GI - Pancreas

CARDIOVASCULAR EFFECTS (COMPLICATIONS?) OF ACUTE PANCREATITIS

Medical Grand Rounds

The University of Texas Health Science Center at Dallas

December 8, 1983

TABLE OF CONTENTS

I. INTRODUCTION

1. Moynihan, B.: Acute pancreatitis. Ann. Surg. 81:132, 1925.
2. Thal, A.P., Kobold, E.E., Hollenberg, M.J.: The release of vasoactive substances in acute pancreatitis. Am. J. Surg. 105:708, 1963.
3. Fordtran, J.S.: Pancreatitis. Medical Grand Rounds, Parkland Memorial Hospital, September 12, 1974.
4. Pollock, A.V.: Acute pancreatitis; analysis of 100 patients. Brit. Med. J. January 3, 1959, p. 6.
5. Carey, L.C., Rodgers, R.E.: Pathophysiologic alterations in experimental pancreatitis. Surgery 60:171, 1966.
6. Gliedman, M.L., Bolooki, H., Rosen, R.G.: Acute pancreatitis. Curr. Prob. Surg. 26:3, 1970.
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8. Carey, L.C.: Extra-abdominal manifestations of acute pancreatitis. Surgery 86:337, 1979.
9. Bradley, E.L., III: Overview. In: Complications of Acute Pancreatitis; Medical and Surgical Management. Philadelphia: W.B. Saunders Co., 1982, p. 1.
10. Buja, L.M., Personal Communication.
11. Anderson, M.C., Schoenfeld, F.B., Iams, W.B., et al.: Circulatory changes in acute pancreatitis. Surg. Clin. N. Am. 47:127, 1967.
12. Zollinger, R.M.: Pancreatic problems. 1. Acute pancreatitis. Postgrad. Med., March 1971, pp. 91.
13. Keith, L.M., Jr., Watman, R.N.: Blood volume deficits in pancreatitis. Surg. Forum 5:380, 1954.
14. Werner M.H., Hayes D.F., Lucas C.E., et al.: Renal vasoconstriction in association with acute pancreatitis. Am. J. Surg. 127: 185, 1974.
15. Caini, B., Modigliani, V.: Cardiovascular syndrome of acute pancreatitis. Sett. Med. 44:349, 1956 (abst. JAMA 162:1499, 1956).

In 1925, Sir Berbey Moynihan stated "acute pancreatitis is the most terrible of all the calamities that occur in connection with the abdominal viscera". It has long been recognized that this condition has widespread protean manifestations and that acute pancreatitis frequently has marked effects on the cardiovascular system. Because of these extensive and potentially lethal effects, Thal et al. have stated "Small wonder is it that the *Surgeon* * looks upon the pancreas as the powder keg of the abdomen".

The *Internist* also has a great respect for and fear of pancreatic disease in his patients. In 1974, Dr. John Fordtran presented a very scholarly and exhaustive Medical Grand Rounds entitled "Pancreatitis". At that time he pointed out the diversity of presentations of acute pancreatitis.

Some patients with acute pancreatitis are admitted in shock with a decreased arterial blood pressure and cardiac output and an increased systemic or peripheral vascular resistance. In these cases the loss of blood volume can be quite severe. Zollinger found a 1500 cc deficit of blood volume in about two-thirds of the patients he studied. Keith and Watman found a mean deficit in blood volume of 1806 cc and a maximal deficit of 2510 cc in patients with acute

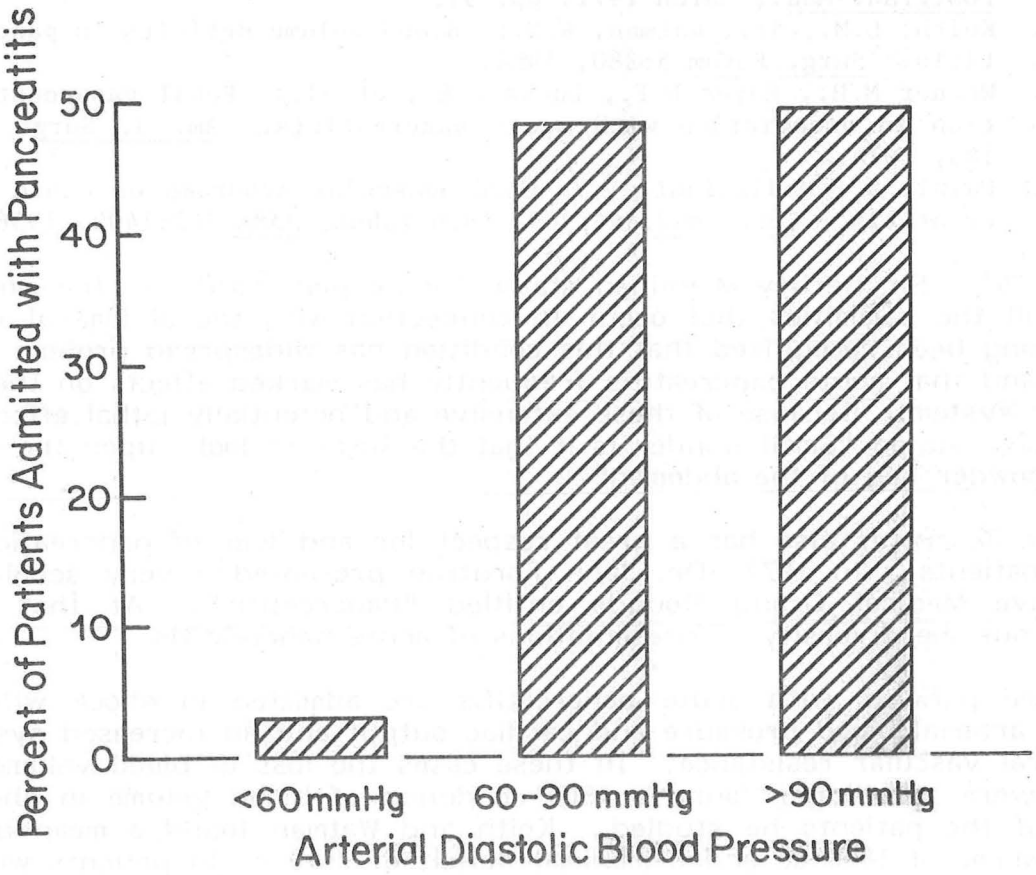
* Italics are Author's

pancreatitis. In such cases, the pancreas is markedly necrotic and filled with blood. With extensive hemorrhagic pancreatitis, blood volume loss may also extend into the retroperitoneal space.

However, such widespread destruction of and hemorrhage into the pancreas is not present in many patients. In these cases the pancreas is markedly edematous with no evidence of hemorrhage. Fat necrosis may be seen in the surrounding connective tissue due to the leakage of pancreatic enzymes. Such pathological findings occur in acute alcoholic pancreatitis. In these cases the blood volume loss may be absent or very minimal. Zollinger found no measurable blood volume deficit in about one-third of the patients with acute pancreatitis that he studied. Werner et al. recently studied patients with acute edematous alcoholic pancreatitis and found a normal extracellular fluid space as measured by means of the inulin space technique.

One section in Dr. Fordtran's Medical Grand Rounds was entitled "Hemodynamic Problems in Acute Pancreatitis". He reported that in a 1972 survey of patients admitted to Parkland Memorial Hospital with acute pancreatitis few of them were hypotensive. In fact, in patients who showed no evidence of decreased blood volume, he discussed the occurrence of a transient increase in systemic arterial blood pressure. The arterial diastolic blood pressures in 172 patients with pancreatitis who were admitted to Parkland Memorial Hospital in 1972 are shown in Figure 1.

Figure 1



In this series, 3% of the patients were admitted with an arterial diastolic blood pressure below 60 mmHg, 48% had diastolic pressure between 60-90 mmHg, and 49% had pressures greater than 90 mmHg.

There are four possible ways in which acute pancreatitis can affect the cardiovascular system and these are shown in Figure 2.

Figure 2

POSSIBLE CAUSES OF THE CARDIOVASCULAR EFFECTS OF ACUTE PANCREATITIS

(1) Decrease in Effective Blood Volume

(2) Electrolyte Disturbances

(3) Release of Vasoactive and Inotropic Agents

(4) Pressor Reflex from Pancreas

In some cases of acute pancreatitis, the cardiovascular effects are dominated by the loss in effective blood volume and the ensuing neural and humoral response to the hypotensive state. In such cases one is unable to determine the pure effects on the cardiovascular system of the inflammation of the pancreas, per se. Also, electrolyte disturbances can have cardiovascular effects when they occur in patients with acute pancreatitis. The cardiovascular effects of these two conditions, however, are not unique to patients with acute pancreatitis and can be prevented with appropriate therapy.

Patients with acute pancreatitis who do not have a marked loss of effective blood volume or an electrolyte disturbance have been shown to have transient elevations of arterial blood pressure. This could be due to either the release of vasoactive and inotropic agents or to a pressor reflex from the pancreas, or to both of these mechanisms.

In this Grand Rounds, we will examine the cardiovascular effects that are caused by acute inflammation of the pancreas, per se. This is not being done to minimize the extreme importance of the loss of effective blood volume and electrolyte disturbances that often occur in patients with acute pancreatitis. It is thought, however, that it is important to understand the marked cardiovascular effects that occur in patients with acute pancreatitis who do not have a significant loss in effective blood volume or an electrolyte disturbance.

II. CARDIOVASCULAR EFFECTS (COMPLICATIONS?)

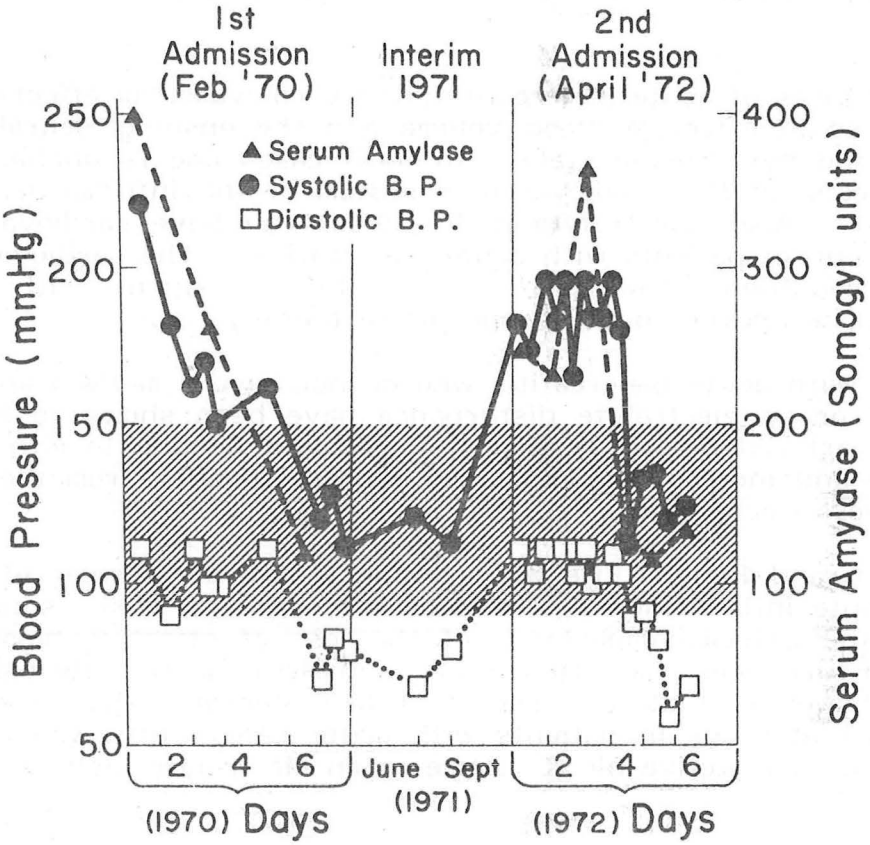
A. Systemic Circulation

1. Systemic Hemodynamics

3. Loc. cit.
14. Loc. cit.
16. Sakaran, S., Lucas, C.E., Walt, A.J.: Transient hypertension with acute pancreatitis. Surg. Gynecol. Obstet. 138:235, 1974.
17. Ito, K., Ramirez-Schon, G., Shah, P.M., et al.: Myocardial function in acute pancreatitis. Ann. Surg. 194:85, 1981.
18. Interiano, B., Stuard, I.D., Hyde, R.W.: Acute respiratory distress syndrome in pancreatitis. Ann. Int. Med. 77:923, 1972.
19. Lucas, C.E., Ledgerwood, A.M.: Shock and renal failure. In: Complications of Acute Pancreatitis; Medical and Surgical Management. Philadelphia: W.B. Saunders Co., 1982, p. 33.

Several studies have now reported transient elevations of arterial blood pressure in patients admitted to the hospital with acute pancreatitis. An example of this finding in one of the patients with acute pancreatitis studied by Sakaran et al. is shown in Figure 3.

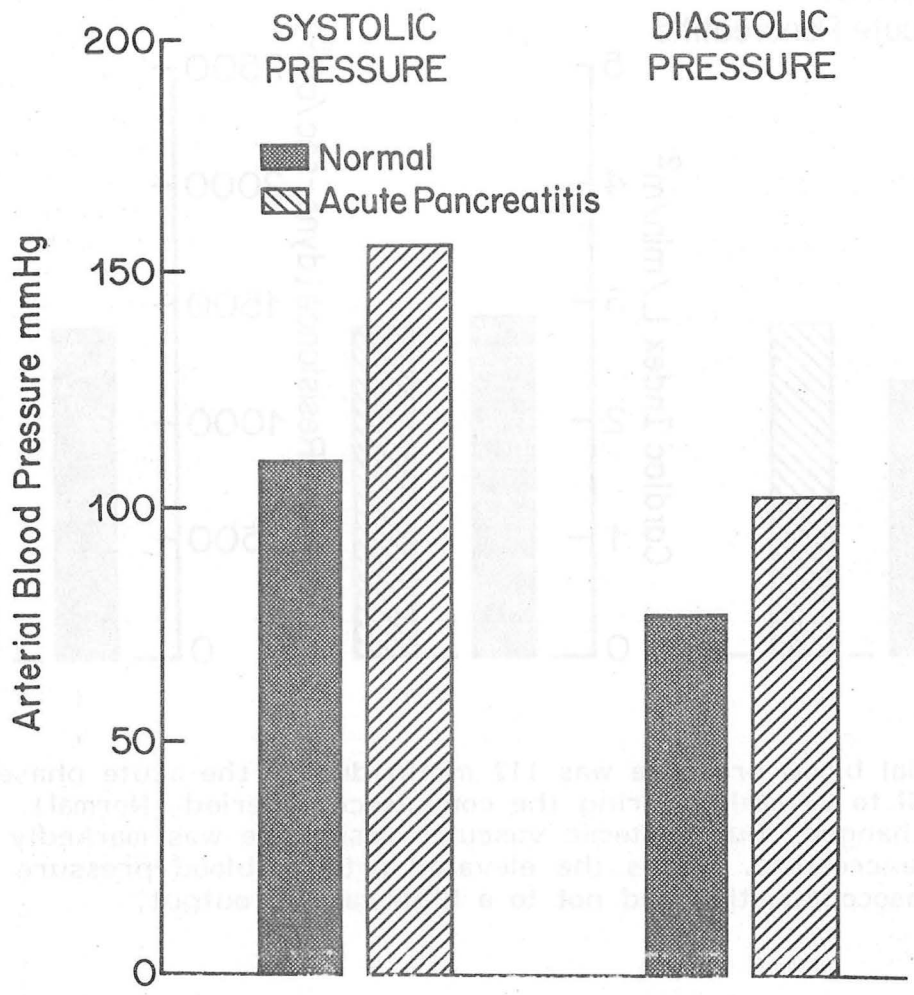
Figure 3



The patient was admitted to the hospital in 1970 with a history and physical findings that suggested acute pancreatitis and with a serum amylase of 400 Somogyi units. The arterial blood pressure was 220/110 mmHg on admission and fell to a normal value as the symptoms and signs subsided and the serum amylase returned to normal. The patient was seen in the emergency room twice during 1971 and on both occasions the arterial blood pressure was normal. The patient was admitted for a second episode of acute pancreatitis in 1972 and again the arterial blood pressure and the serum amylase were both elevated. The blood pressure fell to normal as the symptoms and signs of acute pancreatitis subsided and the serum amylase returned to normal.

Sakaran et al. have reported the arterial blood pressures in 42 consecutive patients admitted to their hospital. Forty of the patients were noted to have an elevated arterial blood pressure which fell to normal and the mean values for this group are shown in Figure 4.

Figure 4

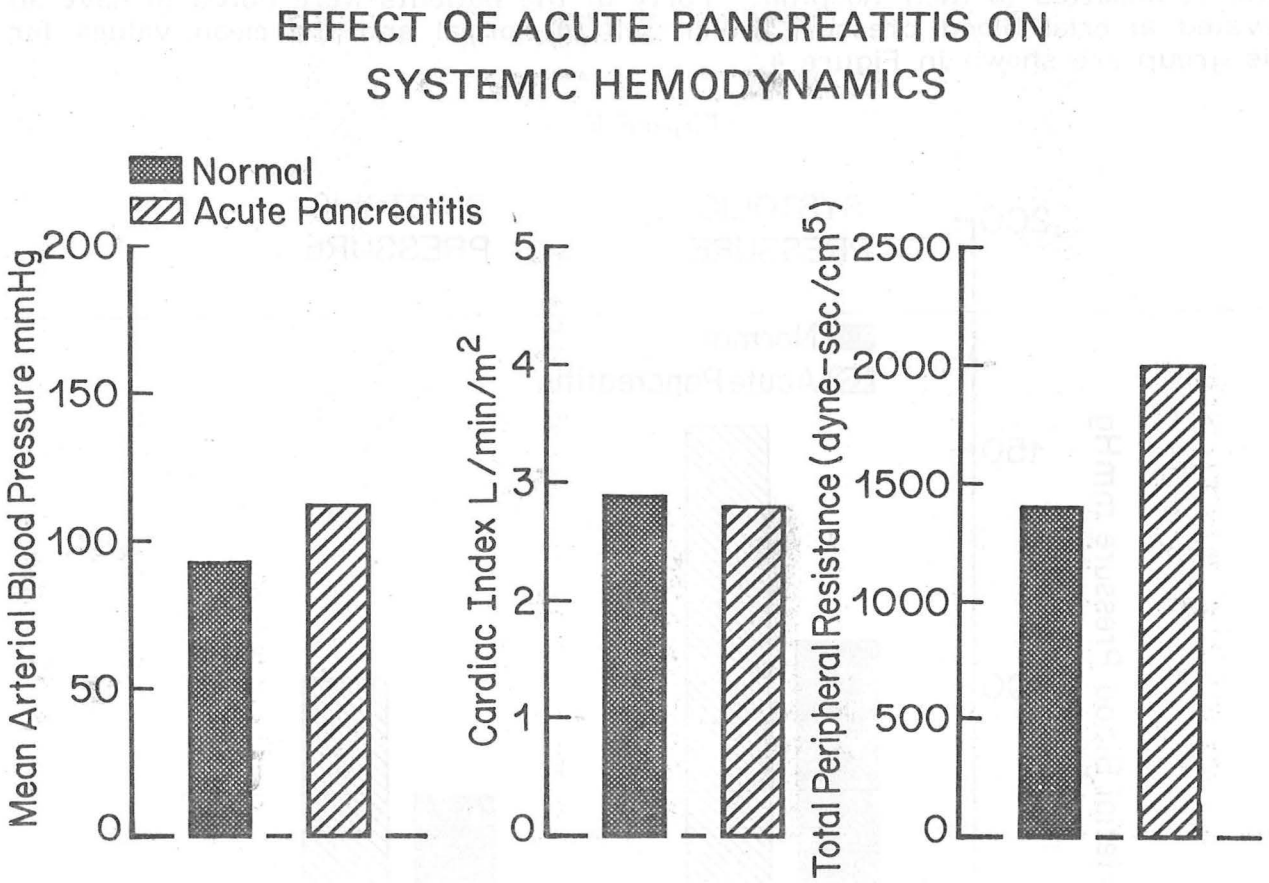


During the episode of acute pancreatitis the systolic pressure averaged 156 and the diastolic pressure 102 mmHg. During the recovery phase (Normal) the systolic pressure averaged 120 and the diastolic 77 mmHg. None of the patients required anti-hypertensive medications after discharge from the hospital. Such

elevations in blood pressure were not seen in patients admitted to the hospital with severe pain from other acute abdominal catastrophes.

Werner et al. studied patients admitted to the hospital with acute edematous alcoholic pancreatitis and with a normal extracellular fluid space. All had an elevated mean arterial blood pressure. They investigated the cause of this transient increase in arterial blood pressure and the results of their study are shown in Figure 5.

Figure 5



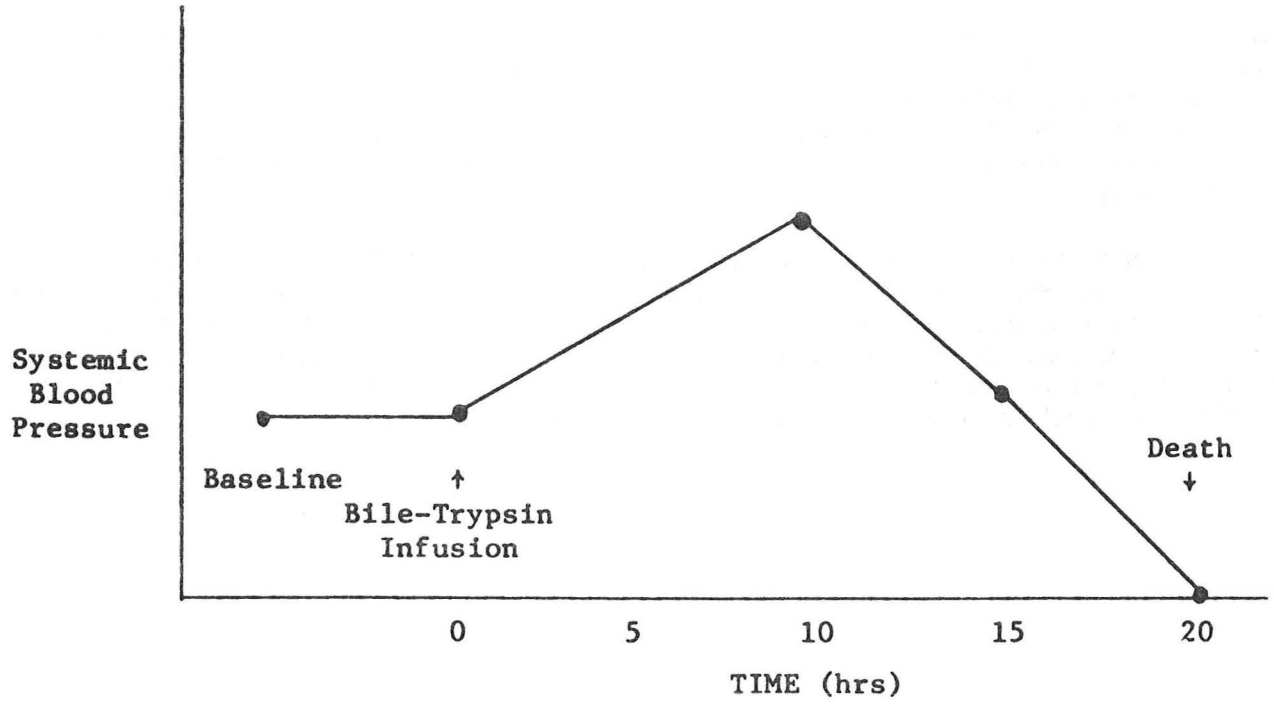
The mean arterial blood pressure was 112 mmHg during the acute phase of pancreatitis and fell to 93 mmHg during the convalescent period (Normal). Cardiac output was unchanged, but systemic vascular resistance was markedly elevated during acute pancreatitis. Thus the elevated arterial blood pressure was due to peripheral vasoconstriction and not to a high cardiac output.

19. Loc. cit.
20. Halmagyi, D.F.J., Karis, J.H., Stenning, F.G., et al.: Pulmonary hypertension in acute hemorrhagic pancreatitis. Surgery 76:637, 1974.

Experimental studies in dogs performed by Sakaran have been reported by Lucas and Ledgerwood. These studies also demonstrated a transient increase in arterial blood pressure when lethal acute pancreatitis was experimentally induced. These data are shown in Figure 6.

Figure 6

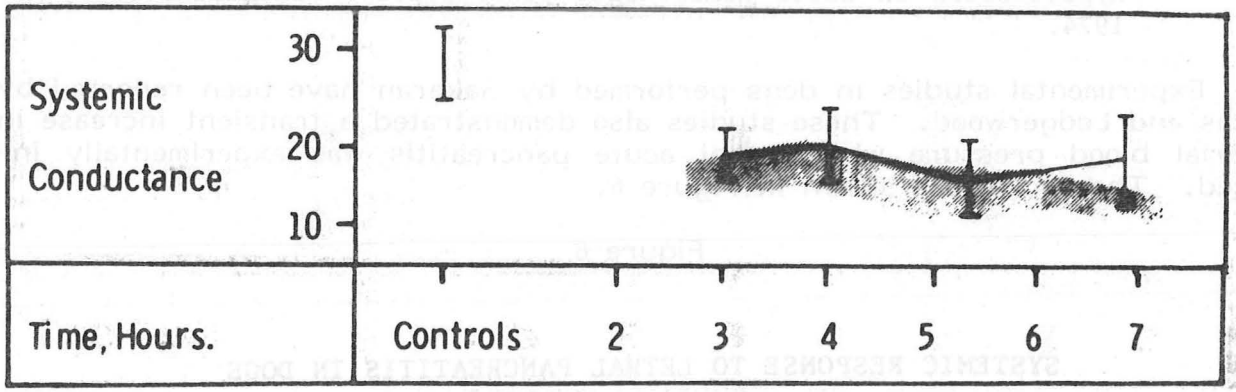
SYSTEMIC RESPONSE TO LETHAL PANCREATITIS IN DOGS



The infusion of bile-trypsin into the pancreatic duct caused an early hypertensive response even when fluids were not given to replace the probable loss into the inflamed pancreas. Replacement of fluids caused an even greater rise in arterial blood pressure in a study by Sakaran of dogs with non-lethal acute pancreatitis.

Halmagyi et al. have studied systemic vascular conductance, which is the reciprocal of systolic vascular resistance, when acute pancreatitis was experimentally induced in dogs. These findings are shown in Figure 7.

Figure 7



The shaded area represents the values in the sham operated dogs and the vertical lines with bars represent the values in the dogs with acute pancreatitis. Systemic conductance, which is the reciprocal of systemic vascular resistance, was decreased or the systemic vascular resistance was increased in the dogs with induced pancreatitis. However, similar elevations were found in the sham operated dogs.

It seems quite clear that systemic arterial blood pressure can be transiently elevated in some patients with acute pancreatitis and in dogs with experimentally induced acute pancreatitis. Further, these elevations in arterial blood pressure are due to an increase in systemic or peripheral vascular resistance. Thus a transient peripheral vasoconstriction seems to occur during acute pancreatitis even when blood volume losses are minimal or absent.

2. Renal Blood Flow

14. Loc. cit.
19. Loc. cit.
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22. Dankner, A., Heifetz, C.J.: The interrelationship of blood and urine diastase during transient acute pancreatitis. Gastroenterology 18:207, 1951.
23. Thal, A.P., Perry, J.F., Jr., Egner, W.: A clinical and morphologic study of forty-two cases of fatal acute pancreatitis. Surg. Gynecol. Obstet. 105:191, 1957.
24. Beisel, W.R., Herndon, E.G., Myers, J.E., et al.: Acute renal failure as a complication of acute pancreatitis. Arch. Int. Med. 104:539, 1959.
25. Freidell, V.H.: Pancreatitis and renal insufficiency. Am. J. Gastroenterology 34:487, 1960.
26. Balslov, J.T., Jorgensen, H.E., Rodmundur, N.: Acute renal failure complicating severe acute pancreatitis. Acta Chir. Scand. 124:348, 1962.
27. Frey, C.F.: Pathogenesis of nitrogen retention in pancreatitis. Am. J. Surg. 109:747, 1965.
28. Lee, H.A., Hills, E.A.: Acute pancreatitis and renal failure. Postgrad. Med. J. 41:471, 1965.
29. Gordon, D., Calne, R.Y.: Renal failure in acute pancreatitis. Brit. J. Med. 3:801, 1972.
30. Gjessing, J.: Renal failure in acute pancreatitis. Brit. Med. J. Nov. 11, 359, 1972.
31. Goldstein, D.A., Llach, F., Massry, S.G.: Acute renal failure in patients with acute pancreatitis. Arch. Int. Med. 136:1363, 1976.
32. Moffatt, T.L.: Incidence of acute renal failure in alcoholic pancreatitis. Virginia Med. 107:143, 1980.

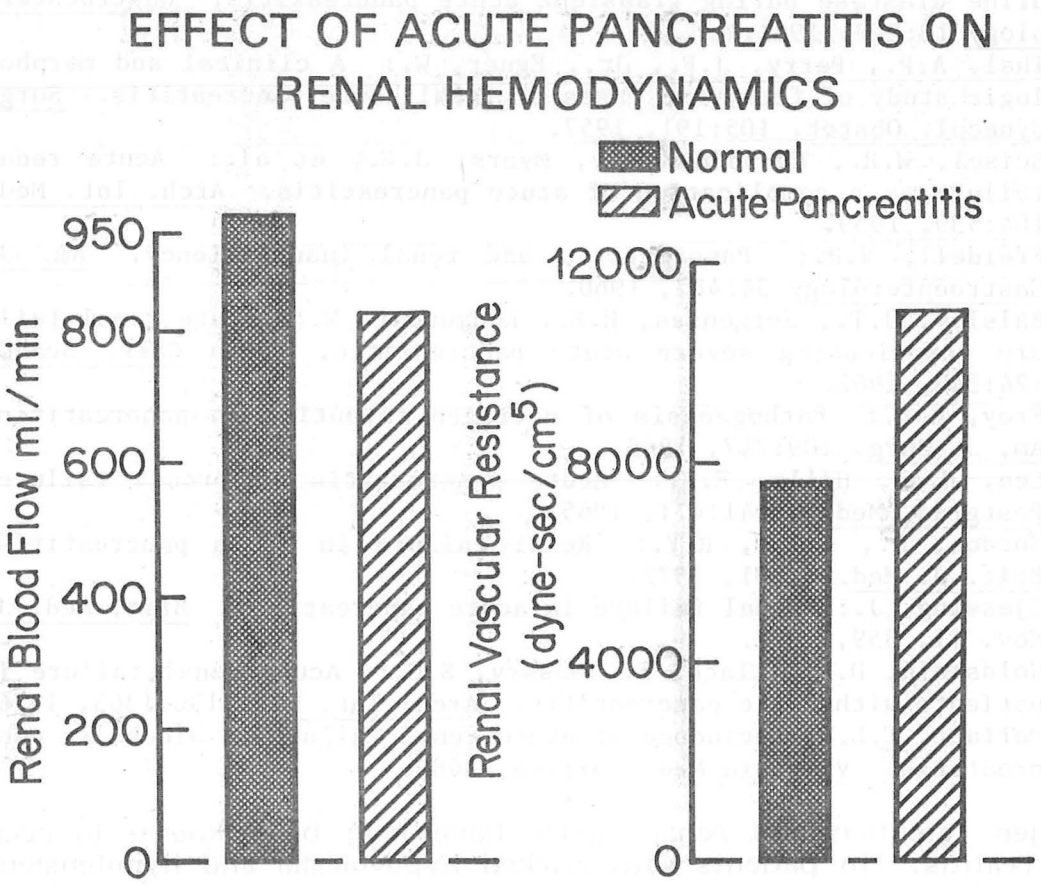
Nitrogen retention and renal failure have long been known to occur in acute pancreatitis. In patients with marked hypovolemia and hypotension, reduced renal blood flow with ensuing ischemia is the probable cause. However, renal failure has been well documented in patients with acute pancreatitis who are not hypotensive and have no evidence of hypovolemia.

Lee and Hills reported four cases of renal failure during acute pancreatitis which occurred without documented hypotension. All four of these patients died and were autopsied. The kidney of all four patients revealed acute renal tubular necrosis.

Goldstein et al. have reported five cases of acute pancreatitis who developed acute renal failure in the absence of hypotension or any evidence of a reduced effective blood volume. All of these patients had complete recovery of renal function with only one requiring peritoneal dialysis.

Werner et al. also studied renal hemodynamics in the same 11 patients who were admitted with acute edematous alcoholic pancreatitis and with an elevated mean arterial pressures and increased peripheral vascular resistance. The results are shown in Figure 8.

Figure 8



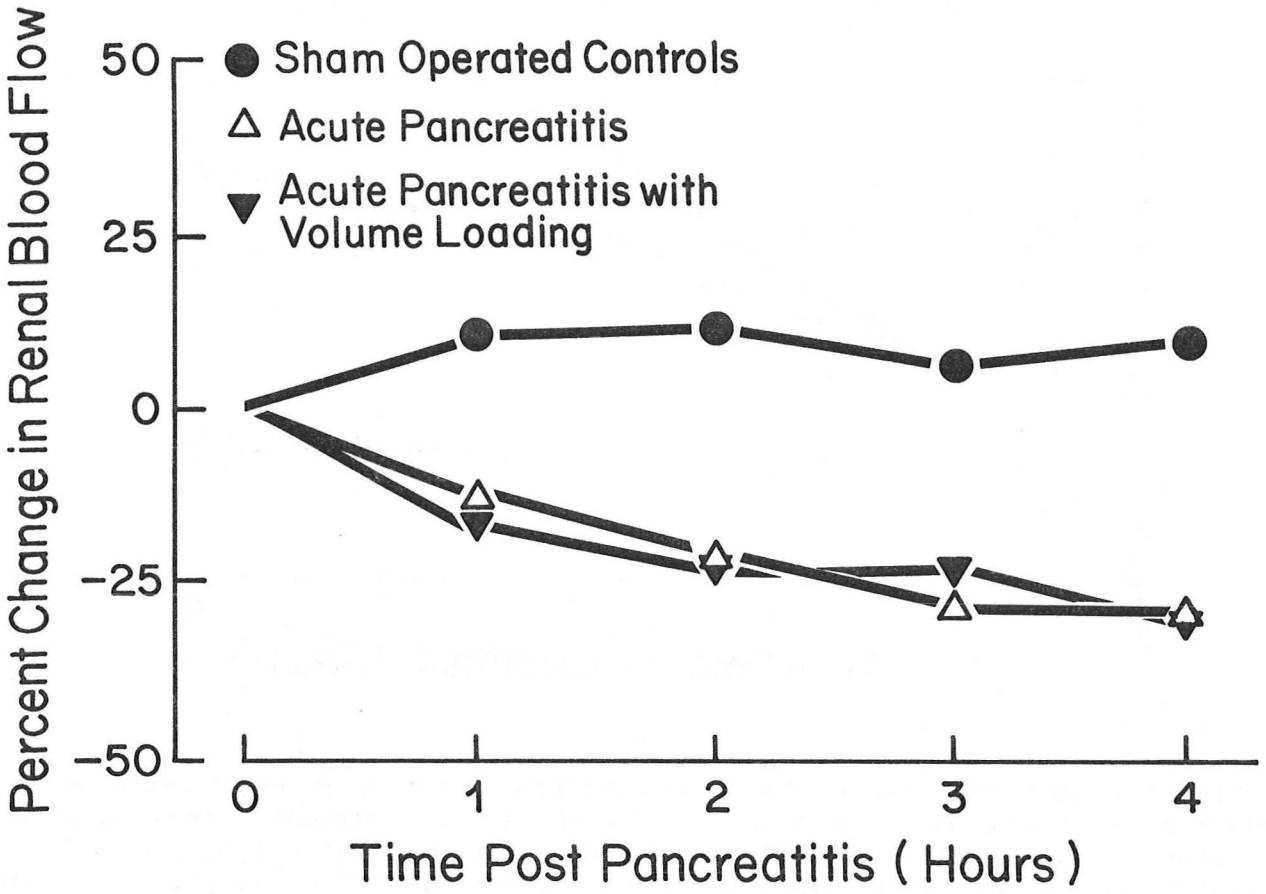
The renal blood flow was 827 ml/min during acute pancreatitis and rose to 979 ml/min during convalescence (Normal). Renal vascular resistance was very high (11,006 dyne-sec/cm^5) during acute pancreatitis and fell toward normal (7,814 dyne-sec/cm^5) during convalescence (Normal). This study strongly suggests that renal vasoconstriction is present in patients with acute pancreatitis.

33. Frey, C.F., Brody, G.L.: Relationship of azotemia and survival in bile pancreatitis in the dog. Arch. Surg. 93:295, 1966.
34. Bourland, W.A., Tobin, H.M., Reynolds, D.G., et al.: Pancreatitis induced renal vasoconstriction. Am. Surgeon 48:369, 1982.

In 1966 Frey and Brody measured cardiac output, renal blood flow, and systemic arterial pressure in dogs before and after producing bile pancreatitis. The greater reduction in renal blood flow as compared with systemic arterial pressure indicated an increased renal vascular resistance. Also, dogs who had bilaterally splanchectomy and sympathectomy from T5 to T12 had decreased incidence of azotemia and reduced mortality.

The renal and systemic cardiovascular effects of acutely inducing bile pancreatitis in dogs has been reported by Bourland et al. and the effect on renal blood flow is shown in Figure 9.

Figure 9

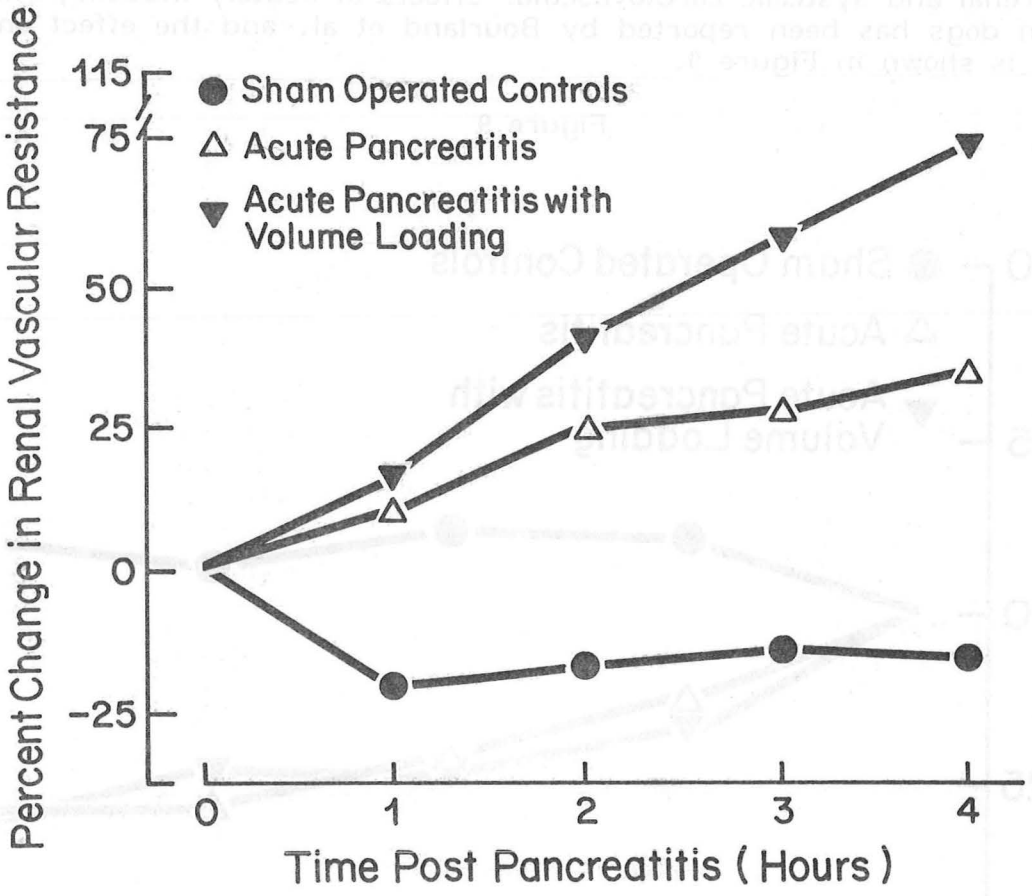


Cardiac output was measured by the thermodilution technique and renal blood flow by an electrocardiographic flow probe. Measurements were made on sham operated control dogs, dogs in which acute pancreatitis was induced and no fluids were administered, and dogs with pancreatitis in which cardiac output was maintained by fluid replacement. In this last group, mean arterial blood pressure increased. Renal blood flow was unaltered in the sham operated

controls. In the animals in which bile pancreatitis was induced and no fluids were administered renal blood flow decreased about 25%. In the animals in which bile pancreatitis was induced and cardiac output was maintained by fluid replacement renal blood flow still decreased 25%. It is thus clearly shown that renal blood flow is decreased in experimentally produced acute pancreatitis in dogs even when cardiac output is maintained and arterial pressure is increased.

The effect on renal vascular resistance in the same animals in the study by Bourland et al. is shown in Figure 10.

Figure 10



In the sham operated controls there was a slight decrease in renal vascular resistance; however, in animals with induced bile pancreatitis, there was an increase in renal vascular resistance in both the dogs without and with fluid replacement. It was also noted in these studies that the increase in renal vascular resistance was greater than the increase in total peripheral vascular resistance.

These studies in dogs clearly demonstrated that renal vasoconstriction occurs during acute pancreatitis. In addition, the magnitude of the renal vasoconstriction seems to be out of proportion to that of total peripheral vasoconstriction.

B. Heart

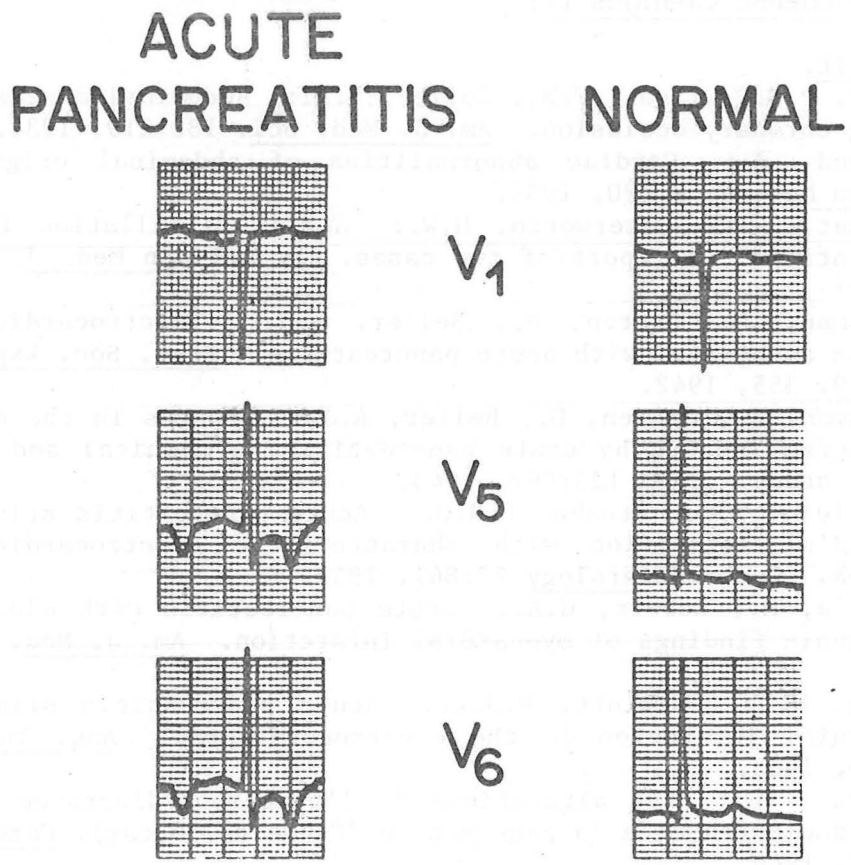
1. Ischemic Changes (?)

15. Loc. cit.
35. Barker, P.S., Wilson, F.N., Coller, F.A.: Abdominal disease simulating coronary occlusion. Am. J. Med. Sci. 188:219, 1934.
36. Drummond, J.: Cardiac abnormalities of abdominal origin. S. African Med. J. 8:520, 1934.
37. Barbezat, G.O., Waterworth, M.W.: Atrial fibrillation in acute pancreatitis. A report of two cases. S. African Med. J. 53:554, 1978.
38. Gottesman, J., Casten, D., Beller, A.J.: Electrocardiographic changes associated with acute pancreatitis. Proc. Soc. Exp. Biol. Med. 49: 355, 1942.
39. Gottesman, J., Casten, D., Beller, A.J.: Changes in the electrocardiogram induced by acute pancreatitis, a clinical and experimental study. JAMA 123:892, 1943.
40. Baugerlein, T.C., Stobbe, L.H.O.: Acute pancreatitis stimulating myocardial infarction with characteristic electrocardiographic changes. Gastroenterology 27:861, 1954.
41. Shamma'a, M., Rubeiz, G.A.: Acute pancreatitis with electrocardiographic findings of myocardial infarction. Am. J. Med. 32:827, 1962.
42. Fulton, M.C., Marriott, H.J.L.: Acute pancreatitis stimulating myocardial infarction in the electrocardiogram. Ann. Int. Med. 59:730, 1963.
43. Lambert, P.H.: Les alterations de l'electrocardiogramme dans la crise douloureuse de la pancreatite (Etude de 50 cas). Cardiologia 48:387, 1966.
44. Mautner, R.K., Siegel, L.A., Giles, T.D., et al.: Electrocardiographic changes in acute pancreatitis. So. Med. J. 75:317, 1982.
45. Dittler, E.L., McGavack, T.H.: Pancreatic necrosis associated with auricular fibrillation and flutter. Report of a case simulating coronary thrombosis (autopsy findings). Am. Heart J. 16: 354, 1938.
46. Spritzer, H.W., Peterson, C.R., Jones, R.C., et al.: Electrocardiographic abnormalities in acute pancreatitis: Two patients studied by selective coronary arteriography. Military Med. 134:687, 1969.
47. Cohen, M.H., Rotsztain, A., Bowen, P.J., et al.: Electrocardiographic changes in acute pancreatitis resembling acute myocardial infarction. Am. Heart J. 82:672, 1971.

It has been known for some time that abdominal disease can cause electrocardiological changes which indicate myocardial ischemia and infarction. Also many studies of patients with acute pancreatitis have reported electrocardiographic findings of atrial and ventricular ectopy, ST segment and T-wave changes, and transient Q-waves.

Mautner et al. reviewed the electrocardiograms of patients admitted with the clinical diagnosis of acute pancreatitis. The tracings from a 57 year old male are shown in Figure 11.

Figure 11



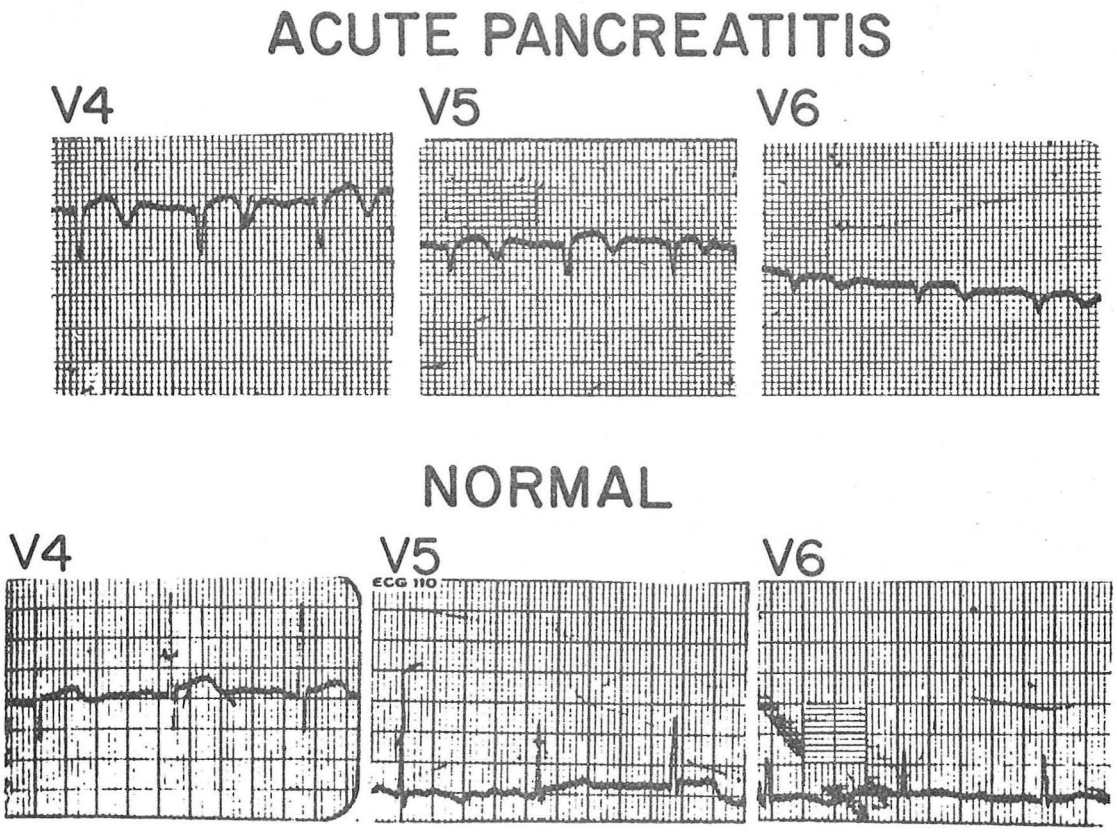
During acute pancreatitis (left panel), the EKG shows ST segment depression and T-wave inversion in leads V5 and V6. After recovery from the acute episode (right panel), there is marked improvement in the ST segments and T-waves. The patient had no evidence of coronary artery disease, and coronary arteriography was not performed.

Dittler and McGavack reported a patient with acute pancreatitis whose early clinical course suggested an acute myocardial infarction. Serial electrocardiograms revealed atrial fibrillation and flutter and slurring of the R-waves. The patient died, and at autopsy the coronary arteries were completely normal.

Spritzer et al. have reported one patient with acute pancreatitis whose electrocardiographic changes were consistent with myocardial ischemia or infarction. On admission, the electrocardiogram was normal. During an episode of chest pain, an electrocardiogram revealed marked ST segment elevation and the appearance of a Q-wave in 2, 3 and AVF. Within 36 hours, the electrocardiogram had returned to normal. Coronary arteriography in this patient showed no evidence of coronary artery disease.

Cohen et al. have also published the electrocardiographic changes in a patient with acute pancreatitis who was studied with coronary arteriography. The electrocardiographic findings are shown in Figure 12.

Figure 12



On admission (upper panel) there was loss of anterior forces with elevation of the ST segment and inversion of the T-waves in leads V4, V5, and V6. Three days later the anterior forces had returned but the T-wave remained inverted. Several months later (lower panel), there were only residual findings on the electrocardiogram with non-specific T-wave changes in leads V4, V5, and V6. Later coronary arteriography was performed and revealed normal coronary arteries.

It has been demonstrated quite convincingly that electrocardiographic changes of myocardial ischemia and even infarction can occur during acute pancreatitis in patients who have normal coronary arteries. The mechanism for these changes is not clear. Mautner has suggested that the cause may be coronary "spasm" in some patients.

48. Pollock, A.V., Bertrand, C.A.: Electrocardiographic changes in acute pancreatitis. Surgery 40:951, 1956.

Few animal experiments have been performed to study the electrocardiographic changes that occur during acute pancreatitis. Pollock et al. noted transient depression of the ST segment and inversion of the T-wave when acute pancreatitis was experimentally produced by injecting bile into the pancreatic duct of dogs. Somewhat similar changes could be produced by the IV injection of pancreatic "juices". Studies of myocardial blood flow in an animal model of acute pancreatitis are needed.

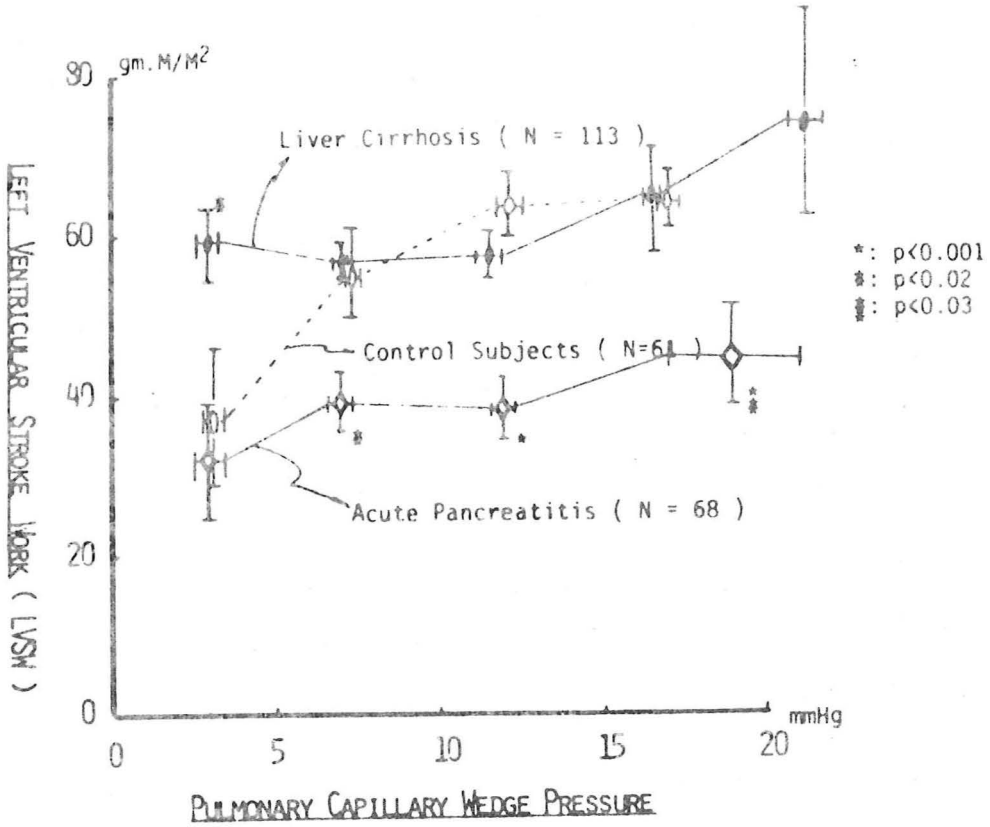
2. Contractile State

17. Loc. cit.
49. Ito, K., Ramirez-Schon, G., Shah, P.M., et al.: The myocardial depressant factor (MDF) in acute hemorrhagic pancreatitis. Trans. Am. Soc. Artit. Int. Organs 26:149, 1980.
50. DiCarlo, V., Nespoli, A., Chiesa, R., et al.: Hemodynamic and metabolic impairment in acute pancreatitis. World J. Surg. 5:329, 1981.
51. Bevilacqua, G., Chiara, O., Bigatello, L., et al.: Hemodynamic and metabolic impairment in acute pancreatitis. In: Controversies in Acute Pancreatitis. Hollander, L.F. (ed.), Berlin: Springer-Verlag, 1982, pp. 18.
52. Siegel, J.H., Cerra, F.B., Peters, D., et al.: The physiologic recovery trajectory as the organizing principle for the quantification of hormonometabolic adaptation to surgical stress and severe sepsis. Adv. Shock Res. 2:177, 1979.
53. Siegel, J.H., Giovannini, I., Coleman, B.: Ventilation:perfusion maldistribution secondary to the hyperdynamic cardiovascular state as the major cause of increased pulmonary shunting in human sepsis. J. Trauma 19:432, 1979.

Clinically few studies have been done to determine the effect of acute pancreatitis on the contractile state of the heart; and, in those published, interpretation of the findings is difficult. Even though many studies have found that a "hyperdynamic" phase exists, most investigators have concluded that a decrease in the contractile state of the left ventricle occurs during acute pancreatitis.

A study by Ito et al. suggests that acute pancreatitis causes a decrease in the contractile state of the left ventricle and these data are shown in Figure 13.

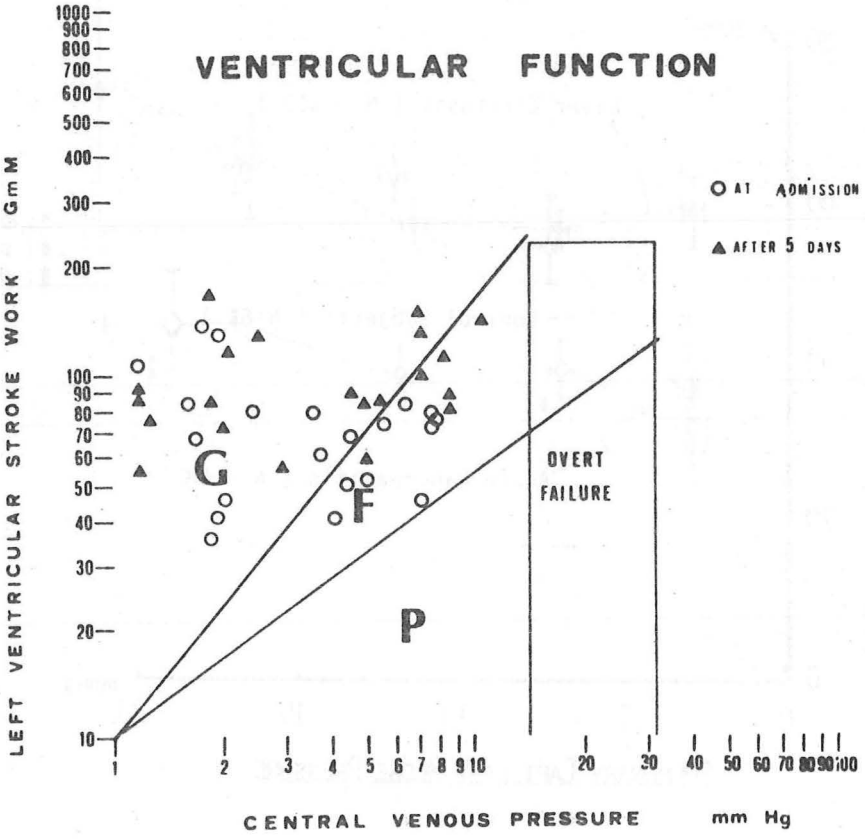
Figure 13



Ventricular function curves in which left ventricular stroke work was plotted against pulmonary capillary wedge pressure were constructed for patients with liver cirrhosis, controls, and patients with acute pancreatitis. The downward shift of the curve for the patients with acute pancreatitis as compared to the patients with liver cirrhosis and the controls was interpreted as demonstrating a decrease in the contractile state of the left ventricle. However, the patients with acute pancreatitis were not studied during their convalescent phase; thus the control level of the contractile state in these patients is not known.

A study of left ventricular function by Bevilacqua et al. suggests little, if any, effect of acute pancreatitis on ventricular function, and this data is shown in Figure 14.

Figure 14



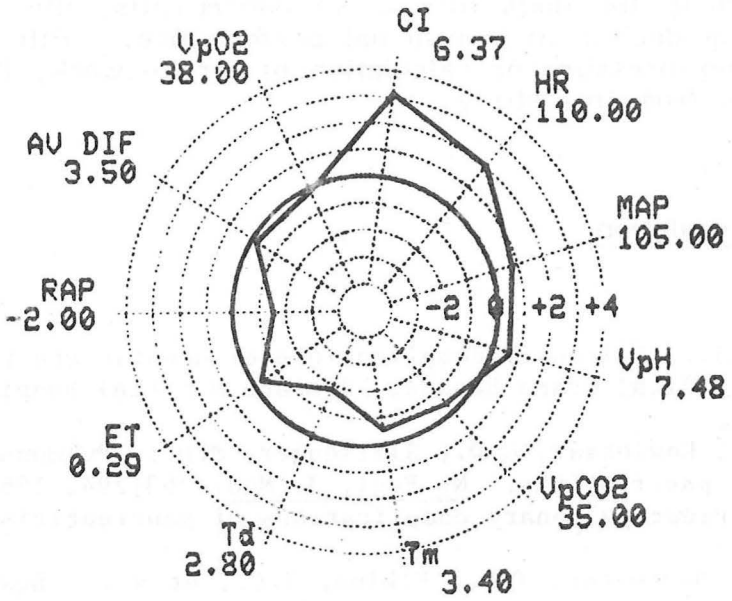
Left ventricular stroke work is plotted against central venous pressure both as log-log values. In this figure, G indicates good, F indicates fair, and P indicates poor left ventricular function. Both at admission (open circle) and after five days of hospitalization (solid triangle), ventricular function falls into the good to fair range.

Siegel et al. have described a "hyperdynamic" state in patients with acute pancreatitis by utilizing a rather complicated method to display the hemodynamic response which is called the "State Classification Circle Diagram". This is shown in Figure 15.

Figure 15

PATIENT: 44 YEAR FEMALE WITH PANCREATITIS

HYPERDYNAMIC



The solid circle represents normal values for each of the plotted variables. The dotted circles represent + or - one standard deviation from the normal. In this patient with acute pancreatitis, the cardiac index (CI) and mean arterial pressure (MAP) were high, and mean right atrial pressure (RAP) was low. This indicates that left ventricular stroke work was relatively high and right sided filling pressure was relatively low, a finding which vaguely suggests an increase in the contractile state of the left ventricle. Also, the time of dye clearance from the left ventricle (Tm) and the ejection time (ET) were decreased, findings which further indicate an increased sympathetic drive to the heart. Finally, total body arteriovenous oxygen difference (AV DIF) was low which indicates that the cardiac output was high relative to the level of oxygen consumption by the body.

From these various clinical studies, it is impossible to come to any firm conclusion concerning the effect of acute pancreatitis on the contractile state of the left ventricle. However, it is suggested that a transient increase in the contractility of the left ventricle may occur.

54. Lefer, A.M., Glenn, T.M., O'Neill, T.J., et al.: Inotropic influence of endogenous peptides in experimental hemorrhagic pancreatitis. Surgery 69:220, 1971.

Animal studies have added little insight to our understanding of the effects of acute pancreatitis on the contractile state of the heart. Lefer et al. measured central venous pressure (right sided filling pressure) and cardiac output in dogs who had either a sham operation or the experimental production of acute pancreatitis. Since cardiac output fell significantly lower at a comparable central venous pressure in the dogs with acute pancreatitis, the authors concluded that there was a decline in myocardial performance. With no measurement of left sided filling pressure or calculation of stroke work, it is difficult to make any conclusions from this study.

C. Pulmonary Circulation

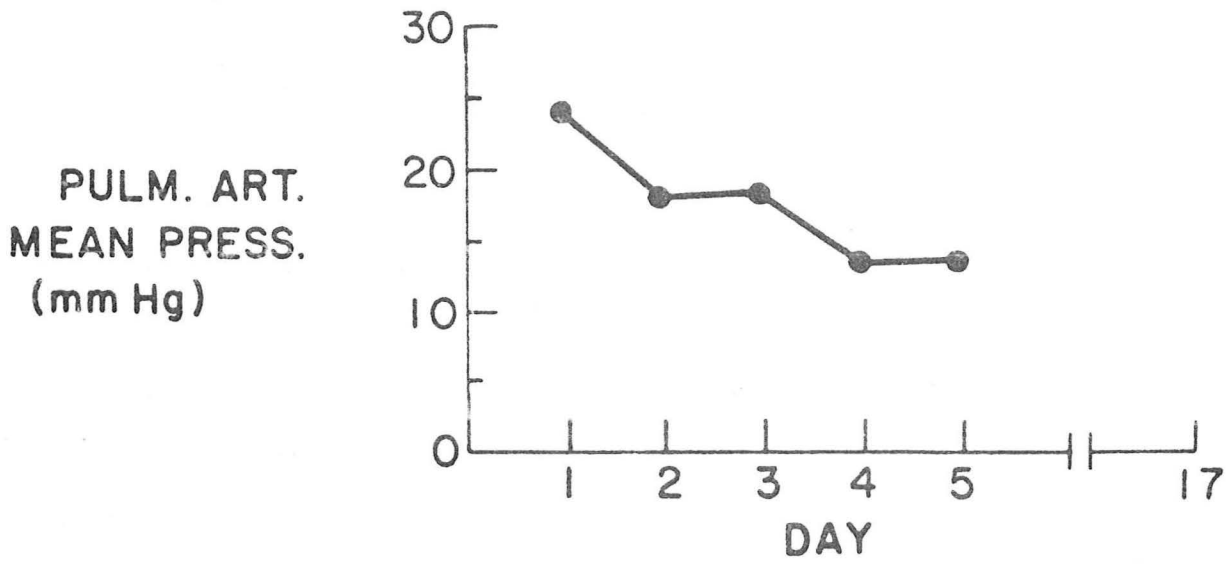
18. Loc. cit.
20. Loc. cit.
55. Robertson, K.J.: Pulmonary complications of hepatic and pancreatic disease. Medical Grand Rounds, Parkland Memorial Hospital, May 24, 1979.
56. Roseman, D.M., Kowlessar, O.D., Sleisenger, M.H.: Pulmonary manifestations of pancreatitis. N. Engl. J. Med. 263:294, 1960.
57. Kaye, M.D.: Pleuropulmonary complications of pancreatitis. Thorax 23:297, 1968.
58. Kellum, J.M., DeMeester, T.R., Elkins, R.C., et al.: Respiratory insufficiency secondary to acute pancreatitis. Ann. Surg. 172: 657, 1972.
59. Hayes, M.F., Jr., Rosenbaum, R.W., Zibelman, M., et al.: Adult respiratory distress syndrome in association with acute pancreatitis: evaluation of positive end expiratory pressure ventilation and pharmacologic doses of steroids. Am. J. Surg. 127:314, 1974.
60. Warshaw, A.L., Lesser, P.B., Rie, M., Cullen, D.J.: The pathogenesis of pulmonary edema in acute pancreatitis. Ann. Surg. 182: 505, 1975.
61. Rovner, A.J., Wescott, J.L.: Pulmonary edema and respiratory insufficiency in acute pancreatitis. Radiology 118:513, 1976.
62. Miyashiro, A., Grosberg, S.J., Wapnick, S.: Reversible pulmonary hypertension and cardiac failure with chronic recurrent pancreatitis. Chest 71(5):669, 1977.
63. Nath, B.J., Warshaw, A.L.: Pulmonary insufficiency. In: Complications of Pancreatitis; Medical and Surgical Management. Bradley, E.L. (ed.), W.B. Saunders Co., Philadelphia, 1982.
64. Malik, A.B.: Review Article: Pulmonary edema after pancreatitis: role of humoral factors. Circulatory Shock 10:71, 1983.

In 1979, Dr. Joy Robertson presented an excellent Medical Grand Rounds entitled "Pulmonary Complications of Hepatic and Pancreatic Disease". In this presentation, she discussed the severe and sometimes lethal changes that occur in the lungs of patients with acute pancreatitis. These complications included pleural effusion, pulmonary emboli, hypoxia, and pulmonary edema. Many studies have been published concerning these problems and it is now clear that acute respiratory distress syndrome (ARDS) can occur in patients with acute

pancreatitis. However, in this Medical Grand Rounds, we will limit our discussion to the effects on the pulmonary hemodynamics in less ill patients who are not in pulmonary edema and who have minimal pulmonary parenchymal changes.

There are few studies which have made hemodynamic measurements in the pulmonary circulation of patients with uncomplicated acute pancreatitis. Miyashiro et al. have reported a patient with reversible pulmonary hypertension and right heart failure during an episode of recurrent chronic pancreatitis. The results of this study are shown in Figure 16.

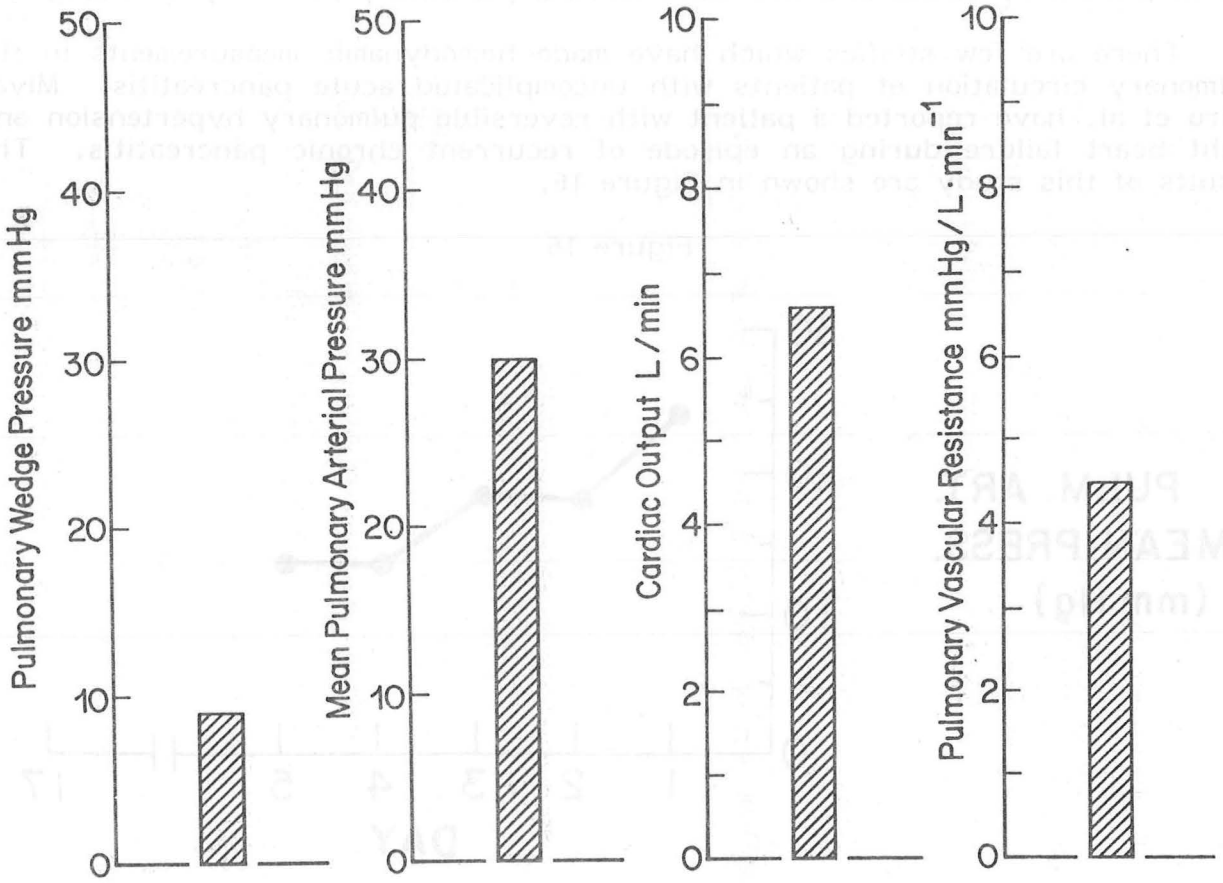
Figure 16



On admission the mean pulmonary artery pressure was 25 mmHg and the patient was in right heart failure. During the next five days the pancreatitis subsided and the mean pulmonary artery pressure fell to normal. There was no evidence of pulmonary emboli. Clinically the right heart failure disappeared as the pulmonary artery pressure fell.

Halmagyi et al. measured pulmonary pressures with a Swan-Ganz catheter and cardiac output by the Fick method in three patients who were admitted with acute hemorrhagic pancreatitis. Some of the results of their study are shown in Figure 17.

Figure 17



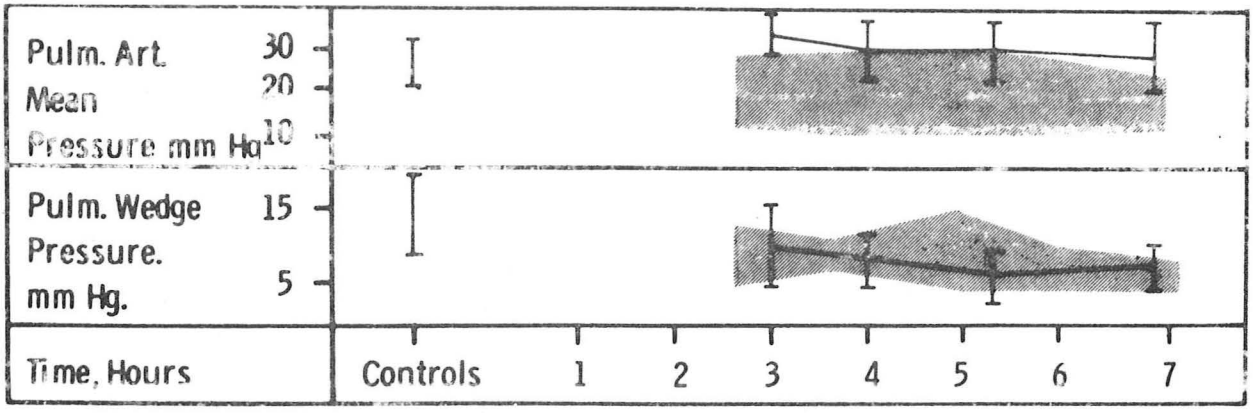
On admission the pulmonary wedge pressure was 9 mmHg, the mean pulmonary artery pressure was 30 mmHg, the cardiac output was 6.6 liters, and the pulmonary vascular resistance was 4.5 mmHg/L/min. Thus, these three patients had pulmonary hypertension which was principally due to an increased pulmonary vascular resistance.

20. Loc. cit.

65. Lee, B.C., Malik, A.B., Barie, P.S., Minnear, F.L.: Effect of acute pancreatitis on pulmonary transvascular fluid and protein exchange. Am. Rev. Respir. Dis. 123:618, 1981.

Several studies in animals have examined the effect of acute pancreatitis on pulmonary hemodynamics. Halmagyi et al. have also studied the pulmonary circulation during the experimental production of acute pancreatitis. Some of the results of their studies in dogs are shown in Figure 18.

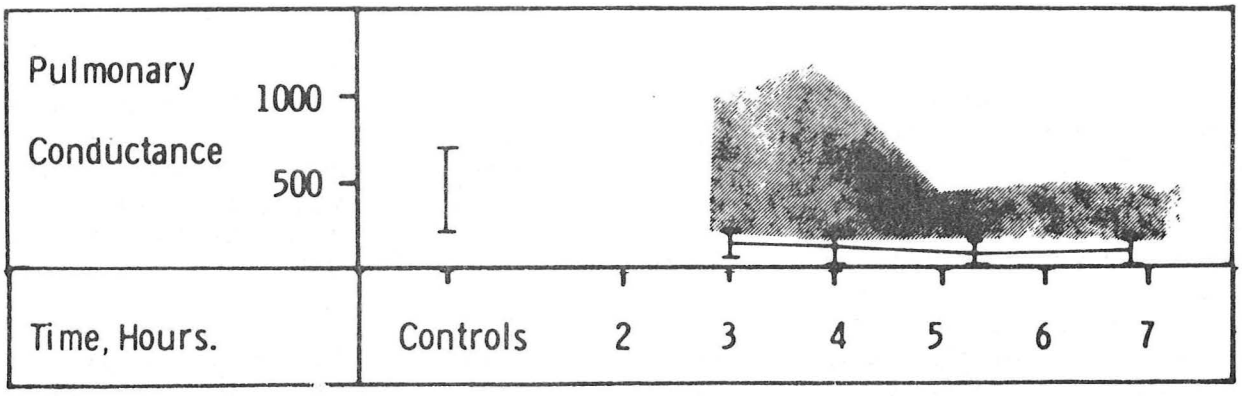
Figure 18



The shaded area represents the values in the sham operated dogs and the vertical lines with bars represent the values in the dogs with acute pancreatitis. Mean pulmonary artery pressure tended to increase in the dogs with acute pancreatitis and to decrease in the sham operated animals. Pulmonary wedge pressure was decreased in both groups.

Since Halmagyi et al. also measured cardiac output in these studies on dogs, they could calculate pulmonary vascular conductance which is the reciprocal of pulmonary vascular resistance. These data are shown in Figure 19.

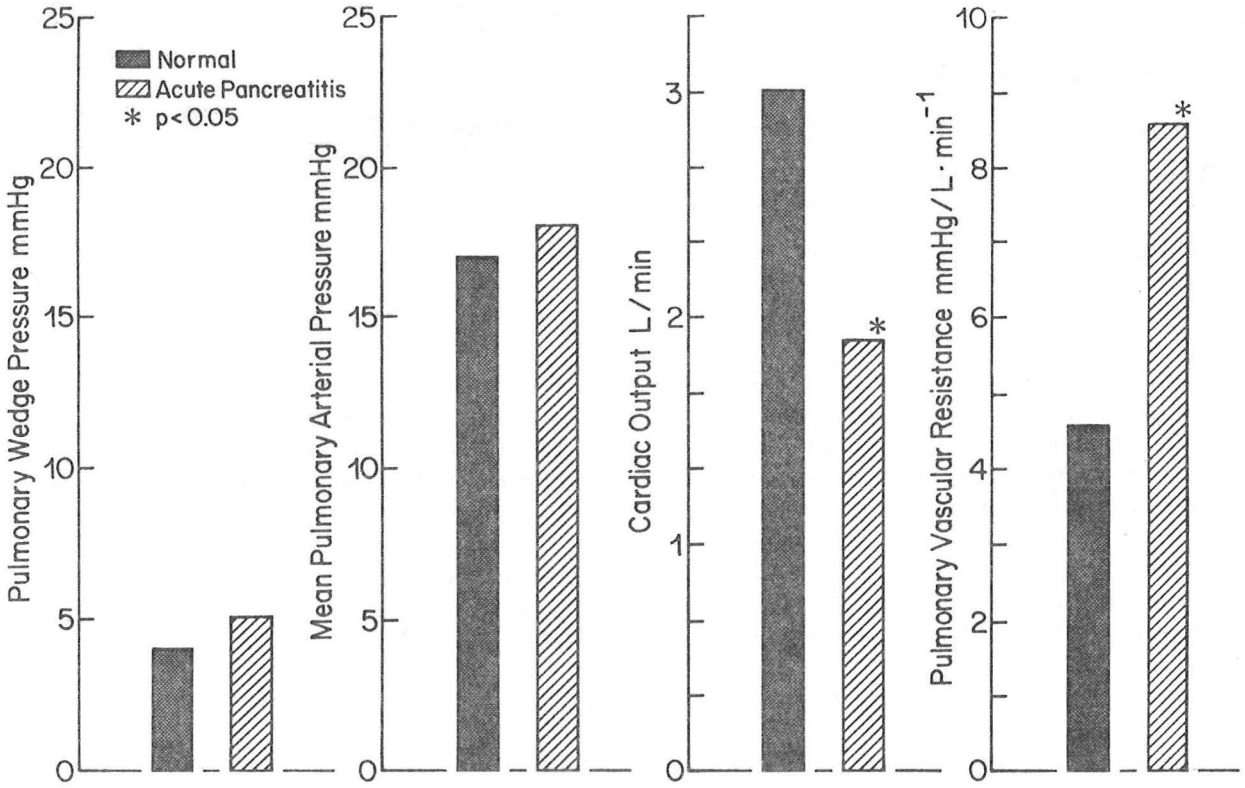
Figure 19



Pulmonary conductance was increased in the dogs with induced acute pancreatitis and was essentially unchanged in the sham operated controls. Thus an increase in pulmonary vascular resistance caused by pulmonary vasoconstriction occurred in the dogs with experimentally produced acute pancreatitis.

Lee, Malik, et al. have studied the response of the pulmonary circulation to induced acute pancreatitis in sheep and some of their results are shown in Figure 20.

Figure 20



During control conditions the pulmonary wedge pressure was 4 mmHg, mean pulmonary artery pressure 17 mmHg, cardiac output 3.0 liters/min, and pulmonary vascular resistance 4.6 mmHg/L/min. After inducing acute pancreatitis the pulmonary wedge pressure and mean pulmonary artery pressure were unchanged; however, the cardiac output had decreased to 1.9 liters/min, and the pulmonary vascular resistance had increased to 8.6 mmHg/L/min.

It therefore seems clear that pulmonary as well as systemic arterial pressure can be transiently elevated in both patients and animals with acute pancreatitis. Also, this elevation is due to an increase in pulmonary vascular resistance and not to an increase in pulmonary wedge pressure. It is therefore suggested that a transient pulmonary vasoconstriction occurs during acute pancreatitis.

III. PATHOPHYSIOLOGICAL MECHANISMS

The combination of increased mean arterial pressure, increased systemic or peripheral vascular resistance, increased renal vascular resistance, and increased pulmonary vascular resistance suggests that a generalized pressor mechanism is present during acute pancreatitis. Also, the ischemic changes in the myocardium and in the intestines are compatible with this hypothesis. As was mentioned earlier in this Grand Rounds, these responses could be due either to the release of vasoactive and inotropic agents from the pancreas during pancreatitis, or to a pressor reflex from the pancreas which is activated during acute pancreatitis, or to both of these mechanisms. We will now discuss the experimental studies concerning these two possibilities.

A. Vasoactive and Inotropic Substances

2. Loc. cit.
14. Loc. cit.
16. Loc. cit.
19. Loc. cit.
54. Loc. cit.
63. Loc. cit.
66. Maxwell, G.M., Elliott, R.B., Kneebone, G.M.: Effects of bradykinin on the systemic and coronary vascular bed of the intact dog. Circ. Res. 10:359, 1962.
67. Montague, D., Rosas, R., Bohr, D.F.: Bradykinin: vascular relaxant, cardiac stimulant. Science 141:907, 1963.
68. Ryan, J.W., Moffat, J.G., Thompson, A.G.: Role of bradykinin in the development of acute pancreatitis. Nature 204:1212, 1964.
69. Ryan, J.W., Moffat, J.G., Thompson, A.G.: Role of bradykinin in acute hemorrhagic pancreatitis. Arch. Surg. 91:14, 1965.
70. Lovett, W.L., Wangensteen, S.L., Glenn, T.M., et al.: Presence of a myocardial depressant factor in patients in circulatory shock. Surgery 70:223, 1971.
71. Wangensteen, S.L., Ramey, W.G., Ferguson, W.W., et al.: Plasma myocardial depressant activity (shock factor) identified as salt in the cat papillary muscle bioassay system. J. Trauma 13:181, 1973.

Both vasodilator and vasoconstrictor substances have been postulated to be released from the pancreas during acute pancreatitis. The most likely vasodilator substances are bradykinin and kallidin. They both produce extreme vasodilitation and increased capillary permeability. It has been postulated that these substances may play a role in the development of shock when it occurs in patients with acute pancreatitis. However, if these substances are present in patients with elevated arterial pressure, they are acting in an opposite direction to the rise in arterial blood pressure.

Lucas and Ledgerwood have postulated the release of a "cryptic pressor" substance which is responsible for the pressor mechanism during acute pancreatitis. However, studies of serum and urine catecholamine levels, urinary vanillylmandelic acid levels, and peripheral and renal vein renin levels have all been negative in patients with acute pancreatitis. Also, in dogs in which pancreatitis was experimentally induced and a transient increase in arterial blood pressure occurred, no changes have been found in plasma renin, serum epinephrine, or serum dopamine beta-hydroxylase levels.

Thus, there are no studies in either patients or animals which have been able to identify a "cryptic pressor" substance which is released by the pancreas during acute pancreatitis. More clinical and basic studies are needed to determine whether or not a pressor substance is present during acute pancreatitis.

Various inotropic agents have also been reported to be released by the pancreas when it is inflamed. An agent which decreases the contractile state of the heart has been described by Lefer et al. and is known as the myocardial depressant factor (MDF). However, it has been reported that MDF is due to an artifact of the cat papillary muscle bioassay system.

Bradykinin has been reported to increase the cardiac output and this finding was interpreted to indicate an increase in the contractile state of the heart. However, since bradykinin is a powerful vasodilator, the increase in cardiac output may be due to afterload reduction and not to an increase in the contractile state.

More studies are needed to determine whether any substances are released from the pancreas during acute pancreatitis and cause either an increase or a decrease in the contractile state of the heart.

B. Pancreatic Pressor Reflex

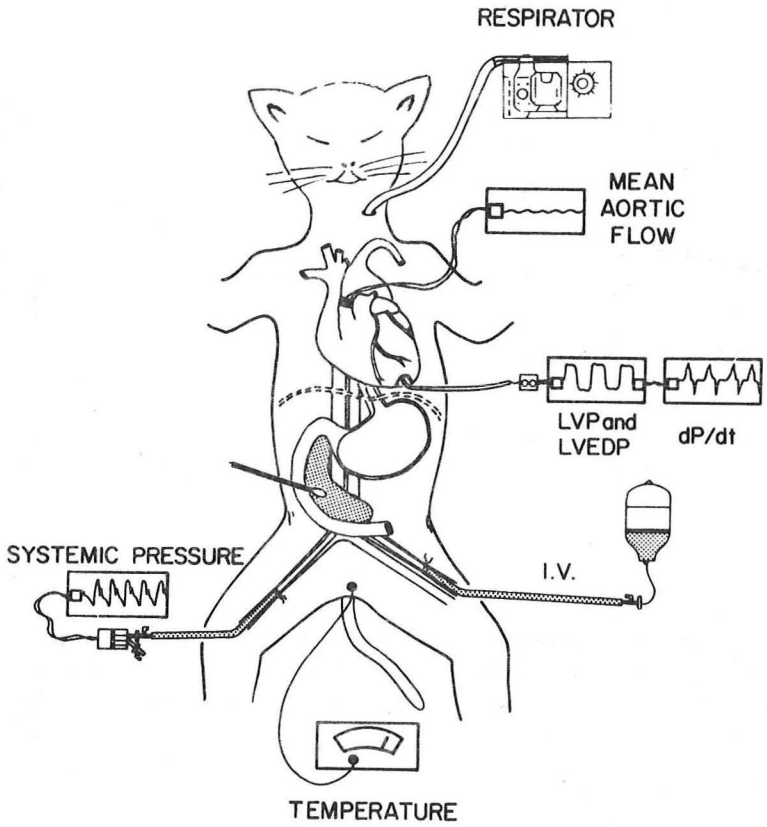
72. Chernigovsky, V.N.: Investigation of the receptors of certain internal organs. J. Physiol. U.S.S.R. 29:2, 1940.
73. Chernigovsky, V.N.: Afferent Systems of the Internal Organs. Kirov: Military Maritime Medical Academy, 1943.
74. Heymans, C., Neil, E.: Reflexogenic Areas of the Cardiovascular System. London: Churchill, 1958.
75. Chernigovsky, V.N.: Interoceptors, Lindsley, D.B., ed., Washington: American Physiological Association, 1967.
76. Saphir, R., Rapaport, E.: Cardiovascular responses of the cat to mesenteric intra-arterial administration of nicotine, cyanide, and venous blood. Circ. Res. 25:713, 1969.
77. Frank, M.H.: Cardiovascular chemoreflexes from the perfused innervated ileum of the cat. Am. J. Physiol. 228:944, 1975.
78. Ashton, J.H.: Cardiovascular reflexes elicited by stimulation of neural receptors in the liver of the dog. Ph.D. Thesis, UTHSCD, May, 1980.
79. Coleridge, H.M., Coleridge, J.C.G., Kidd, C.: Cardiac receptors in the dog, with particular reference to two types of afferent endings in the ventricular wall. J. Physiol. (London) 174:323, 1964.
80. Coleridge, H.M., Coleridge, J.C.G., Luck, J.C.: Pulmonary afferent fibers of small diameter stimulated by capsaicin and by hyperinflation of the lungs. J. Physiol. (London) 179:248, 1965.
81. Kaufman, M.P., Iwamoto, G.A., Longhurst, J.C., Mitchell, J.H.: Effects of capsaicin and bradykinin on afferent fibers with endings in skeletal muscle. Circ. Res. 50:133, 1982.
82. Ashton, J.H., Iwamoto, G.A., Longhurst, J.C., Mitchell, J.H.: Reflex cardiovascular depression induced by capsaicin injection into canine liver. Am. J. Physiol. 242:H955, 1982.
83. Longhurst, J.C., Ashton, J.H., Iwamoto, G.A.: Cardiovascular reflexes resulting from capsaicin-stimulated gastric receptors in anesthetized dogs. Circ. Res. 46:780, 1980.

84. Ordway, G.A., Longhurst, J.C.: Cardiovascular reflexes arising from the gallbladder of the cat; effects of capsaicin, bradykinin, and distension. Circ. Res. 52:26, 1983.
85. Ordway, G.A., Mitchell, J.H., Longhurst, J.C.: Bradykinin stimulates pancreatic afferents to activate the cardiovascular system. Trans. Assn. Am. Physicians 45:229, 1983.
86. Ordway, G.A., Longhurst, J.C., Mitchell, J.H.: Stimulation of pancreatic afferents reflexly activates the cardiovascular system in cats. Am. J. Physiol., in press, 1983.
87. Waldrop, T.G., Ordway, G.A., Mitchell, J.H.: Unpublished data.

The cardiovascular effects that can be reflexly activated from receptors in the abdominal viscera were first studied by Russian investigators. This area of research has largely been neglected in this country. During the last several years our laboratory has been investigating the hemodynamic changes that can be reflexly induced by activating receptors in the liver, stomach, and gallbladder. More recently, the cardiovascular effects that can be reflexively elicited by stimulation of receptors in the pancreas have been reported.

The experimental preparation for studying the cardiovascular effects of stimulating afferents in the pancreas is shown in Figure 21.

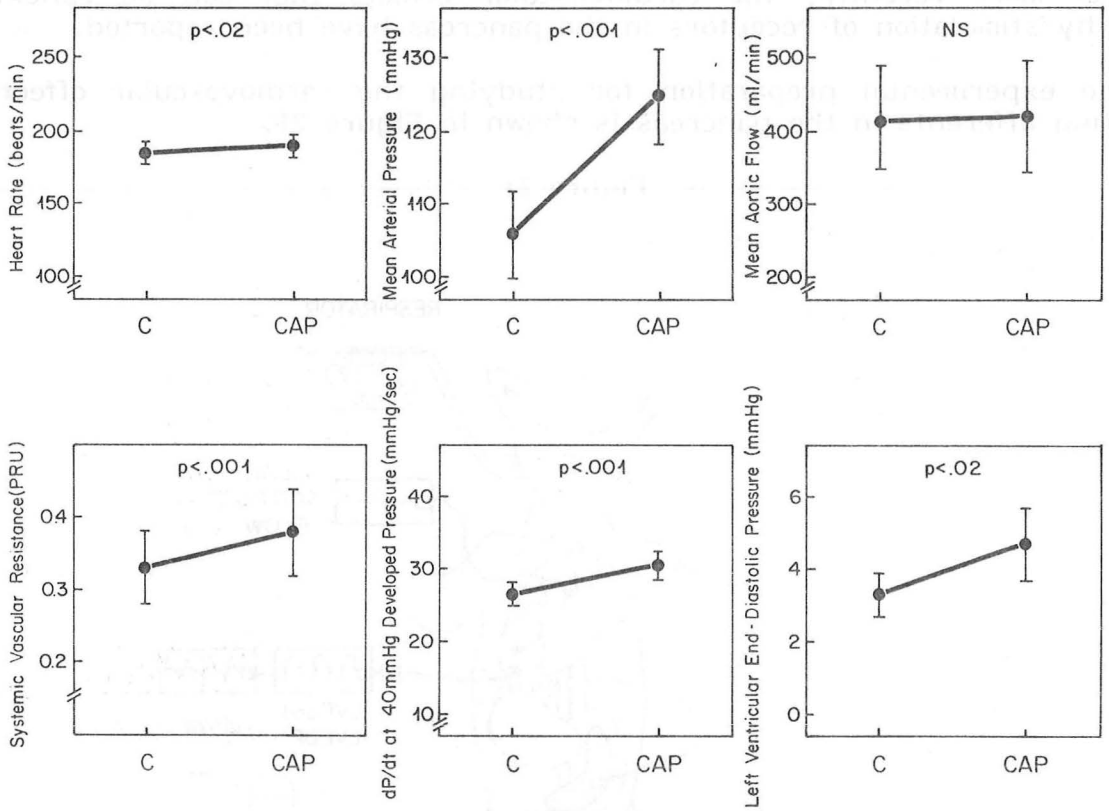
Figure 21



Cats were anesthetized with methoxyflurane and then instrumented to measure aortic flow, aortic pressure, left ventricular pressure and its derivative, and heart rate. In our initial investigations, capsaicin, was painted on the surface of the pancreas with a cotton swab. Capsaicin, which is a noxious substance extracted from paprika, has been used to activate unmyelinated afferent fibers or Group IV (C) fibers from the cardiopulmonary receptors (heart and lungs) and from the skeletal muscle receptors. In our studies measurements were made during control conditions and after the application of capsaicin to the surface of the pancreas.

The averaged values for the cardiovascular effects elicited in 11 cats by the application of capsaicin (200 µg/ml) to the pancreas are shown in Figure 22.

Figure 22

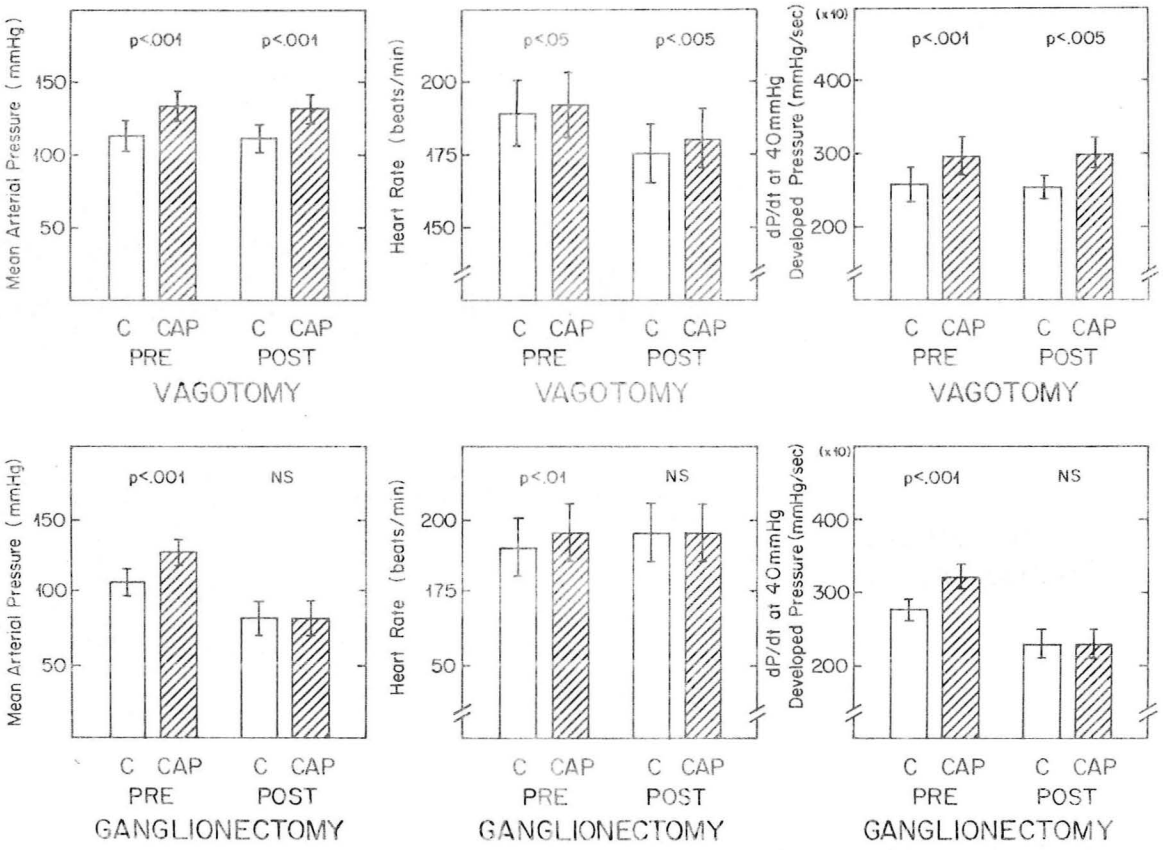


There is an increase in mean arterial pressure and systemic vascular resistance with no change in cardiac output. This indicates an increase in vasoconstrictor activity to the peripheral vessels. Also there is an increase in dP/dt at a developed pressure of 40 mmHg, an index of the contractile state of the left ventricle which is largely independent changes of preload and afterload. There is also a slight increase in heart rate and left ventricular end-diastolic pressure.

In order to prove that these cardiovascular effects were reflex in origin, it was necessary to determine the effect by interruption of the afferent fibers from the pancreas. Pancreatic afferents could reach the cardiovascular control areas through the abdominal vagus (vagal afferents) or through the celiac and

superior mesenteric ganglion (spinal or so-called "sympathetic" afferents). The results of the study to determine the route of the afferent pathways in nine cats are shown in Figure 23.

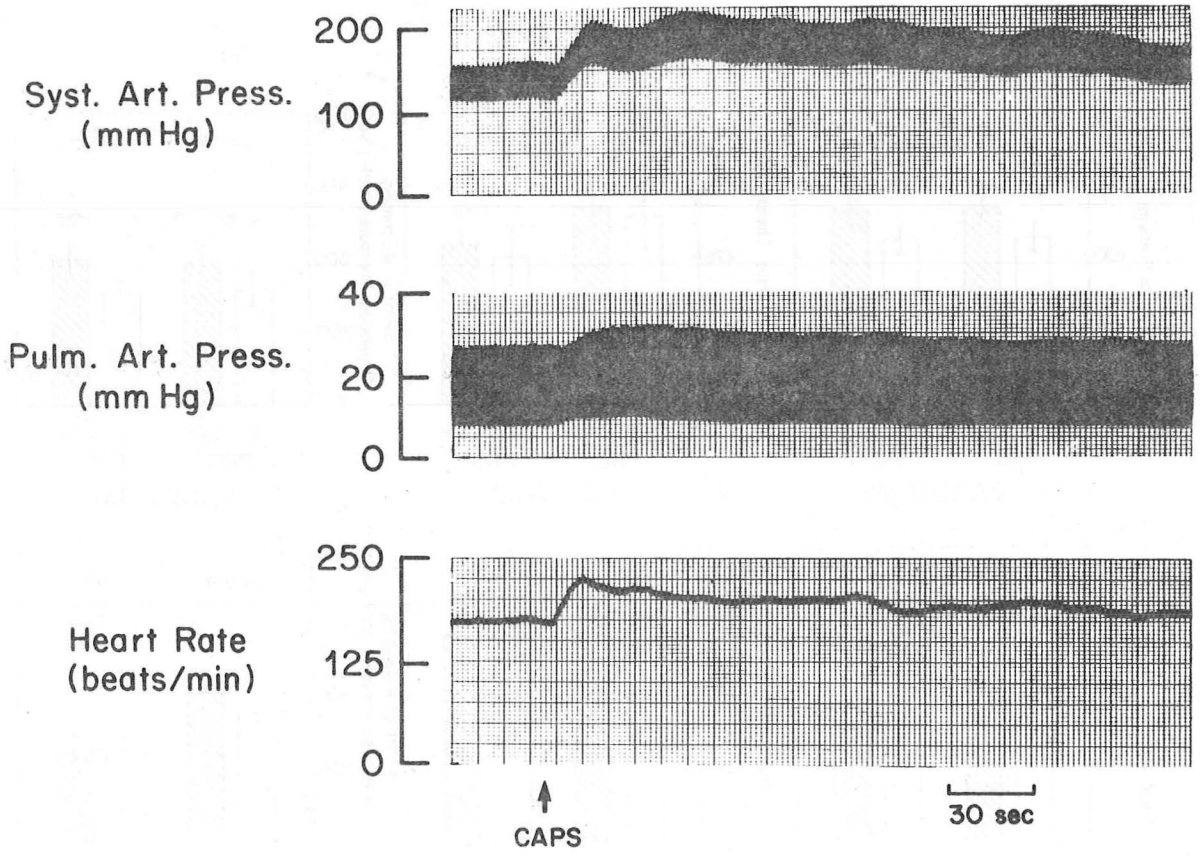
Figure 23



The effect of abdominal vagotomy are shown in the upper panels. Comparing pre- to post-vagotomy studies, there was no difference in the increase in mean arterial pressure, heart rate, or dP/dt at 40 mmHg developed pressure. Though not shown in this figure, the increase in systemic vascular resistance was also unchanged by abdominal vagotomy. The effects of ganglionectomy are shown in the bottom panels. Before ganglionectomy, there were significant increases in mean arterial pressure, heart rate, and dP/dt at 40 mmHg. These changes were abolished by ganglionectomy. This study clearly demonstrates that the cardiovascular effects are reflex in origin and further that the afferents responsible for the changes reach the cardiovascular control areas via the celiac and superior mesenteric ganglia (spinal afferents).

The cardiovascular effects reflexly induced by stimulation of pancreatic receptors with capsaicin were clearly present but not of great magnitude. Mean arterial pressure increased by about 20 mmHg and systemic vascular resistance by .08 PRU. However, these studies were performed under methoxyflurane anesthesia. To better define the true magnitude of the response, we have performed similar studies in decerebrate cats without anesthesia. The results of one of these studies are shown in Figure 24.

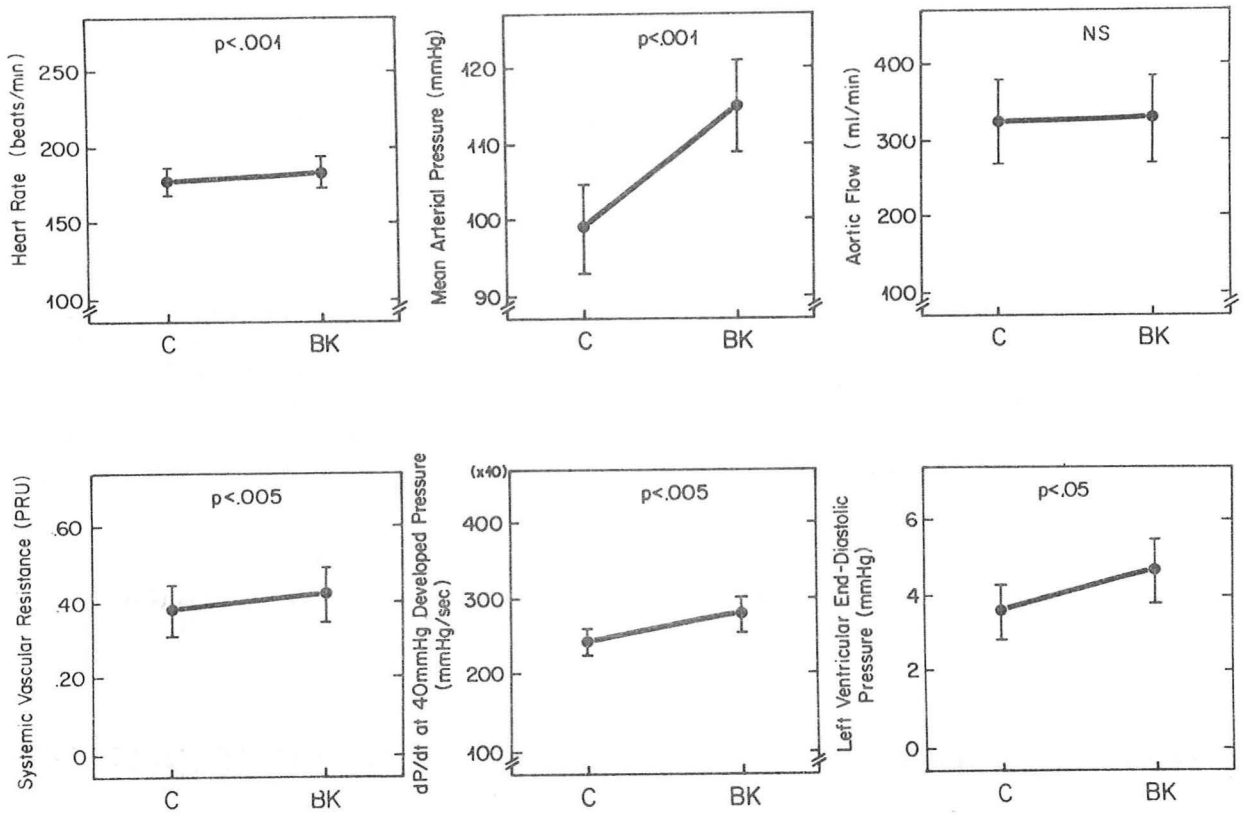
Figure 24



In this study the application of capsaicin to the pancreas caused an increase in systolic arterial blood pressure of 65 mmHg, in diastolic pressure of 50 mmHg, and in mean arterial pressure of 60 mmHg. In addition, there was an increase in pulmonary artery pressure and in heart rate.

Capsaicin was used in these studies as a pharmacological probe to demonstrate for the first time that activity of afferent fibers from the pancreas can reflexly activate the cardiovascular system. However, since capsaicin is not a substance normally present in the body, these studies do not demonstrate whether these same reflex effects might be produced under physiological or pathophysiological conditions. To address this point, the cardiovascular effects of the topical application of bradykinin, an endogenous polypeptide associated with an inflammatory process in the pancreas, was studied. The averaged values for the cardiovascular efferents elicited in 18 cats by the application of bradykinin (10 µg/ml) to the pancreas are shown in Figure 25.

Figure 25



The application of bradykinin after a longer latency period, significantly increased heart rate, mean arterial pressure, systemic vascular resistance, dP/dt at 40 mmHg, and left ventricular end-diastolic pressure. Also, as in the studies of the cardiovascular effects of capsaicin, these changes were not affected by sectioning of the abdominal vagus but were abolished by removal of the celiac and superior mesenteric ganglia. Further, it has also been shown that the cardiovascular effects that are reflexly evoked when bradykinin was applied to the pancreas are dose-dependent. The peak effect occurred at a concentration of 100 μg/ml or a total dose of 5 μg. The reflex cardiovascular effects of the application of bradykinin in decerebrate cats have not been studied, but it seems likely that the effects would be enhanced as they were with capsaicin.

These studies clearly demonstrate that a potent pressor response can be reflexly activated by stimulation of receptors in the pancreas. They cause a marked increase in both systemic and pulmonary vascular resistance. In addition, there is an increase in the contractile state of the left ventricle. The pancreatic pressor reflex may play a role in the widespread vasoconstriction that occurs in acute pancreatitis.

IV. THERAPEUTIC IMPLICATIONS

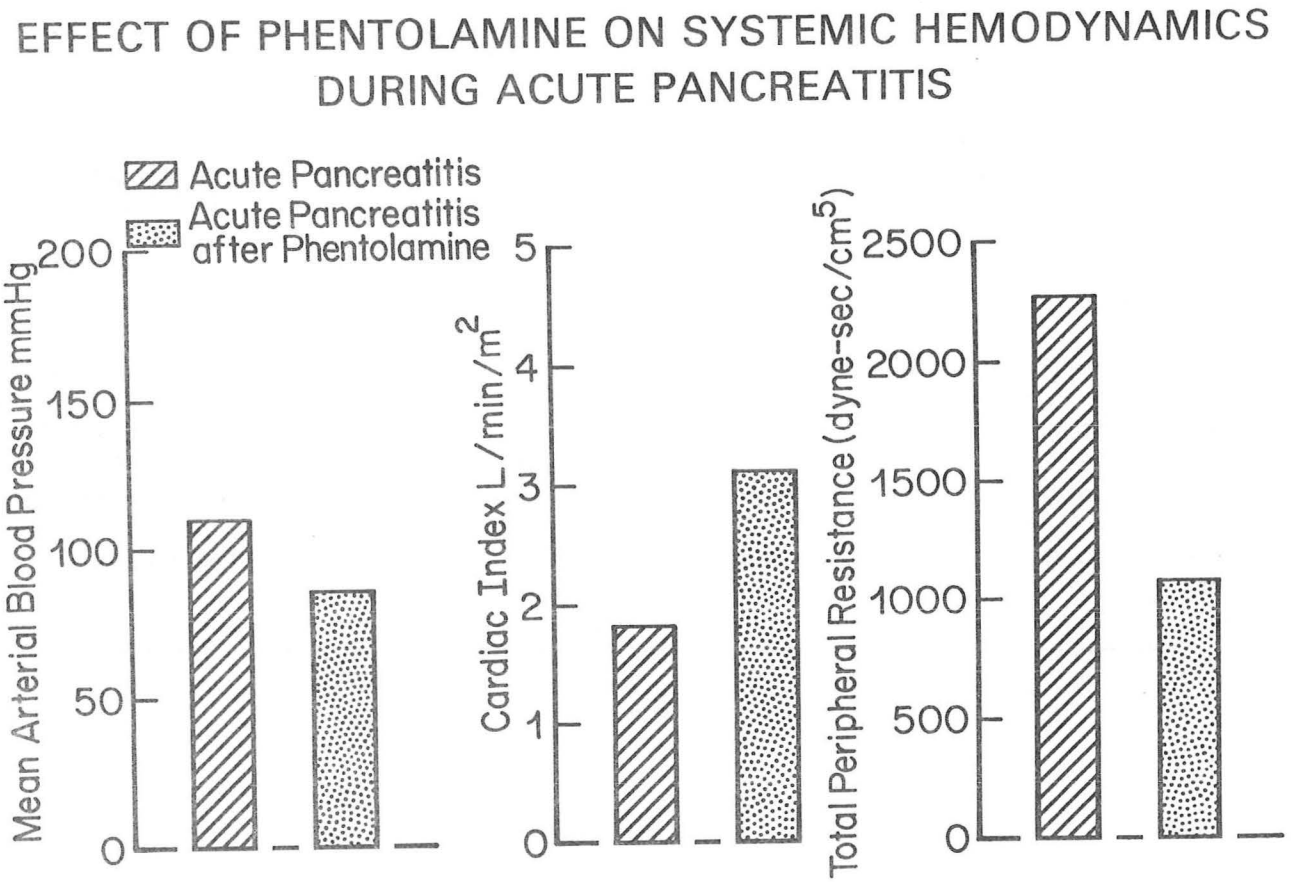
A. Vasodilator Therapy

14. Loc. cit.
19. Loc. cit.
88. Thal, A.P., Wilson, R.F.: Shock. Curr. Prob. Surg. September, 1965, p. 1.

Substantial evidence has been presented which demonstrates that a pressor mechanism is present during acute pancreatitis. Since such widespread vasoconstrictor activity is present, vasodilators have been used on a small scale to treat patients with acute pancreatitis. Thal and Wilson were the first to treat a patient who had an elevated arterial blood pressure, increased systemic vascular resistance, low cardiac output, and low urine output with phentolamine, which is an alpha-adrenergic receptor blocker. In their patient, the administration of phentolamine decreased systolic vascular resistance, increased cardiac output, and increased urine output. Renal hemodynamics were not measured in their patient.

Werner et al. were also able to improve systemic hemodynamics in one patient by administering phentolamine and their results are shown in Figure 26.

Figure 26

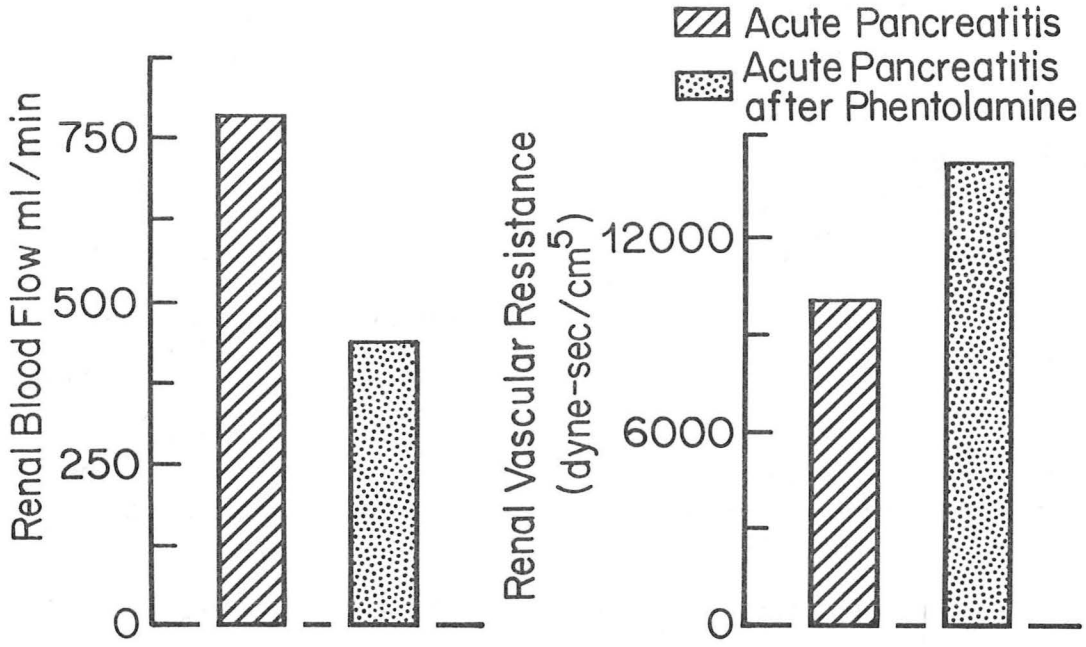


During acute pancreatitis the mean arterial blood pressure was 110 mmHg, the cardiac index was low, and the total peripheral resistance was high. After treatment with phentolamine, there was a slight fall in mean arterial blood pressure with a marked increase in cardiac output and a marked decrease in systemic vascular resistance. Also, the patient appeared to be clinically improved and urine output increased.

Since urine output increased in this patient, it was assumed that renal vascular resistance had probably decreased and renal blood flow increased. However, when such measurements were made by Werner et al., this was not the case, and their results are shown in Figure 27.

Figure 27

EFFECT OF PHENTOLAMINE ON RENAL HEMODYNAMICS DURING ACUTE PANCREATITIS

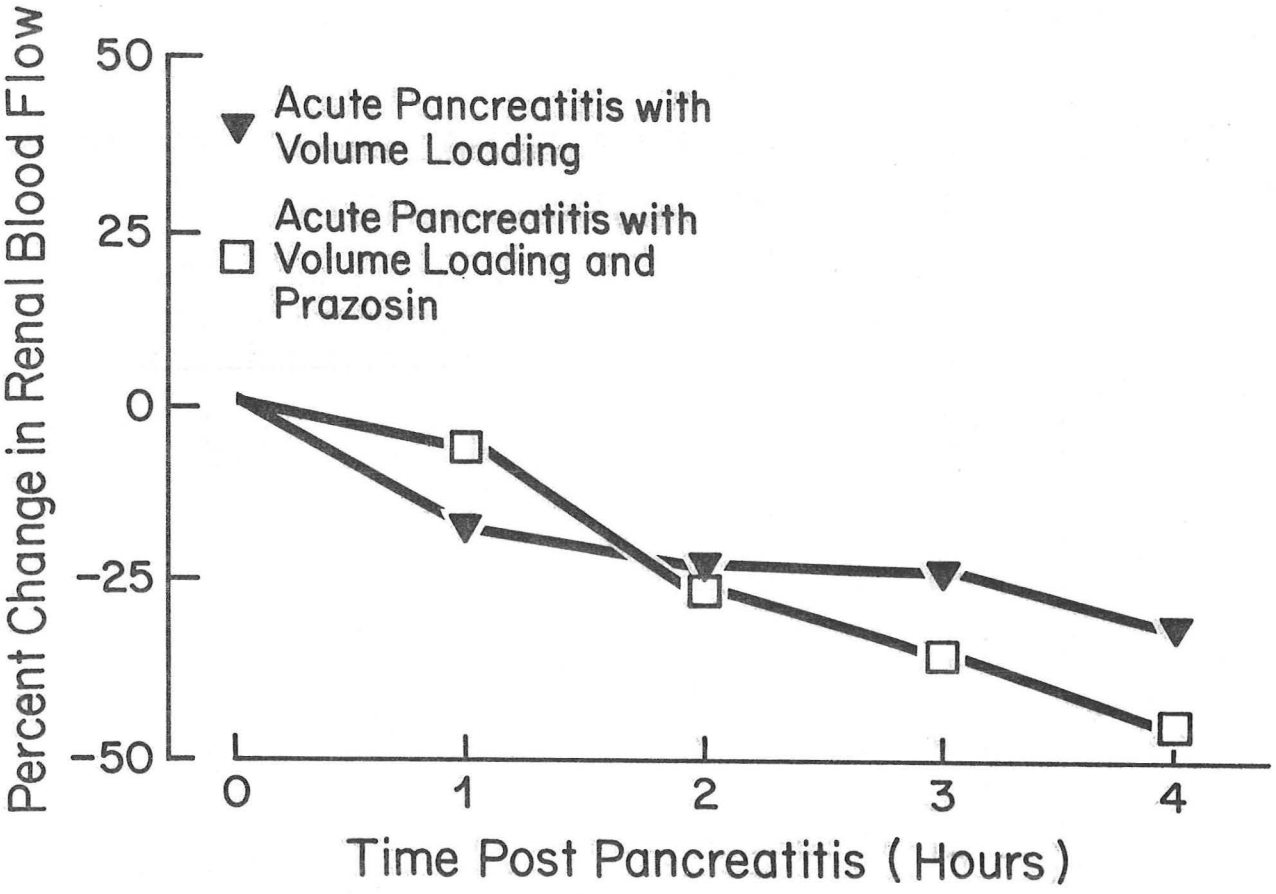


During acute pancreatitis renal blood flow was 786 ml/min and fell to 439 ml/min after the infusion of phentolamine. Also, there was a further increase in renal vascular resistance. This is a very surprising finding in that the renal vasoconstriction was thought to be due to alpha-adrenergic receptor stimulation by either a neural or humoral route.

34. Loc. cit.

Bourland et al. have investigated the effect of alpha-adrenergic receptor blockade in their dog model of acute pancreatitis by the administration of prazosin. As found in the clinical study by Werner et al., they noted an improvement in systemic hemodynamics in dogs who received the alpha-adrenergic blockade. Also, they measured changes in renal blood flow and these results are shown in Figure 28.

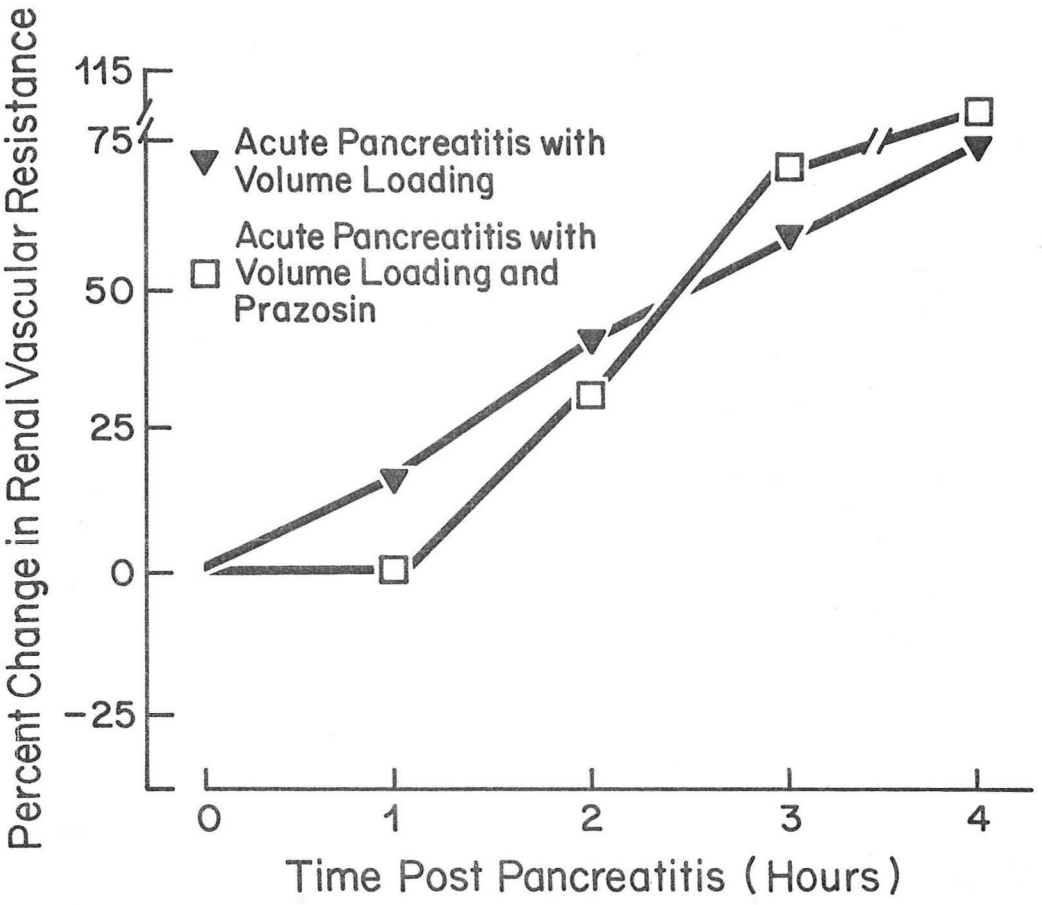
Figure 28



As seen earlier, renal blood flow was markedly decreased during acute pancreatitis. The administration of prazosin had no effect on the reduction in renal blood flow which occurred during acute pancreatitis.

Bourland et al. also measured the effect of prazosin on the renal vascular resistance changes that occurred during acute pancreatitis, and these results are shown in Figure 29.

Figure 29



As seen earlier, renal vascular resistance was markedly increased during acute pancreatitis. The administration of prazosin had no effect on the increase in renal vascular resistance that occurs during acute pancreatitis.

It thus appears that the administration of an alpha-adrenergic receptor blocker improves systemic hemodynamics both in patients and in dogs with acute pancreatitis. That is, there is a decrease in peripheral vascular resistance and an increase in cardiac output with little change in arterial blood pressure. However, even though urine output may increase, alpha-adrenergic receptor blockade appears to be detrimental to the renal circulation during acute pancreatitis. The reason for this finding is not apparent. It would be of great interest to determine whether the infusion of an alpha-adrenergic receptor blocker directly into the renal artery would reduce renal vascular resistance in patients with acute pancreatitis. Also the effect of renal nerve section on the increase in renal vascular resistance should be investigated in an animal model of acute pancreatitis.

B. Volume Loading

19. Loc. cit.
89. Lankisch, P.G.: Current status of diagnosis and conservative treatment of acute pancreatitis. In: Controversies in Acute Pancreatitis. Holander, L.F. (ed.), Berlin: Springer-Verlag, 1982, p. 143.
90. Bradley, E.L., III: Current treatment of acute pancreatitis. In: Complications of Acute Pancreatitis; Medical and Surgical Management. Philadelphia: W.B. Saunders Co., 1982, p. 16.

The recognition that a pressor mechanism is a feature of acute pancreatitis has important clinical implications in the treatment of this disease. Lucas and Ledgerwood have suggested that the pressor mechanism in acute pancreatitis is similar to that seen in pheochromocytoma. Because of the presence of the potent pressor mechanism, the patient with acute pancreatitis may appear to be "normotensive or without hypovolemia" even though he has a marked loss of effective blood volume. Patients with hypertension and oliguria secondary to a pheochromocytoma are optimally treated with a combination of alpha-adrenergic receptor blockade and volume loading; however, alpha-adrenergic receptor blockade appears to be detrimental to the renal circulation in patients with acute pancreatitis. Volume loading is the only choice for treatment. Since many patients with renal failure during acute pancreatitis are hypovolemic even though arterial blood pressure is normal or high, fluid volume must be administered with monitoring of left sided filling pressure and with urine output used as the end point.

The case report of a patient treated by Lucas and Ledgerwood is described in Figure 30.

Figure 30

A 35-year-old white male was admitted with acute relapsing pancreatitis attributed to alcohol. Physical examination revealed marked epigastric guarding with diminished bowel sounds. Amylase creatinine clearance ratio was 7.2% (normal <4%). Vital signs on admission included a blood pressure of 130/80, pulse rate of 90, and temperature of 99.6°F. Over the next 24 hours, he was given a total of 4,200 cc of Ringer's lactate. Blood pressure had risen to 150/100 and pulse to 100, but urine output had gradually declined to less than 10 cc/hr. A Swan-Ganz catheter was introduced into the pulmonary outflow tract, demonstrating reduced central filling pressure. Vigorous fluid therapy was then begun, monitoring the central filling pressure until urine output began to rise. After administration of an additional 5000 cc of balanced salt solution within the second 24 hours, urine output rose to 70 cc/hr. The pulse decreased to 86, but the blood pressure remained somewhat elevated at 140/90. As the pancreatitis resolved, the patient became normotensive.

COMMENT: "Normal" blood pressure does not reflect the adequacy of renal perfusion in the face of a circulating vasopressor in patients with pancreatitis. Fear of overloading the "hypertensive" patient with fluids is one of the major causes of renal failure in these patients. Fluid therapy is best adjusted in acute pancreatitis by monitoring central filling pressure and urine output.

This patient clearly illustrates the clinical implications of a pressor mechanism being present in patients with acute pancreatitis.

V. CONCLUSIONS

The evidence seems convincing that a pressor mechanism is present during acute pancreatitis. To date there is no evidence for a vasopressor substance being released by the pancreas; however, a pancreatic pressor reflex has been described and this reflex may play a role in the widespread vasoconstriction that occurs during acute pancreatitis. Vasodilator therapy with an alpha-adrenergic blocker improves the systemic hemodynamics both in patients and in animals with acute pancreatitis. However, renal vasoconstriction, which is present during acute pancreatitis, appears to become greater after alpha-adrenergic blockade. The reason for this finding is not apparent. It is clear that more studies are needed in both the clinical arena and in the research laboratory in order to better understand the cardiovascular effects (complications?) of acute pancreatitis.