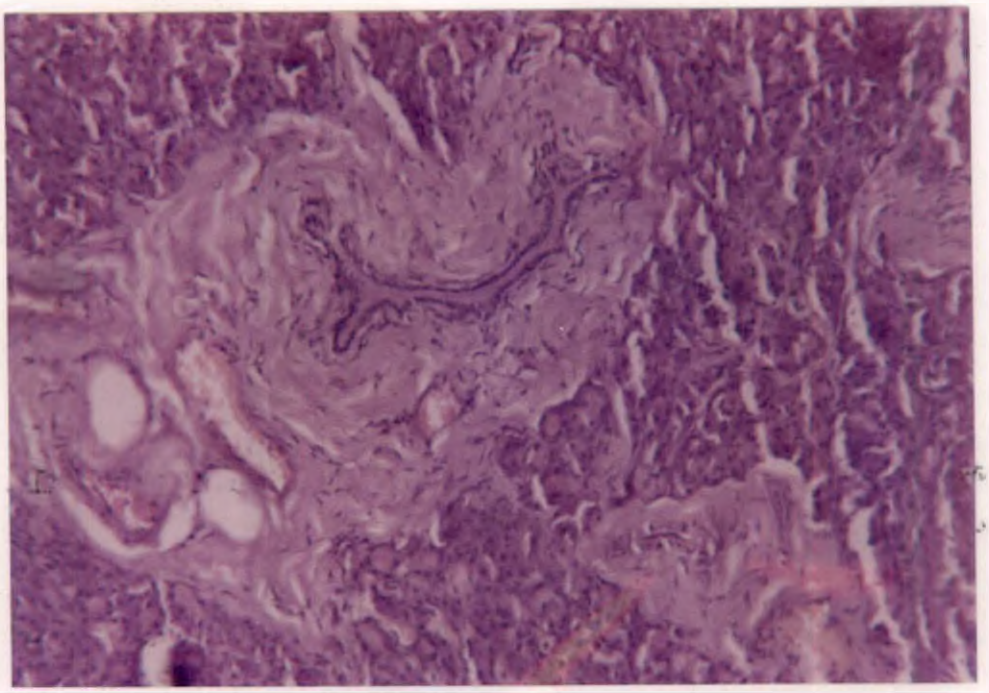


Fig. 13. Pancreas: Fibrosis of the duct wall. (H&Ex 160)

Fig. 14. Pancreas: Ductular epithelial proliferation. (H&Ex 160)



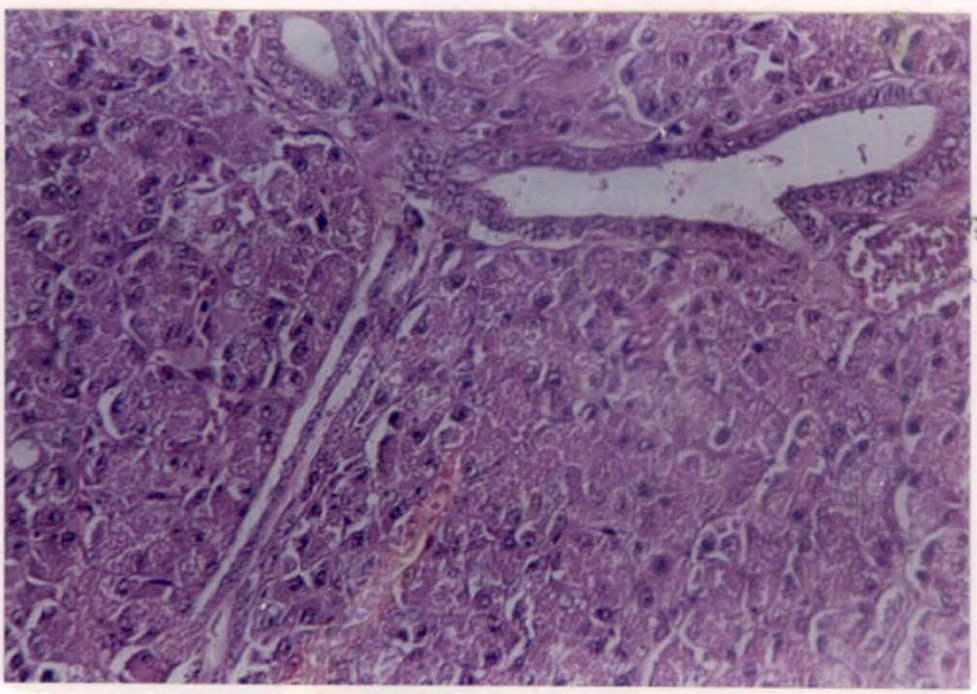
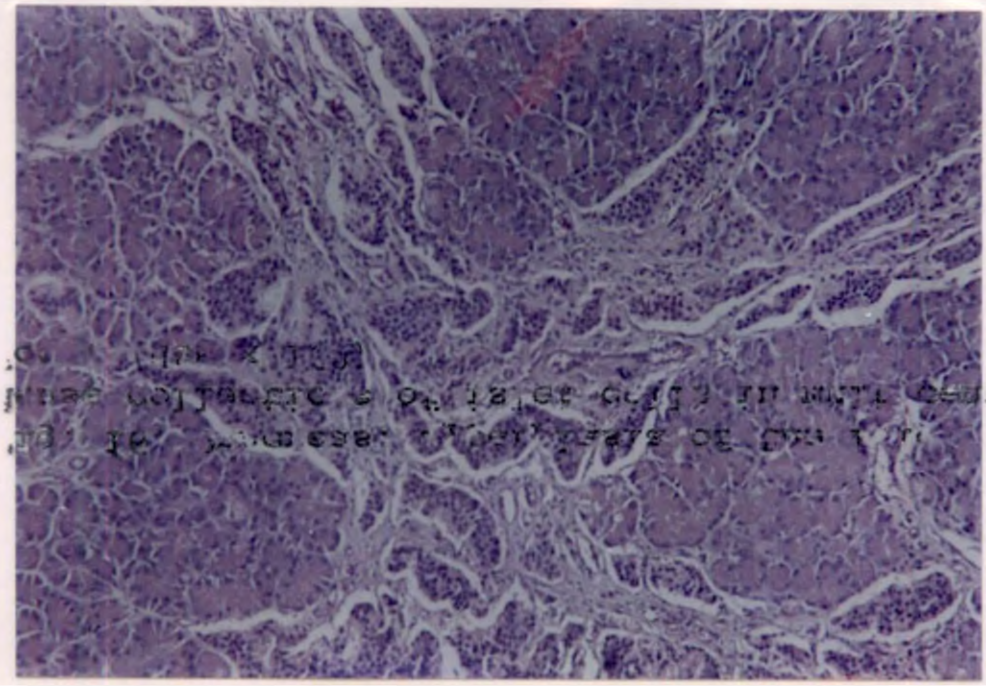


Fig. 15. Pancreas: Papillary projection of the ductular epithelium. (H&E x 160)

Fig. 16. Pancreas: Hyperplasia of the islet cells-dense collections of islet cells in multicentric foci. (H&E x 160)



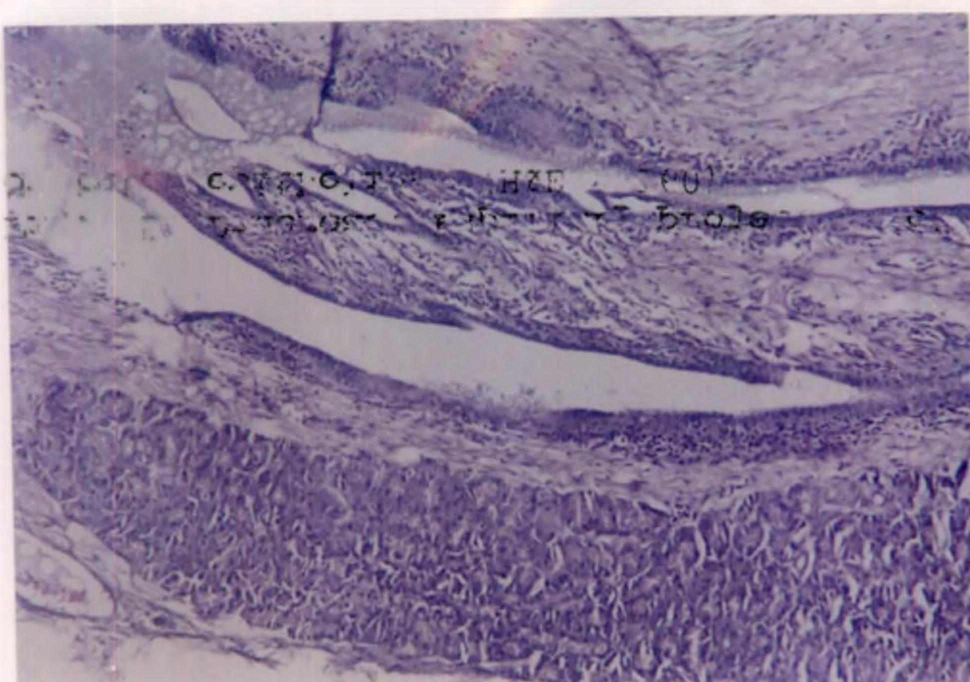
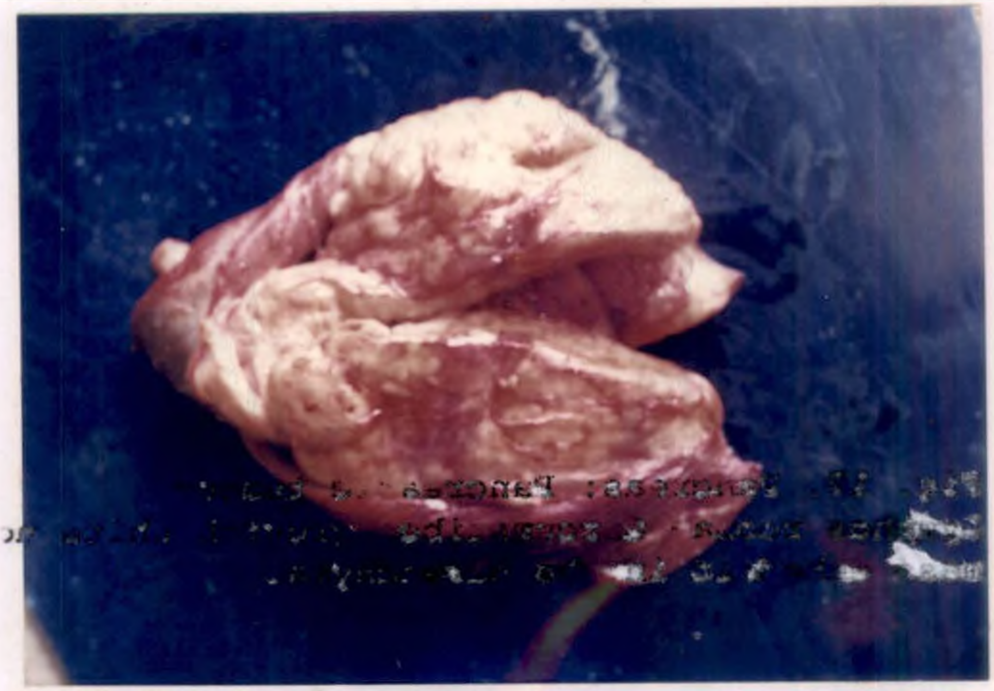


Fig. 17. Pancreas: Pancreatic tumour- lymphosarcoma- Circumsribed greyish white nodular mass embedded in the parenchyma.

Fig. 18. Pancreas: Metastatic lymphosarcoma in the pancreas- Invasion of neoplastic cells into the pancreatic parenchyma. (H &E)



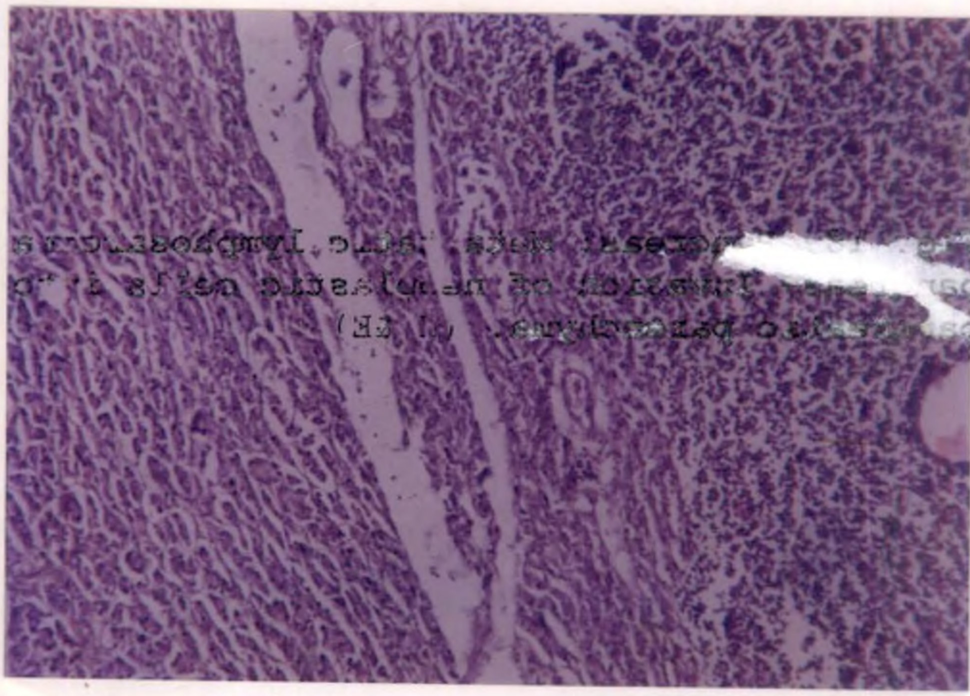
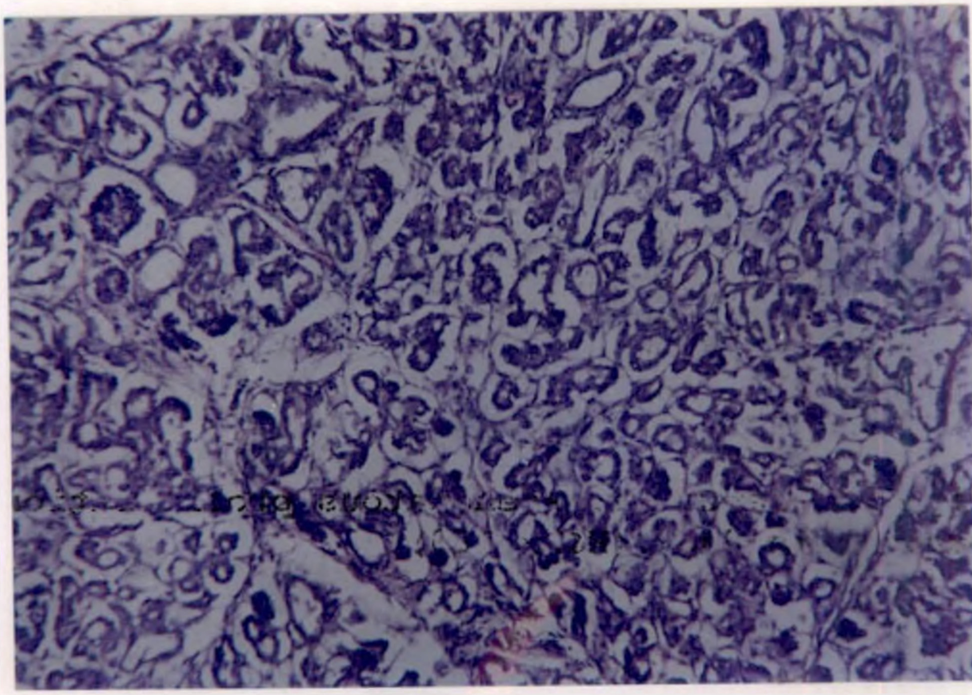


Fig. 19. Pancreas: Adenomatous proliferation of the pancreatic duct. (H&Ex 160)

Fig. 20. Pancreas Adenoma: Higher magnification. (H&Ex 250)



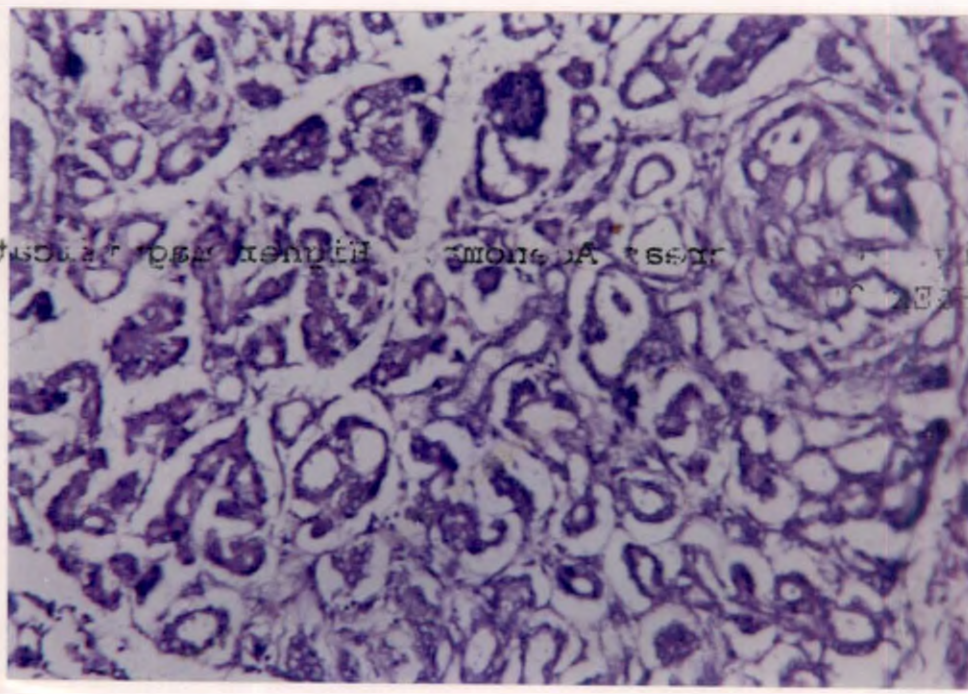
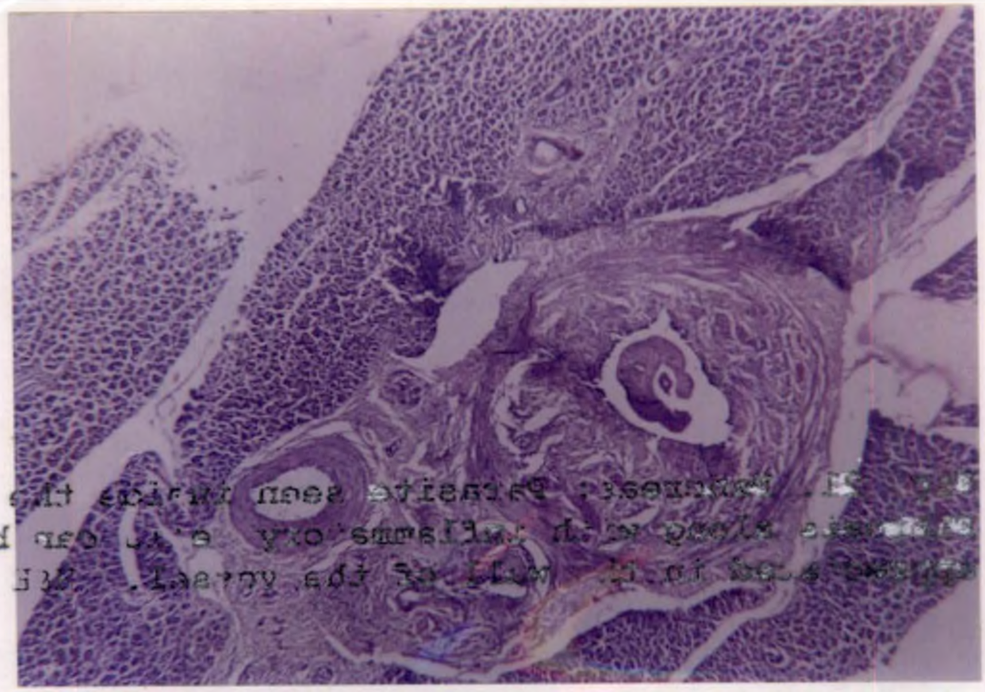


Fig. 21. Pancreas: Parasite seen inside the vein. Fibrosis along with inflammatory cells can be appreciated in the wall of the vessel. (H&Ex 60)

Fig. 22. Pancreas: Parasite seen inside the dilated pancreatic veins. No reaction is seen in the surrounding parenchyma. (H&E x 60)



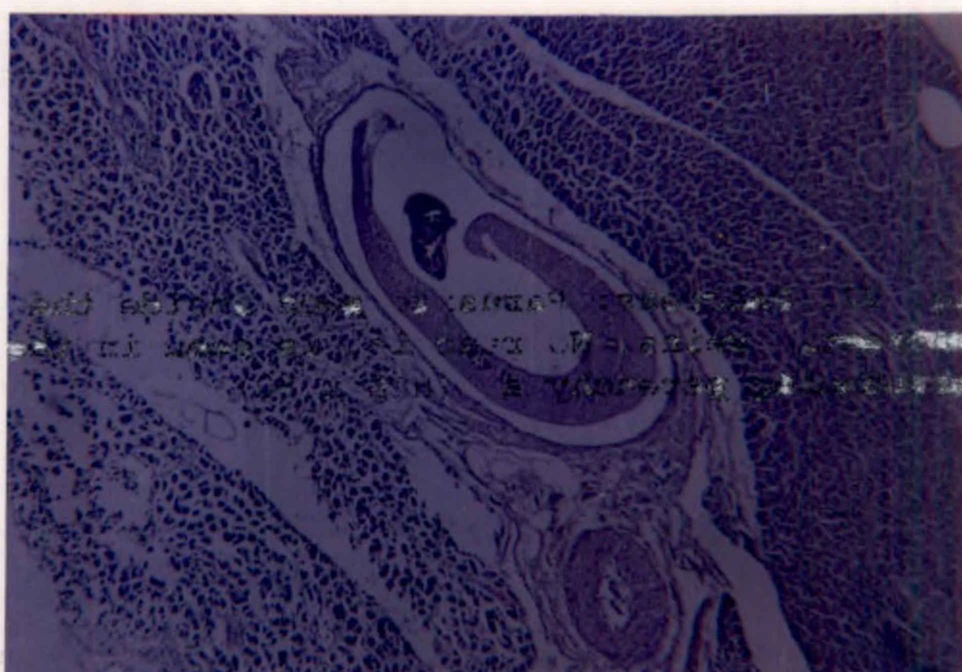


Fig. 23. The pancreoliths stained blue with haematoxylin are seen inside the dilated pancreatic duct. (H&Ex 160)

Fig. 24. Pancreas: Calculi seen inside the pancreatic duct stained red. (Alizarin red x 60)

Fig. 23. The pancreoliths stained blue with haematoxylin are seen inside the dilated pancreatic duct. (H & E x 150)

Fig. 24. Pancreas Calculus seen inside the pancreatic duct stained red. (Fibrin red

DISCUSSION

5. DISCUSSION

The present study which is the first of its kind in Kerala / India was undertaken to evaluate the prevalence and nature of pathological disorders of the pancreas in cattle. Along with the pancreas, blood and urine were collected from the slaughter house specimens for clinico-pathological studies. There has not been any systematic investigations on the diseases of the pancreas in cattle in India and this investigation has, therefore, enabled to catalogue and categorise the disorders of the pancreas. The information gathered from this investigation have made it abundantly clear that disorders of the pancreas in cattle are much more than expected and the clinical diagnosis and assessment of these conditions are very difficult.

The systematic histopathological examination showed that 51 per cent of the pancreas were having lesions of varying degree. Of this, 17 per cent showed severe lesions and 14 per cent and 20 per cent showed moderate and mild lesions respectively. Among this, chronic pancreatitis was the most common condition encountered.

Although a few cases of this condition have been reported no single cause has been identified and the etiology appeared to be complex or multifactorial. In human beings, a variety of factors like autodigestive destruction, ductular obstruction like parasitic infection, toxic and nutritional factors have been identified (Kloppel and Heitz, 1984). Autodigestion due to reflux regurgitation of the duodenal contents into the main pancreatic duct and consequent ductal inflammation and leakage and activation of enzymes into the pancreatic parenchyma has been suggested as a cause by Hendrick(1980). Regurgitation of bile through ampulla of Vater has also been pointed out as a possible factor. This destroys the phospholipid of the cell membrane leading to inflammatory response in the tissue. In cattle, all these are possible as a result of impaction or tympany which causes pressure on the duct system. It is also pertinent to point out that in cattle impaction and tympany are common disorders. Besides these, in cattle, parasitic infections of the duodenum and pancreatic duct are relatively common conditions particularly the former. The parasites can pass from the duodenum into the pancreatic duct through the ampulla of

Vater. Bossaert et *al.* (1989) have reported a case of *Euretrema coelomaticum* infection in bovines with subacute periductular pancreatitis. It is relevant to mention here that parasites were seen on histological examination in the pancreatic vessels in two instances. The role of the parasites in causing chronic pancreatitis cannot be ruled out. Bacterial and viral infections can be an aetiological factor in precipitating pancreatitis, particularly virus with epitheliotropic properties. Deeb *et al.* (1987) observed focal pancreatitis in cattle associated with Foot and mouth disease and Seong and Seo (1996) in Canine distemper in dogs. According to Longnecker (1982), varying degrees of acute pancreatitis can be induced in animals by chemicals that are cytotoxic to acinar cells. Smith and Embling (1993) reported periductular inflammation in sheep with zinc toxicity. Saunders *et al.* (2000) reported that citrus pulp toxicity causes lymphocytic to lymphogranulomatous inflammation of the pancreas in dairy cattle. Panciera *et al.* (1992) reported cellular infiltration in the pancreas in Hairy Vetch poisoning in cattle. However, in this

investigation no etiological association between pancreatitis and toxicity could be identified.

Dzhurov and Jourov (1975) observed inflammatory changes of the pancreas of fattening calves in ruminal acidosis. Ivanov (1974) stated that recurrent acute or chronic ruminal acidosis caused lesions in the pancreas. Ruminal acidosis, which has been recorded as a common clinical condition in the state of Kerala can therefore be a factor of significance in the etiology of pancreatitis. However, in this study no correlation could be established between ruminal acidosis and pancreatitis. Hence there is a need to undertake a detailed investigation to clarify the association between ruminal acidosis and pancreatitis. It is significant to clarify the prevalence and nature of pancreatic damage in ruminal acidosis, since the latter condition is common in this state and if it involves the pancreas, the pathological implications of ruminal acidosis attains substantial importance as this will have an important bearing on the pancreatic exocrine function and therapeutic approach. Experimental studies

to delineate the pathological features in the pancreas in ruminal acidosis, is therefore, warranted.

In this context it is relevant to point out Ritchie's (1979) finding that nutritional deficiencies can cause pancreatitis in humans. He opined that chronic pancreatitis can be caused by eating unripe cassava which contains cyanide and if the diet is deficient in sulphur containing aminoacids, it can damage the pancreatic acinar cells which leads to pancreatitis. The investigation undertaken in Kerala (McMillan and Geevarghese, 1979) has also indicated an association between pancreatitis and consumption of tapioca in the human population. In the state of Kerala, tapioca is an important ingredient of the livestock ration. There is therefore, a possibility that tapioca with its varying amounts of cyanide content can lead to pancreatic damage and pancreatitis. Documentation of 10 per cent of cases of pancreatitis out of 100 cases examined is certainly high and needs detailed investigation on this problem. Pancreatitis is not being diagnosed clinically in veterinary practice as it needs laboratory examination in hospitals and facilities are inadequate in veterinary

hospitals to undertake laboratory investigations. The cases of pancreatitis go unnoticed and undiagnosed but the poor digestability and intestinal malabsorbtic diseases, associated with this, cripples the growth and production in livestock leading to economic losses. It has not been possible to identify any association between tapioca consumption and pancreatitis in this preliminary investigation. However, the results of this investigation certainly emphasises the need for a thorough investigation to clarify the magnitude of involvement of tapioca in the causation of pancreatitis in cattle.

Pseudocyst was encountered in nine per cent of cases. This was associated with inflammatory response in three per cent of cases. According to Kane and Krejs (1984) pseudocysts are formed by leakage of activated pancreatic enzymes into the tissues and subsequent digestive degradation of the acinar cells. Ritchie (1979) observed that the cysts were generally filled with murky fluid resulting from the liquefaction of the acinar tissue by the digestive enzymes and they are surrounded by the neighboring connective tissue and the

pseudocysts do not have a lining epithelial cell wall. He also pointed out that often, an elevated serum amylase level is associated with the condition and the level persists for some time and do not come down within a few days as in the case of acute pancreatitis. In this investigation, the mean value of serum amylase level in these cases of pseudocysts was within the normal range. However, in the pseudocysts associated with inflammation, there was significant increase in the amylase value. This would suggest that the inflammatory response led to severe destruction of the tissues causing regurgitation of the enzyme into the blood.

Nodular hyperplasia was recorded in four per cent of the cases. According to Jubb *et al.*(1993) it is relatively a common condition in aged cattle. The animals studied in this case were generally aged adult cattle. The nodular response was involving the acinar tissue and were multicentric in location. On histological examination they were not encapsulated, but appeared as distinct circumscribed foci consisting of hypertrophic acinar cell with abundant cytoplasm. The cells were closely packed. The histological features

were similar to those described by Baba *et al.* (1979) in nodular hyperplasia in cattle. The significance of nodular hyperplasia appears to be poorly understood. It would suggest that this is manifestation of compensatory function in the phase of declining cellular activity in senility.

Pancreatic atrophy was documented in 10 per cent of cases and four per cent revealed severe and six per cent had moderate atrophy. Atrophy has been classified as primary and secondary. Primary atrophy has been described as a diffuse change with subtle microscopic changes. Nutritional deficiency or toxicity has been attributed as causative factors (Jubb *et al.*, 1993). In Kwashiorkor in human children, pancreatic acinar atrophy due to protein calorie malnutrition has been described (Kloppel and Heitz, 1984). According to Jubb *et al.* (1993), when there is reduction in protein and energy intake to sub-optimal levels there is atrophy of cells and organs. Specific nutritional deficiencies also cause atrophy. Atrophy of the pancreas was reported in zinc toxicity in sheep (Allen *et al.* 1983; Smith and Embling, 1993). Fell *et al.*(1985) reported atrophy of acinar

cells in the pancreas in cattle deficient in copper. Jubb *et al.* (1993) observed that lack of essential amino acids, copper and vitamin A can lead to atrophy of the acinar tissue. The possible role of these factors in the causation of primary atrophy cannot be ruled out.

Secondary atrophy results from the obstruction of the ductal system and manifests grossly as an uniform lesion (Jubb *et al.*,1993). Shien *et al.* (1979) reported acinar atrophy due to the obstruction of the duct by pancreatic parasite. Those cases in which parasite and pancreolith was seen, no atrophic changes could be seen in the parenchyma. There was no indication of any obstructive lesion in the pancreatic duct in the atrophic pancreas encounter in this investigation.

Acinar cell degeneration was another disorder recorded in the pancreas. This is a non-specific change which can occur from a variety of local and systemic diseases (Vegad, 1998). Deeb *et al.* (1987) reported degenerative changes in the acinar cells in Foot and mouth disease. Zhaurov *et al.* (1987) observed degenerative changes in the pancreas in metabolic

disorders while, Dzhurov and Jourov (1975) documented degenerative changes in the pancreas in fattening calves with ruminal acidosis. However, in this investigation in none of the slaughter house materials, these could be established. Ruminal acidosis and Foot and mouth disease are common in dairy cattle in Kerala. There is a possibility that these disorders might have triggered the degenerative acinar changes. There is scope to investigate into the role of these factors in the etiology of degenerative acinar changes. These degenerative changes can lead to digestive disorders, temporary or permanent, as the case may be, leading to reduced productivity in livestock.

Haemosiderosis characterised by intralobular and interacinar deposition of haemosiderin pigments which stained characteristic Prussian blue with Pearl's stain was also observed in three cases. There was also haemosiderin deposits in the veins. This is a situation generally seen in chronic passive venous congestion, although it can be due to a genetic defect. Haemosiderosis can be primary or secondary. House (1994) observed that in primary, there will be fibrosis along

with haemosiderosis, whereas fibrosis will be absent in the secondary haemosiderosis. The cases recorded here could therefore be a secondary haemosiderosis resulting from chronic venous congestion and haemorrhage.

In two instances parasites were seen in the pancreatic vessels. On gross examination, the parasites could not be identified, but they were detected on histological examination. Although live parasites were not available for speciation on the basis of morphological features, by histological examination, the parasite was identified as *Schistosoma* sp. Presence of parasites in the pancreatic duct was reported by many workers and mostly, they were *Eurytrema* sp. (Ashizawa *et al.*, 1971; Shien *et al.*, 1979; Harada *et al.*, 1980; Kono *et al.*, 1980; Sakamoto *et al.*, 1980; Pereira *et al.*, 1988). In these cases, there were significant pathological changes characterised by periductular pancreatitis, fibrosis of the pancreatic duct and pancreatic cirrhosis (Kono *et al.*, 1980; Bossaert *et al.*, 1989). Hussein and Haroun(1977) reported a case of fascioliasis in which lesions were found in the pancreas. Lawrence (1978) recorded lesions in the

pancreas produced by the eggs of *Schistosoma matheei*. There has been no authentic reports on the incidence of pancreatic Schistosomiasis in cattle in India. It would appear that Schistosoma sp. identified might be *Schistosoma spindalis* which has migrated aberrantly into the pancreatic veins. The lesions were insignificant and it was characterised by mild perivascular fibrosis in one case. This observation focuses attention on the need for a thorough search for the parasite in the pancreas. The search will certainly help to identify more number of cases of parasitic infection in the pancreas. *E. pancreaticum* infection has not been so far reported either from Kerala or India.

A case of pancreatic calculi was identified from an eight year old Jersey cross bred cow slaughtered at the slaughter house. It was seen as a gritty hard mass on incision in a cavity. During processing of tissue for histopathological examination, a portion of the hard stone like mass was washed off. In H & E stained sections, remnants of blue calcareous materials could be detected in a duct. There was slight fibrosis of the wall surrounding this calculi. There were four such

cavities containing bluish material with fibrosis of the wall in one section. On staining with Alizarin red, the mass stained red confirming that it contained calcium. The calculi was associated with periductular fibrosis and hyperplasia of the ductular epithelium. Verine (1970) has recorded several cases of bovine pancreatic lithiasis. He observed that in most of the cases, the animals were in good condition and no symptoms were manifested clinically and therefore, no clinical diagnosis was made. The histological changes, in these cases were similar to those described by Verine (1970), Velling (1975) and Groom (1994). Groom (1994) reported prominent acinar atrophy in the pancreas associated with lesions in the duct. There was no change in the parenchyma in the present case. The pancreatic calculi were found to contain calcium carbonate (Velling, 1975; Moore and Verine, 1987; De Caro *et al.* 1988; Groom, 1994). The chemical analysis of the calculi in the case reported here was not carried out and its exact composition could not be verified. Possibly, it also contained calcium carbonate as reported by earlier workers.

Fatty infiltration of the pancreas was recorded in seven per cent of the cases. The acinar tissue was seen compressed and adipose tissue was displacing the parenchyma. Whether it is associated with obesity or has it got any clinico pathological significance remains to be investigated.

The changes in the duct system were seen in 16 per cent of the cases and consisted of fibrosis, hyperplasia of the ductular epithelium and dilatation of the duct. Similar changes were reported in zinc toxicity in sheep (Smith and Embling, 1993), in pancreatic lithiasis (Velling, 1975; Groom, 1994) and in *Eurytrema pancreaticum* infection (Kono *et al.*, 1980).

Sixteen per cent of the animals examined had lesions in the Islets of Langerhans. These included clumping, degeneration, necrosis and cellular infiltration in the Islets with lymphocytes and plasma cells. Ivanov (1974) stated that recurrent sub-acute or chronic ruminal acidosis can induce degenerative lesions in the Islets leading to diabetes and lymphocytic infiltration in the Islets has been reported in

diabetes. The degenerative lesions observed in the Islets is certainly a high incidence. However, it could not be ascertained whether these animals had clinical diabetes mellitus. However, observation points out the need for undertaking laboratory tests to detect diabetes in dairy animals. It is generally believed that diabetes mellitus is relatively a rare condition in cattle. If ruminal acidosis can lead to Islet cell degeneration and diabetes mellitus as reported by Ivanov (1974) certainly, diabetes as a clinical condition can exist in cattle since ruminal acidosis is a common condition in cattle. There is, therefore, good scope to investigate into the prevalence and nature of diabetes in cattle.

Islet cell hyperplasia was seen in one case. Proliferation of pancreatic endocrine tissue is a poorly defined phenomenon in animals. A similar condition has been reported in an aged spider monkey by Brunnert *et al.* (1990). In human beings hyperplastic islets were associated with pancreatic fibrosis (Bartow *et al.*,1981). But in this particular case it was not seen. In human beings it is associated with idiopathic hyperinsulinaemia hypoglycemia in infants (Jaffe *et al.*,

1980). The etiology for islet cell hyperplasia in this case could not be determined. A possible pathogenesis might include compensatory hyperplasia due to decreased production of endocrine hormones by islet cells. Islet cell hyperplasia has not been reported in cattle yet, hence this appears to be the first record.

Haemorrhagic foci in the pancreas were seen in nine per cent of the cases. Variety of factors like bacterial and chemical toxins, hypoxia and passive congestion have been indicated to cause haemorrhage. Massive haemorrhage in the pancreas and sudden death in dogs has been reported in Canine distemper (Vegad, 1995). However, in this study in cattle, massive haemorrhages has not been observed. These were mainly small foci. For this, no specific cause could be incriminated. It could also be a terminal manifestation before death.

Congestion and oedema were seen in 30 per cent and nine per cent of cases respectively. This could be a local manifestation of a general disease. However, the changes could not be related to any disease specific or non-specific. This may be a focal manifestation of

impaction or tympany resulting in chronic passive venous congestion and consequent oedema. There was no indication of any inflammatory reaction.

A case of metastatic lymphosarcoma was encountered in the pancreas during the course of this investigation. All the lymph nodes, superficial and deep seated were enlarged and greyish white fleshy nodular lesions were seen in the pancreas. Histopathologically, the tumor was diagnosed as lymphosarcoma. Lymphosarcoma is a very common tumor of cattle (Prasad and Chandrasekharan, 1963). This tumor primarily affects both peripheral and visceral lymph nodes. Metastasis can occur in any organ as no organ is immune.

A case of cystadenoma was diagnosed on histological examination. This was small and grossly it could not be appreciated much. Cystic spaces of various dimensions lined with cuboidal epithelial cells were seen and occasionally small papillary projections were seen projecting into the lumen. The histological picture was characteristic of cyst adenoma and the possible origin could have been the pancreatic duct.

Glucose was detected in eight cases in the urine out of 84 samples examined. However, only in three cases the serum glucose level was above the threshold value of 100 mg/ dl. On histological examination none of these cases revealed any direct islet cell change. Therefore, the glycosuria appears to be not related to pancreatic islet cell changes. Glycosuria can occur due to factors like hyperadrenalism and transient glycosuria during drug administration. However, in these three cases, there were inflammatory changes, pseudocyst formation, atrophy and fatty infiltration. These could cause indirect changes in the islet cells leading to hyperglycaemia and glycosuria.

Increase in the serum amylase was seen in 18 cases and out of these 10 cases had lesions in the pancreas. Therefore, there was correlation between amylase value and changes in the pancreas. In eight cases although amylase level was increased, there was no gross or histological changes in the pancreas. This increase can be due to some obstructive lesion in the lower duct

system or in the intestine itself. However this could not be ruled out.

The investigation undertaken has helped to elucidate the pathological features of the pancreas. The pancreas is an organ which is deep seated and in autopsies, lesions of these organs are overlooked. The literature review has only revealed very scanty reports on the prevalence of pancreatic disorders in cattle. Functionally, this is an important gland with exocrine and endocrine functions and it has a direct bearing on the productivity of cattle. The systematic investigation undertaken on the pathology of pancreas has helped to focus attention on the prevalence of various pancreatic disorders in cattle. As believed, pancreatic disorders in cattle are not less frequent. The pancreas also manifests various pathological disorders and there is need to a have well drawn out research project covering a large population of animals in order to assess the magnitude of the problem. Laboratory tests should be undertaken to identify the disorders clinically. Many of the conditions recorded here like chronic pancreatitis, pancreolith, parasitic infection, islet cell changes

have not been reported in India earlier and observation of all these changes for the first time among a small population of bovines examined points out the prevalence and importance of pancreatic disorders. It is possible that a detailed investigation will help to bring to light the high prevalence rate of many of the known conditions and certain unknown conditions. This study, therefore, has been very fruitful.

SUMMARY

6. SUMMARY

An investigation was undertaken to study the prevalence and pathology of pancreatic disorders in cattle.

One hundred pancreas collected from the Meat Technology Unit, College of Veterinary and Animal Sciences, Mannuthy, as well as Municipal Slaughter House and also from the carcasses brought for autopsy to the Centre of Excellence in Pathology, Mannuthy were used for the study. Blood and urine were collected from those animals whose pancreas were collected from the slaughter house to study the clinico pathological changes. The conditions encountered were classified and pathological features were recorded and the possible pathogenesis was discerned. The study revealed a high prevalence (51per cent) of pancreatic disorders in cattle. The lesions were congestion (30 per cent), chronic pancreatitis (10 per cent), haemorrhage (9 per cent), oedema (9 per cent), atrophy (10 per cent), pseudocyst (9 per cent), fatty change (7 per cent), nodular hyperplasia (4 per cent), fibrosis (4 per cent), haemosiderosis (3 per cent), tumour (2 per cent)

cent) and calculi (1 per cent). Ductular changes included fibrosis (27 per cent), ductular epithelial proliferation (8 per cent), ductular dilatation (8 per cent) and islet changes were seen in 16 per cent of the cases.

The most common lesions encountered were chronic pancreatitis. It was seen in ten per cent of cases, of which four per cent showed severe changes. According to reports, this can be due to several factors like autodigestive disturbances, reflux regurgitation of duodenal contents, regurgitation of bile, ductular obstruction like parasitic infection, toxic and nutritional factors and ruminal acidosis. In the present study, the etiology of one case was traced as parasitic infection. Ruminal acidosis which is a common condition of cattle in Kerala could be a possible cause. But in this study, no correlation could be established between ruminal acidosis and pancreatitis. Therefore, a detailed investigation to clarify the association between these two has to be undertaken.

Nodular hyperplasia was seen in four per cent of cases. But the significance of this lesion appears to

be poorly understood. It could be explained as a compensatory process in the phase of declining cellular activity. Pancreatic atrophy was documented in ten per cent of cases, of which four per cent revealed severe atrophy. Primary atrophy can be due to nutritional deficiency or toxicity. The possible role of these factors in the causation of acinar atrophy could not be ruled out. Degenerative changes was another disorder recorded. The condition should be given due importance, as, such changes can lead to digestive disorders leading to reduced productivity in livestock. Fatty infiltration was seen in seven per cent of cases. Whether it is associated with obesity or has it got any clinico-pathological significance remains to be investigated.

In two cases, parasites were seen in the pancreatic veins. It was identified as Schistosoma sp. based on histological examination. Pancreatic calculi was observed in one case. Staining with Alizarin red the mass stained red, confirming that it contained calcium. The changes in the duct system were seen in 16 per cent of the cases. It included fibrosis of the duct wall, hyperplasia of the ductular epithelium and dilatation of the duct. Islets changes were seen in 16

per cent of the cases. The degenerative lesions observed show a high incidence. However, it could not be ascertained whether these animals had clinical diabetes mellitus. Islet cell hyperplasia was seen in one case. Etiology for this condition could not be determined. A possible pathogenesis might be compensatory hyperplasia due to decreased production of endocrine hormones by islet cells. Islet cell hyperplasia has not been reported in cattle yet. Hence, this appears to be the first record. A case of cystadenoma and a case of metastatic lymphosarcoma were encountered in pancreas during the course of this study.

Urine and serum glucose was estimated to screen diabetes in cattle. But none of the positive cases revealed direct islet cell changes. But there were other changes like pseudocyst formation, inflammation, atrophy and fatty infiltration in these cases. Increase in the serum amylase value was seen in 18 cases and of these, 10 cases showed lesions in the pancreas. This indicates that there is correlation between amylase value and changes in the pancreas.

The systematic investigation undertaken has helped to focus attention on the prevalence of various diseases of the pancreas of cattle. As believed, pancreatic disorders in cattle are not less frequent. Many of the conditions observed in this study like chronic pancreatitis, parasite in the pancreas, islet cell hyperplasia, pancreatic calculi and tumours have not been reported in India earlier. Therefore, a detailed investigation can bring to light the unknown disorders and the aetiopathogenesis of the known conditions can be clarified.

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PREVALENCE AND PATHOLOGY OF PANCREATIC DISORDERS IN CATTLE

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ABSTRACT OF THE THESIS

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ABSTRACT

The present study was undertaken to assess the prevalence and various pathological disorders of the pancreas in cattle. One hundred pancreas collected from the slaughter house and autopsy specimens formed the basis of the study. Serum and urine samples were collected from the slaughtered animals for clinico-pathological evaluation. Fifty one per cent of the pancreas showed lesions of which, 17 per cent severe, 14 per cent showed moderate and 20 per cent showed mild lesions. It was observed that chronic pancreatitis was the most common condition encountered. Other specific conditions encountered were parasitic infections (2), pancreatic tumour (2), pancreatic lithiasis (1) and islet cell hyperplasia (1). Serum amylase value showed correlation with changes in pancreas, while urine and serum glucose values did not show correlation with islet changes. Many of the conditions reported were the first record. The incidence of pathological disorders encountered were relatively high. The need and scope for investigation in to the pathological disorders in cattle were highlighted.