Egyptian Journal of Surgery Vol. (20), No. (1), Jan., 2001

# FUNCTIONAL AND PATHOLOGICAL CHANGES OCCURRING AFTER DUODENUM PRESERVING TOTAL PANCREATECTOMY IN DOGS

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***Background;*** *The aim of this study was to examine clinically the functional changes that may occur in the GIT and the histopathological changes that may occur in different organs after duodenum preserving total Pancreatectomy in dogs .*

***Methods:*** *This was an experimental study on dogs . Total Pancreatectomy without duodenectomy was performed in 15 dogs and 3 were left intact as control . The evolved technique preserved the vascular integrity of the duodenum . All operated dogs were given insulin postoperatively . Five pancreatectomized dogs and one control dog were euthanatized every 10 days post operatively for histopathological study of liver , spleen , lung, kidney, stomach, intestine, urinary bladder and heart. During the postoperative period the dogs were observed for any GIT troubles whether diarrhea, vomiting, or any other abnormal changes.*

***Results:*** *The diabetic dogs survived for period up to 10, 20 and 30 days postoperatively. Loss of weight and dehydration were common findings in the diabetic dogs after 20 to 30 days postoperatively due to the postoperative hyperglycemia that was still present in spite of the daily insulin therapy (single dose). None of the diabetic dogs had any episodes of vomiting or diarrhea and one dog had a black tarry stools twenty days post pancreatectomy that was attributed to ulceration in GIT . However the dog survived till the time of euthanasia . The histopatological study showed that lipidosis was the predominant microscopic lesion , the renal lesion showed nephrosis and glomerulopathy and in one case papillary necrosis was observed . Lymphocytic depletion was observed in the spleen . Small gastric ulcer was seen in one case 20 days post operatively . Other infrequent lesions encompassed pulmonary congestion , interstitial pneumonia and pleural squamous metaplasia were recorded . No pathological changes were recorded in sections of intestine , urinary bladder and heart .*

***Conclusion:*** *There were no functional problems in GIT associated with duodenum preserving total pancreatectomy and almost all histopathological changes that occurred in different organs were due to the resulting diabetes secondary to the removal of the pancreas .The safety of such technique in humans need to be more meticulously evaluated due to the complexity of human surgical anatomy .*

## INTRODUCTION

Due to dissatisfaction with the results of pancreatectomy according to Whipple, interest in total pancreatectomy has arisen [8]. As a trial to minimize exising nearby gastrointestinal tract (GIT) organs to improve the functional results and decrease the mortality and morbidity, surgeons started conserving the pylorus by introducing the pylorus preserving pancreatoduodenectomy [9, 18]. Even such procedure did not influence much the postoperative weight gain [21]. Early and even more recent studies suggested that postoperative gastric emptying maybe delayed with such modification [11,22,23]. As a trial to minimize such morbidity, surgeons started resecting only the head or the whole pancreas and preserved the GIT including the duodenum. In contrast to the Whipple procedure, the duodenum preserving total pancreatic head resection enables the preservation of the stomach, biliary tract and duodenum. Early and late

morbidity after the Whipple procedure is related to the reduction in insulin secretion, the occurrence of early and late dumping complaints, and attacks of cholangitis [7].

Duodenum preserving total pancreatectomy is indicated in certain cases of chronic pancreatitis [7] and cancer [8]. Duodenum preserving resection leads to less pain, a greater weight gain, and a significantly better glucose tolerance than patients do after pylorus preserving Whipple resection [2]. Thus the more GIT preservation during pancreatectomy the more physiological and less morbidity is the outcome. By follow up period of up to 22 years it has been demonstrated that late morbidity and mortality after duodenum preserving head resection are surprisingly low [7].

Considering the reaction of different animals to resection of the pancreas, dogs were found to be the most suitable model [16]. Total pancreatectomy in dogs without insulin substitution resulted in rapid development of severe diabetes and death within one week [14]. Pancreatectomized animals might survive for longer periods when insulin and a meat - carbohydrate diet is given [13]. The present study was designed to analyze the handicaps of total pancreatectomy without duodenectomy in dogs and to assess the side effects of such technique on the pertaining visceral organs and the general condition as a whole. Hopefully, this will be useful to the prospective remedies on human patients.

## MATERIALS AND METHODS

### *Anatomical background*

Five dogs were anesthetized by 2.5% sodium thiopental intravenously. Then sanguination was done via common carotid arteries. Thoracotomy was proceeded for cannulation of thoracic aorta. Flank laparotomy was then made for cross clamping of aorta prior to renal artery. A colored latex 150-200 ml (gum milk latex 60%, colored red with carmine) was infused via the aortic cannula. The surgical anatomy of the resected specimens was demonstrated (Fig. 1 a, b, c).

### *Experimental subjects*

Eighteen healthy male and female native breed mongrel dogs, weighing 10-12 kg, aging more than five years old were used in this study. Fifteen dogs were subjected to total pancreatectomy without duodenectomy and the rest were left intact as control. Five pancreatectomized and one control dogs were euthanatized every 10 days postoperatively using rapid I.V. shots of thiopental sodium 10%.

### *Surgical approach*

Following anesthesia with atropine sulfate (0.2 mg/kg.), diazepam (0.5 mg/kg.), ketamine 10% (15 mg/kg.) and xylazine HCL 2% (1.1 mg/kg.) intravenously, dogs were placed on dorsal recumbence position and the abdomen was prepared for surgery. Through a midline incision the duodenum was identified and exteriorized into the wound. The mesentery of both the right lobe and body of pancreas was resected close to the pancreas with bipolar electrocautery. The caudal pancreatico-duodenal branches (Fig. 2a) of the cranial mesenteric vessels were ligated and severed. The continuation of the caudal pancreatico-duodenal vessels were traced through the mesenteric attachment to the wall of the descending duodenum. Their pancreatic branches were cauterized near to the substance of the pancreas (Fig. 2b). The accessory pancreatic duct was isolated by dividing the vessels and gentle blunt dissection then ligated and resected. The pancreatic tissue was bluntly dissected from the mesentery attached to the duodenum, with preserving the branches of caudal pancreatico-duodenal vessels. The body of the pancreas was freed by gentle upward traction thus facilitating its separation, and cutting of the dorsal mesentery with minimal hemorrhage. The peritoneum was divided in between the jaws of a straight sharp pointed mosquito using electrocautery. The part of the body adherent to the duodenum was carefully rubbed to be separated from the surface of duodenum. Surgical dissection was advanced along the duodenum toward the pylorus, dividing vessels with electrocautery. The duodenal branches of the right gastro-epiploic vessel (Fig. 2c) were carefully preserved during the surgical dissection. The greater omentum was then held and manipulated for identifying and dividing the pancreatic branches of the cranial pancreatico-duodenal vessels near the pancreas. To free the left lobe of the pancreas, the branches of the splenic, cranial pancreatico-duodenal and gastro-duodenal vessels were ligated and resected. Subsequently the pancreas was totally removed. The pancreatic lobules encountered behind the duodenal branch of the right gastro-epiploic, on sides of pancreatico-duodenal vessels and adherent to the duodenum were approached gently from behind the vessels without injuring them. These lobules were gathered between the jaws of a mosquito clamp, a ligature was applied, then they were removed. Finally, the greater omentum was sutured to the duodenal wall. The abdominal wall was closed.

### *Postoperative follow up*

The pancreatectomized dogs were given one dose of butorphanol tartrate 1-4 mg (Stadol) intramuscularly, penicillin G sodium 400,000 iu, 0.5 g streptomycin (Neobiotic) and 40 mg. gentamicin sulfate (Garamycin) were given intramuscularly daily for three successive days. Lent insulin (1 unit/kg/day) was administered subcutaneously after each morning meal for control of their blood glucose level. A high protein-carbohydrate diet encompassed of one quarter boiled chicken, one bread and

250 cc milk was given as a daily meal together with an exogenous pancreatic enzymes (zymogen) once daily per os after meal. The water was ad libitum throughout the experiment. Blood samples were taken from dogs five days prior to surgery as control and every day postpancreatectomy till time of euthanatization (once daily morning sample after meal). The glucose level was recorded by Haemo-Glucotest.Dogs were observed for any signs or symptoms of GIT troubles and general health condition.

***Histopathological studies***

The euthanatized dogs were subjected to thorough postmortum examination. Specimens from liver, lung, spleen, kidney, stomach, intestines, urinary bladder and heart were collected. They were fixed in 10% neutral buffered formaline, processed by the routine paraffin embedding technique, sectioned at 4-6 microns thickness and stained with haematoxylin and eosin [(1)].

## RESULTS

The critical point in the sequence of formidable technique was dealing with the adherent pancreas to the duodenum. The pancreas was difficult in dissection so it was carefully rubbed from the surface of the duodenum. Thereafter, the duodenum appeared seemingly cyanosed. However, there were no postoperative complications encountered. Moreover few branches from the gastroduodenal artery sent to the proximal part of left lobe were secured. Attention was paid for avoidance of intra-operative bleeding of these branches.

Total pancreatectomy without duodenectomy required 45 to 60 minutes. Regarding the surgical bleeding, there was insignificant blood loss. The evolved technique preserved the vascular integrity of the duodenum. Thus, there were no postoperative complications related to duodenal ulceration and perforation.

***Functional Findings***

The diabetic dogs survived for a period of 10, 20 and 30 days postpancreatectomy. The surgical wounds healed by primary intention and skin sutures were removed after 10 days.The pancreatectomized dogs showed signs of hyperglycemia which were manifested by polyuria, polydypsia and lethargy. Polyphagia was noticed after daily insulin injection. Loss of weight and dehydration were common findings in the diabetic dogs after 20 to 30 days postoperatively (Fig. 3).

Black tarry stools were passed by one dog 20 days postoperatively and this was attributed to ulceration in the GIT. However, the dog was able to survive till the time of euthanasia.

None of the other dogs showed any signs of GIT disturbances whether vomiting or diarrhea. Despite the daily control of hyperglycemia in diabetic dogs, blood glucose level was significantly increased after the operation ($P<0.01$). Its mean value reached up to 393.6 mg/dl in the fifth day of thirty days diabetic dogs.

***Histopathological Findings***

Histopathological studies demonstrated that lipidosis was the predominant microscopic lesion detected in the examined cases along the observation period. The hepatic cells became greatly swollen by the accumulated fat inside. Many distended hepatic cells were ruptured and fused together forming fat cysts (Fig. 4a). The picture of lipidosis was also seen in four cases in the form of accumulation of large foamy macrophages inside the pulmonary alveoli (Fig. 4b) and spleen. The renal lesions were the most frequent changes encountered in the examined dogs after lipidosis and presented by nephrosis which was characterized by cytoplasmic vacuolation of the tubular epithelial cells in the medullary rays (Fig. 4c). Glomerulopathy began 20 days postpancreatectomy and was marked by thickening of the glomerular capillary basement membrane with aneurysmal dilation (Fig. 4d). Two cases developed glomerulosclerosis with mild interstitial fibrosis at 30 days postpancreatectomy (Fig. 4e). In one case papillary necrosis associated with mild inflammatory reaction and hemorrhage were detected. In eleven examined cases, lymphocytic depletion was observed in the spleen with exposure of the reticular framework (Fig. 4f). Other infrequent lesions encompassed pulmonary congestion, interstitial pneumonia and pleural squamous metaplasia (Fig. 4g). Beside, small gastric ulcer was also seen in one case, 20 days postpancreatectomy. However, no pathological changes were recorded in the sections of the intestine, urinary bladder and heart throughout the observation period.

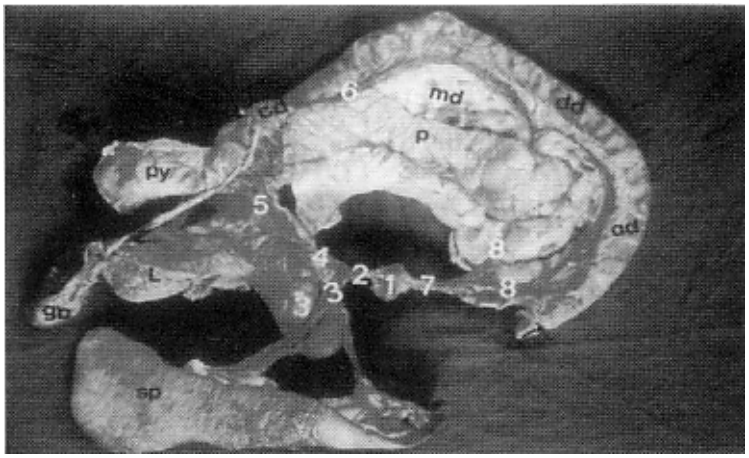



*Fig. (1-a)*

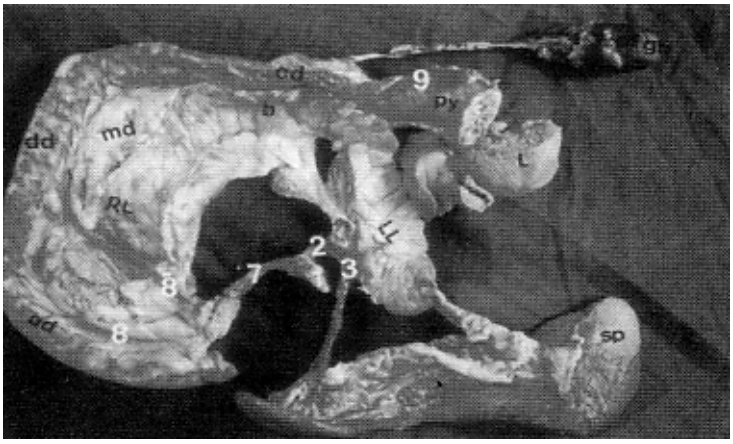



*Fig. (1-b)*

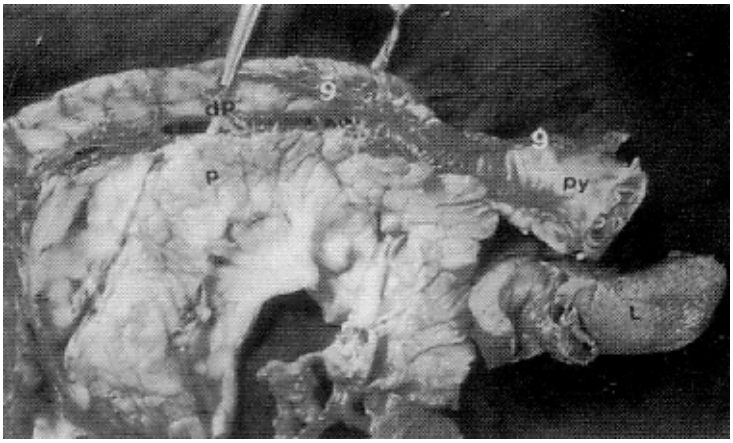
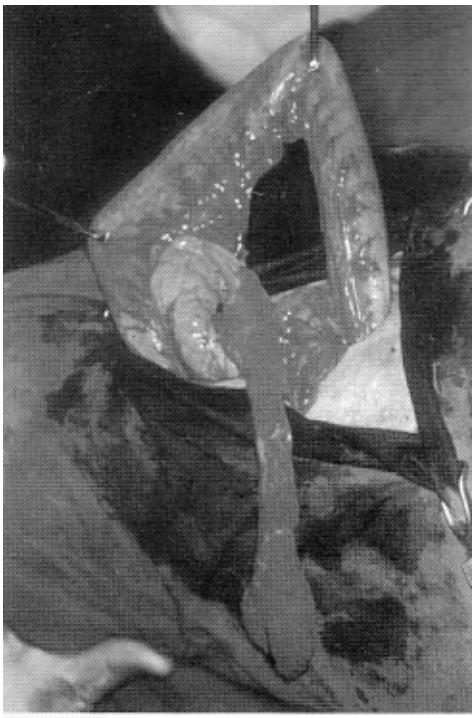



*Fig. (1-c)*

*Fig. (2-a)*



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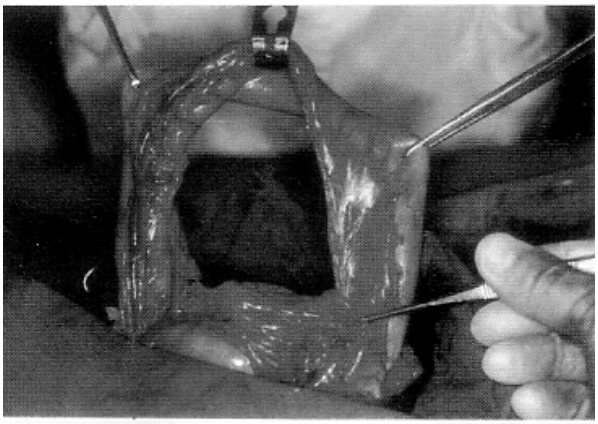


*Fig. (2-c)*

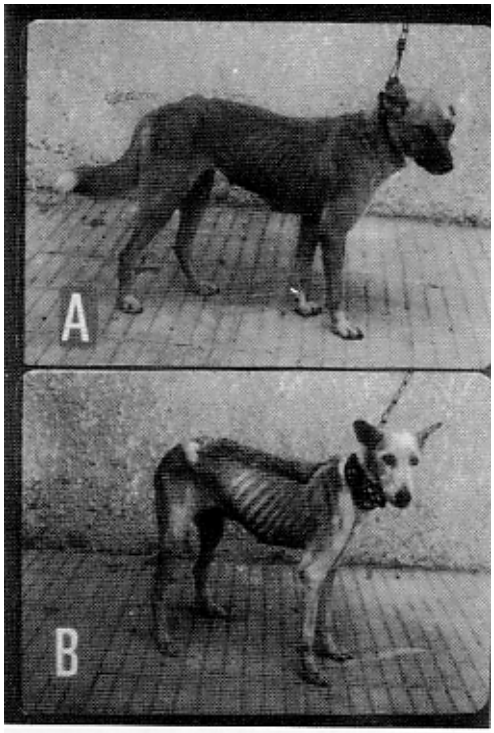



*Fig. (3)*

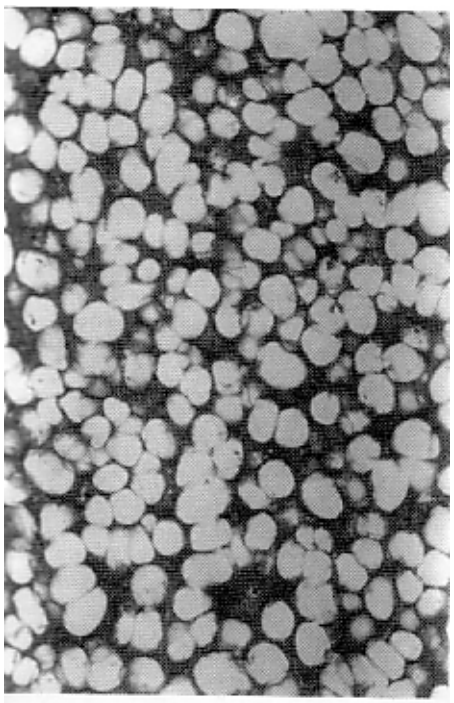
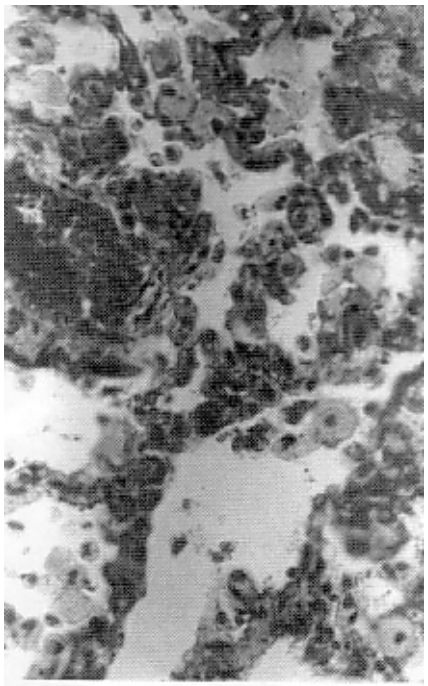


*Fig. (4-a)*



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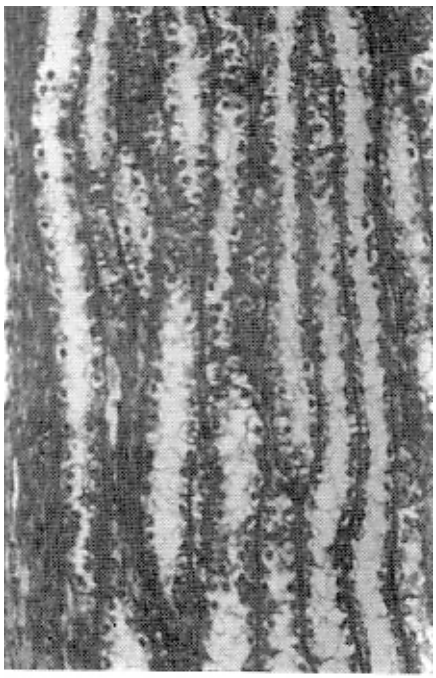

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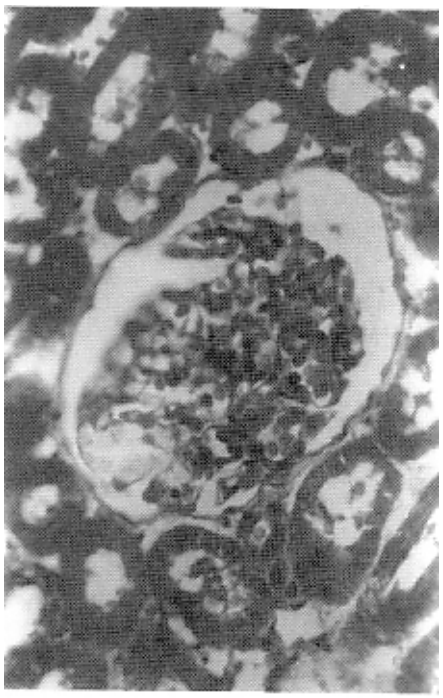
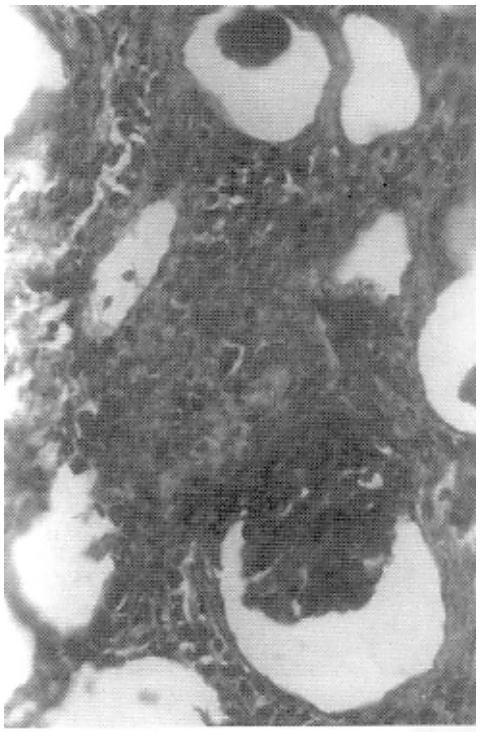


*Fig. (4-d)*



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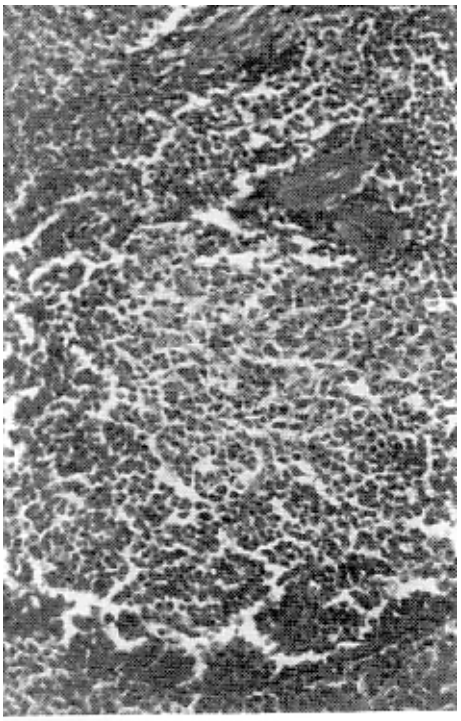

*Fig. (4-f)*

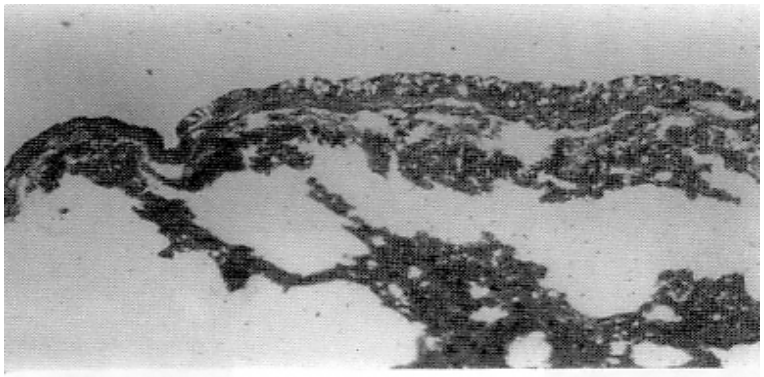

*Fig. (4-g)*

## DISCUSSION

The present study was designed to give an overwhelming view on the concomitant complications of duodenum preserving total pancreatectomy with special study to the technical problems of the procedure in an experimental model.

Concerning the surgical removal of pancreas in dogs. The duodenal branches of the cranial and caudal pancreatico-duodenal arteries as well as the duodenal branches of the right gastro-epiploic artery must be preserved to avoid ischemic necrosis of the duodenum. Haemostasis is of utmost importance to reduce mortality and morbidity. The adopted technique was of short duration as the usual time from initial incision to complete resection of the pancreas was 45 to 60 minutes. The intra-operative problems were substantiated to be related to the adherent part of the pancreas to the duodenum [3], preservation of the vascular integrity of the duodenum [4], and hemostasis of all pancreatic branches supplying or delivering from the pancreatic tissue [5]. The forementioned problems were considered within the methodology of this surgical approach. The described technique permitted an excellent perfusion of the duodenum, with insignificant blood loss and minimal trauma of the vascular organs.

The operated dogs showed significant rise in blood glucose level 24 hours post-pancratectomy. The detectable difference was statistically highly significant ($P<0.01$). Hyperglycemia was ascribed to appancreatic dogs. Thus, they exhibited signs of polyuria, polydypsia and lethargy. Osmotic diuresis occurred, followed by loss of electrolytes and water. This resulted in dehydration and loss of body weight. The operated dogs showed wide fluctuation in the blood glucose level despite the daily insulin therapy. None of the diabetic dogs had episodes of vomiting, diarrhea or any other signs of GIT disturbances. Also none of them had other episodes related to the fluctuation of blood glucose concentration like, sneezing or coughing [6]. Insulin induced post-hypoglycemia hyperglycemia was detected by a wide fluctuation in the blood glucose concentration every morning.

The primary postoperative problem encountered in the control of apancreatic dogs was the endocrine and exocrine function of the pancreas. The disturbance in endocrine function was managed by giving the diabetic dogs intermediate acting insulin (1 unit/kg/day) subcutaneously; onset of action 10-30 minutes, peaking within 2 to 10 hours and lasting 8 to 24 hours [15]. The exocrine function was also controlled by pancreatic enzymes substitute therapy "zymogen". High protein carbohydrate diet were offered daily to improve the general health condition of the diabetic dogs [19].

The picture of lipidosis in the liver, lung and spleen was a constant finding as a result of disturbance in lipid metabolism which occurs in diabetic patients. Similar findings were also recorded in canines [6, 12]. Thus the picture of hepatic lipidosis did not differ by the time of examination and did not show individual variation. It appeared to be directly related to diabetes mellitus.

The diabetic nephropathy varied in its intensity depending on the diabetes time and the individual variation. Such nephropathy was previously mentioned in human patients [17,20]. The present study emphasized that mild diabetic nephropathy occurred. It resulted from angiopathies of the glomerular tufts and from basement membrane injuries. These findings were similar with those described by Kaneko et al. in 1979 [10].

The lymphocytic depletion in the spleen recorded in this study, may give an explanation for the susceptibility of the diabetic patients to infection [20].

## CONCLUSION

There were no functional problems in the GIT associated with duodenum preserving total pancreatectomy and almost all histopathological changes that occurred in the different organs were due to the resulting diabetes mellitus. But the safety of such a procedure in humans need further evaluation due to the more complex human anatomy and the possible differences in pathophysiology.

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