Nonocclusive Mesenteric Vascular Disease:
Clinical and Experimental Observations

LOUIS G. BRITT, M.D., RICHARD C. CHEEK, M.D.

Department of Surgery, University of Tennessee College of Medicine, Memphis, Tennessee 38103

VASCULAR catastrophe involving the mesenteric circulation continues to puzzle the clinician because of bewilderment concerning etiology, diagnosis and therapy. Recognition of organic mesenteric arterial or venous occlusion before the patient becomes moribund coupled with advanced surgical technics makes these patients amenable to treatment.

In contrast the syndrome of nonocclusive mesenteric vascular disease, though widely described [2, 3, 5, 6, 7, 9, 11, 14] remains enigmatic. Initially an alteration in cardiovascular dynamics decreases mesenteric arterial flow. As flow decreases, hydrostatic pressure becomes less than arterial wall tension, and the vessels collapse. Depending on subsequent events, this process may reverse without clinical apparent damage; or may progress through stages to intestinal infarction and death. Reported clinical studies of this syndrome mainly attempt to define the symptom complex with relatively few suggestions for improving patient management. Most experimental models utilize acute or chronic organic occlusion, rather than functional occlusion; these studies provide imperfect understanding of the pathophysiology and recommendations for therapy have been sketchy or of questionable applicability.

Difficulties encountered in managing patients prompted us to analyze our clinical material and attempt to construct an experimental model to study this condition.

Presented at the Annual Meeting of the Southern Surgical Association, December 9–11, 1968, Boca Raton, Florida.

Supported by a grant from the Memphis Heart Association.

Clinical Material

There were 45 patients with acute mesenteric vascular disease admitted to the City of Memphis Hospitals from 1954–1968, 28 of whom were previously reported.[3] Sixteen patients, 36%, had nonocclusive disease, eight of which were recognized in the past 3 years (Table 1). There were nine men and seven women with an average age of 72 years. The diagnosis was proven at operation in eleven patients and at autopsy in five. The mortality rate was 88% in patients with nonocclusive disease and 72% in patients with organic occlusion.

Clinical Picture

Symptoms and signs of nonocclusive disease may be indistinguishable from those of arterial or venous occlusion. Certain aspects of the history may indicate the diagnosis in elderly patients with vague abdominal complaints (Table 2). Most patients had vague abdominal pain accompanied by weight loss in preceding weeks or months. Almost invariably there was a history of organic heart disease, cardiac decompensation, or arrhythmias often poorly controlled by digitalis. Abdominal physical findings were generally less impressive than the complaints would suggest. One striking observation was a changing character of bowel sounds varying at different observations from sounds characteristic of ileus, to normal, or of obstruction. Shock was uncommon initially but varied with the dura-

tion and severity of the process. Laboratory tests were nondiagnostic. Leucocytosis of more than 15,000 was present in 75%, generally reflecting the degree of intestinal necrosis. Atrial fibrillation was present in 63%. Plain abdominal x-ray films usually showed nonspecific ileus. Selective superior mesenteric angiography established the preoperative diagnosis in two patients. There was sudden abnormal tapering and obliteration of intestinal branches, nonvisualization of mesenteric arcades and a lack of definition of intramural vessels, Figure 1.

Operative Findings

Seven patients who were operated upon had extensive intestinal gangrene with a patent, pulsatile superior mesenteric arteries. One patient with infarction survived extensive small bowel and colon resection.

In four patients the process was less severe. The intestines appeared cyanotic or pale, either atonic or with tonic contraction rings present. The superior mesenteric arteries were not occluded, but there were diminished or absent pulsations in distal arterial arcades. In three patients splanchnic block at the time of operation produced return of pulsations, of bowel color, and of peristalsis. One patient had combined epidural block and splanchnic block, and one had epidural block only.

TABLE 1. *Etiology of Acute Mesenteric Vascular Disease*

Diagnosis	No.	%
Nonocclusive	16	36
Arterial thrombosis	15	33
Venous thrombosis	8	18
Arterial embolism	6	13
Total	45	100%

TABLE 2. *Clinical Findings in nonocclusive Mesenteric Vascular Disease*

History	No.	%
Digitalis therapy	15	94
Congestive failure	14	87
Prodromal pain	10	63
Acute colicky pain	10	63
Melena	8	50
Weight loss	6	38
Physical	**No.**	**%**
Tenderness	15	94
Decreased peristalsis	11	69
Dehydration	11	69
Distension	9	56
Hypotension	2	13

Postoperative Course

The patient who had epidural block and direct splanchnic block recovered and was discharged. The patient who had epidural block alone showed marked clinical improvement for 36 hours. He then went into coma and profound hypoglycemia which responded briefly to hypertonic glucose. In-

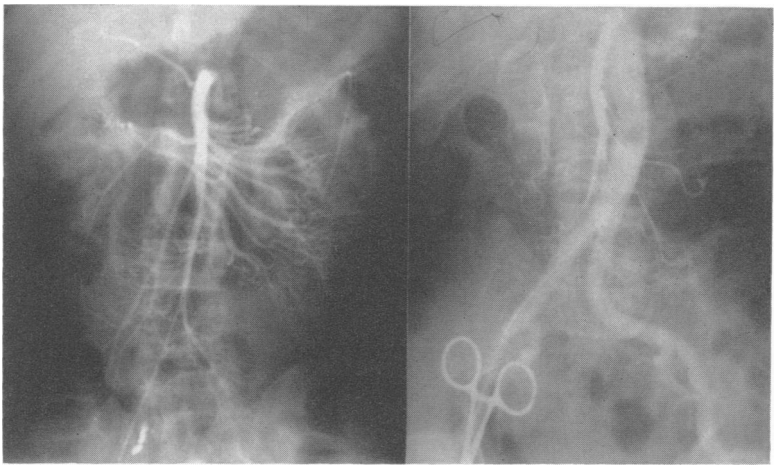

FIG. 1. Superior mesenteric arteriograms. Left: Normal (showing good filling of major branches and arcades). Right: Nonocclusive disease (showing spasm of major branches, no filling of arcades and aortic reflux).

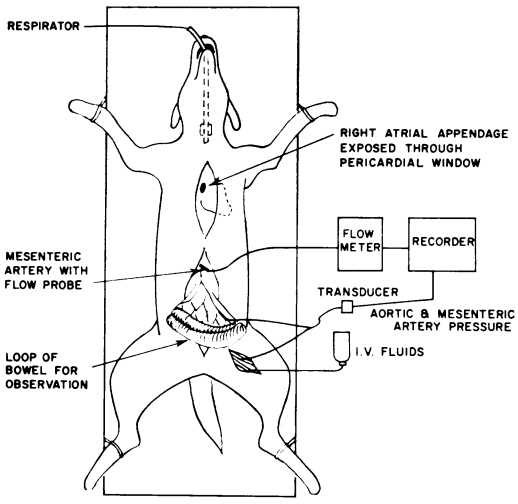

FIG. 2. Experimental preparation.

farcted terminal ileum was present at postmortem examination.

Direct splanchnic block in one patient produced excellent clinical results. A second-look operation after 24 hours disclosed a normal gastrointestinal tract. Eight days later a second episode of nonocclusive ischemia ensued. Re-operation showed intestinal infarction from the ligament of Treitz to the mid-transverse colon, and he died 12 hours later.

One patient with good clinical results from splanchnic block survived 28 days and died of other causes.

Experimental Methods

Thirty-five mongrel dogs weighing 10 to 34 Kg. were anesthetized with intravenous pentobarbital (25 mg./Kg.) and placed on an automatic ventilator with a cuffed endotracheal tube. Catheters were inserted into the femoral vein for fluid administration and into the femoral artery for monitoring systemic arterial pressure with a Statham strain gauge. The chest was opened, and a pericardial window constructed over the right atrial appendage. The superior mesenteric artery was exposed with preservation of the nerve supply, and mesenteric artery flow measured with a Carolina Medical Electronics square-wave electromagnetic flowmeter. A loop of small bowel was delivered onto the abdomen for observation, and an arterial branch cannulated for pressure determination (Fig. 2). Tracings were made on a Sanborn multichannel recorder. Cardiac output was measured with indocyanine green * and a Beckman cardiodensitometer. Rectal temperature was measured with a thermistor, and body heat loss compensated with an electric heating pad.

Experimental procedures were conducted as follows: after establishing baseline arterial pressure and superior mesenteric artery flow, atrial fibrillation was induced by painting the tip of the right atrial appendage with freshly prepared 0.05% tincture of aconitine.[3] At least 15 minutes equilibration time was allowed at each phase of the experiment before measurements were made. Epidural block was produced by percutaneous puncture through the lumbosacral interspace with a special 16 ga. needle. A #4 French ureteral catheter was threaded to the level of the ninth dorsal vertebra and 0.5 cc./Kg. of 0.5% tetracaine injected.[12] Absent knee jerk, loss of hind leg muscle tone and dropping blood pressure were ajudged evidence of satisfactory block. Splanchnic blockade was accomplished by direct infiltration around the root of the mesenteric artery with 20 cc. of 0.5% lidocaine. Regional adrenergic blockade was effected by injecting 0.2 mg./Kg. of phenoxybenzamine *[8] directly into the mesenteric artery with a 27 ga. needle. All animals were sacrificed at the end of the procedure.

Results

All data were computer analyzed within groups and between groups by the Student's "t" test for statistical significance. Atrial fibrillation produced a significant decrease in mesenteric arterial flow, averaging

* Supplied by Hynson, Westcott & Dunning, Inc.

* Supplied by G. June Oswald, Smith Kline & French Laboratories.

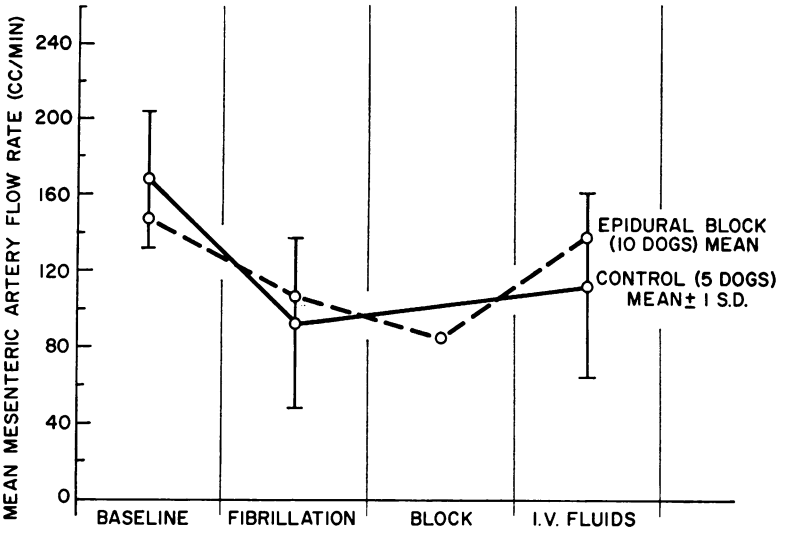

FIG. 3. Epidural block vs. control.

33.5% ($p < 0.01$). There was a corresponding drop in mean blood pressure and mesenteric artery pressure of lesser magnitude.

Cardiac output was determined in various stages of the experiments in dogs subjected to splanchnic or epidural block. There was a mean decrease of 41% in cardiac output in both groups following atrial fibrillation. Epidural block produced an additional 40% decrease ($p < 0.01$) while splanchnic block produced no significant change. Subsequent fluid administration, 1% of body weight, caused an 80% and 65% increase in cardiac output, respectively. Cardiac output was not studied in phenoxybenzamine treated dogs.

Five animals served as controls to establish the efficacy of the model. Intravenous fluids after atrial fibrillation increased mesenteric artery flow 22% which was not statistically significant (Fig. 3). In 10 dogs epidural block after fibrillation produced a 22% decrease in mesenteric artery flow. This was attributed to relative hypovolemia from loss of vasomotor tone since subsequent volume support increased flow 30% ($p < 0.05$) above fibrillation levels. Comparing this increase in mesenteric artery flow to controls receiving equal volume support only, it was not significant (Fig. 3). Direct splanchnic block in 10 dogs after atrial fibrillation produced an effect similar to epidural block, however, intravenous fluids increased flow rate after fibrillation an average of 60% ($p < 0.001$). Compared to controls, this increase was significant ($p < 0.05$) (Fig. 4). The most striking sympathetic blockade was produced in 10 animals treated with intra-arterial phenoxybenzamine. The drug alone caused an average increase in superior mesenteric artery flow of 36% ($p < 0.05$). The addition of intravenous fluids increased the flow rate 134% ($p < 0.001$) above the fibrillation level and 138% ($p < 0.001$) above the flow rate in the control animals (Fig. 5).

Bowel color and amplitude of arterial pulsation in the intestinal arteries were observed. After fibrillation, pulsations in the medium branches, distal arcades and short straight mural vessels disappeared. The bowel became pale, and peristalsis often was either violent or alternated with ileus and tonic contraction rings. Direct splanchnic or epidural block produced variable results but generally, improvement followed. Phenoxybenzamine injection produced excellent pulsations in every instance with distinct improvement in bowel color and peristaltic activity.

Peripheral resistance in the mesenteric

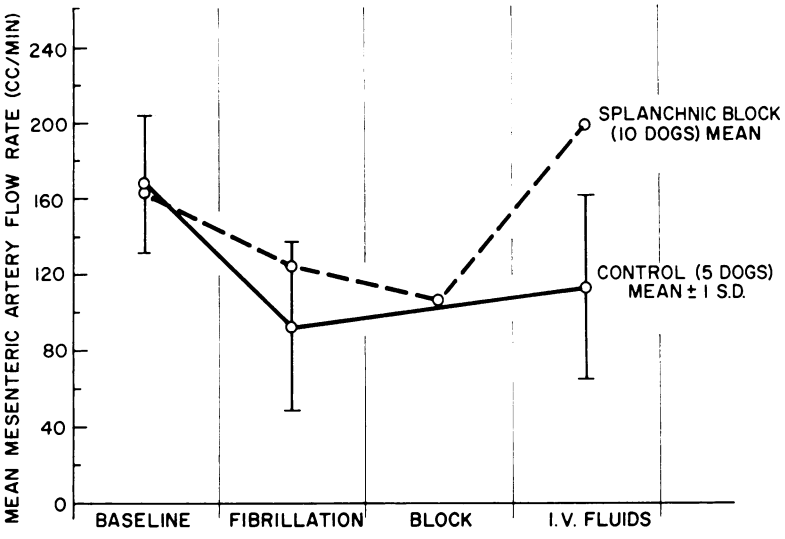

FIG. 4. Splanchnic block vs. control.

circuit was calculated from the formula

$$\text{resistance} = \frac{\text{mesenteric artery pressure (mm. Hg)}}{\text{mesenteric artery flow (cc./min.)}}$$

and expressed as peripheral resistance units (PRU). The average baseline resistance was 0.89 PRU and fibrillation produced a 20% mean increase. Changes in resistance after the various sympathetic blocks alone and after block plus volume support are shown in Table 3. The mean mesenteric artery resistance after any type of sympathetic block combined with volume support was 66% less than controls receiving fluid but no block.

Discussion

There appears to be agreement [2, 5, 6, 7, 9, 11, 14] that the most common precipitating factors in nonocclusive ischemia are severe derangements of cardiac output with especial relationship to congestive heart failure, cardiac arrhythmias, aortic insufficiency, digitalis intoxication and shock. The most plausible etiologic theory is that decreased cardiac output selectively impairs mesenteric arterial flow by redistribution of critical perfusion to more vital organs. Since mesenteric arterioles terminate as preferential channels, much of the mucosal blood

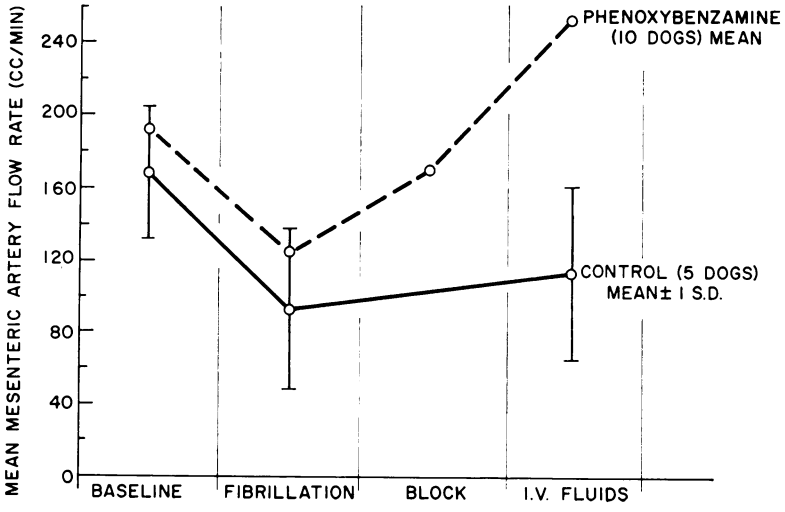

FIG. 5. Phenoxybenzamine vs. control.

flow is shunted away from capillary beds as mesenteric arteriolar resistance increases and mesenteric arteriolar pressure falls below critical closing pressure. Hypoxia results in secondary muscle spasm further reducing effective intestinal blood supply. A vicious cycle ensues as the oxygen deprived mucosal cells are no longer an effective barrier to bacterial migration and the toxic products of the gut.

The composite clinical picture consists of an elderly patient with a history of heart disease, arrhythmias, or unsatisfactory control of digitalis therapy or all three. Vague prodromal abdominal pain with weight loss and changed bowel habits are frequent. Acute severe colicky pain is often described with a paucity of abdominal physical findings. Hypotension is rarely present initially, though Fogarty and Fletcher[6] found this in 78% of their patients. Cardiac arrhythmias are often present,[2, 6, 7, 9] with atrial fibrillation 63% of the time in our patients. X-ray ileus, leucocytosis, and hemoconcentration were usually present and suggestive but non-diagnostic.

"Arterial spasm" in two patients studied by selective superior mesenteric angiography with absent visualization of intestinal branches and diminished or absent mural circulation was as expected if pathophysiologic concepts are correct. Aakhus and Brabrand[1] described selective angiograms in four patients with nonocclusive disease. They found marked constriction of the superior mesenteric arterial bed with short segmental constrictions and reduced filling of the finer arterial branches. The diagnosis was confirmed operatively in three patients and at autopsy in one. Polk[15] found arterial spasm in the mesenteric circulation after experimental venous thrombosis, but there was also venous opacification and staining of the bowel.

Because the presence or absence of necrosis cannot be determined clinically, operative intervention is necessary. Findings at operation may be so variable as to make it impossible to follow any preconceived pattern of surgical attack. Necrotic bowel must be resected. It is difficult to assess the physiologic integrity of intestine as the appearance often belies its pathologic condition.

TABLE 3. *Changes in peripheral resistance*

Procedure	Block Alone	Block and Fluid
Epidural	13%↑	30%↓
Splanchnic	18%↓	45%↓
Phenoxybenzamine	14%↓	36%↓

Most experimental studies used acute or chronic superior mesenteric artery occlusion to produce the ischemia,[12, 16, 17] which is not analogous to the pathophysiology of nonocclusive mesenteric vascular disease. Corday and associates[4] studied the mesenteric circulation during cardiac arrhythmias, hemorrhagic shock and vasopressor infusions. They did not attempt to alter the disturbed physiologic state of the mesenteric circulation. They found a 34% decrease in mesenteric artery flow after atrial fibrillation. They also showed that the increased resistance is in mesenteric arterioles. Liang and associates[12] showed that epidural blockade in experimental mesenteric artery occlusion increases survival, apparently through improved collateral circulation. Jackson and Lykins[10] reported five patients with acute postoperative intestinal ischemia who responded to serial epidural blockade. In our patients in whom infarction had not occurred, epidural block was also beneficial but inability to correct cardiovascular abnormalities limited its effectiveness. Our experimental findings with epidural block support the clinical impression of the value of reducing mesenteric vascular resistance along with volume replacement. The advantages of epidural block are ease of administration and that it may be sustained over an extended period.

Clinically, direct splanchnic block has been used.[2, 3, 6, 14] The data indicate that splanchnic block produces a more signifi-

cant decrease in vascular resistance than does epidural block and results in a greater increase in superior mesenteric artery flow. Unless a catheter is left in the retroperitoneal space splanchnic block cannot be sustained.

Williams and associates[17] utilized systemic phenoxybenzamine (0.5 mg./Kg.) in their experiments with almost uniform survival and a marked decrease in hemorrhagic enteritis. Continued deterioration of cardiac output, precipitous drop in blood pressure and early increases in peripheral resistance were eliminated. Our studies using only one-half this dose of phenoxybenzamine injected directly into the mesenteric artery produced a decrease in mesenteric resistance (36%) and a dramatic increase in superior mesenteric artery flow (136%). There were no systemic blood pressure effects. Gump[8] studied the bolus injection of phenoxybenzamine into the renal artery and showed a decreased resistance in this vascular bed. Phenoxybenzamine appears to be locally tissue-fixed after arterial injection obviating systemic effects. The information at hand indicates a beneficial result from intra-arterial phenoxybenzamine without deleterious side effects, although its duration of action remains unknown. This agent should prove useful as adjunctive therapy in nonocclusive and in occlusive lesions with associated spasm. Phenoxybenzamine could be injected at the time of diagnostic angiography and the catheter left in place for subsequent injection, or for injection directly into the artery at the time of operation.

Summary

1. Clinical findings in nonocclusive mesenteric vascular insufficiency due to an alteration in cardiac output have been described.

2. An acute experimental model simulating the clinical situation has been utilized to study mesenteric arterial flow abnormalities.

3. Epidural block, direct splanchnic block, and intra-arterial administration of phenoxybenzamine combined with support of blood volume increase mesenteric artery flow and decrease mesenteric arterial resistance in spite of continued decreased cardiac output induced by atrial fibrillation.

4. Appropriate management includes direct or indirect splanchnic block, intra-arterial phenoxybenzamine, and support of blood volume in addition to operative intervention.

References

1. Aakhus, Trygve and Brabrand, Georg: Angiography in Acute Superior Mesenteric Arterial Insufficiency. Acta Radiol., **6**:1, 1967.
2. Berger, Robert L. and Byrne, John J.: Intestinal Gangrene Associated with Heart Disease. Surg. Gynec. Obstet., **112**:529, 1961.
3. Britt, Louis G. and Hopson, W. B.: Mesenteric Vascular Insufficiency. Southern Med. J., **58**:1073, 1965.
4. Corday, Elliot, Irving, David W., Gold, Herbert, Bernstein, Harold and Skelton, Robert B. T.: Mesenteric Vascular Insufficiency. Amer. J. Med., **33**:365, 1962.
5. Drucker, William, Davis, John H., Holden, William D. and Reagen, James R.: Hemorrhagic Necrosis of the Intestine. Arch. Surg., **89**:42, 1964.
6. Fogarty, Thomas J. and Fletcher, William S.: Genesis of Nonocclusive Mesenteric Ischemia. Amer. J. Surg., **111**:130, 1966.
7. Glotzer, Donald J. and Shaw, Robert S.: Massive Bowel Infarction. New Eng. J. Med., **260**:162, 1959.
8. Gump, Frank E., Magill, Thomas, Thal, Alan P. and Kinney, John M.: Regional Adrenergic Blockade by Intra-arterial Injection of Phenoxybenzamine. Surg. Gynec. Obstet., **127**:319, 1968.
9. Heer, F. William, Silen, William and French, Samuel W.: Intestinal Gangrene Without Apparent Vascular Occlusion. Amer. J. Surg., **110**:231, 1965.
10. Jackson, Benjamin B. and Lykins, Robert: Serial Epidural Analgesia in Mesenteric Arterial Failure. Arch. Surg., **90**:177, 1965.
11. Laufman, Harold, Nora, Paul F. and Mittelpunkt, Allen I.: Mesenteric Blood Vessels: Advances in Surgery and Physiology. Arch. Surg., **88**:1021, 1964.
12. Liang, Howard, Bernard, Harvey R. and Dodd, Robert B.: The Effect of Epidural Block upon Experimental Mesenteric Occlusion. Arch. Surg., **83**:407, 1961.
13. Nahor, Amos, Milliken, James, Minton, Russell and Fine, Jacob: Technique of Celiac Blockade for Relief of Splanchnic Ischemia. JAMA, **192**:600, 1965.
14. Ottinger, Leslie W. and Austin, W. Gerald:

A Study of 136 Patients with Mesenteric Infarction. Surg. Gynec. Obstet., 124:251, 1967.
15. Polk, Hiram C., Jr.: Experimental Mesenteric Venous Occlusion: Diagnosis and Treatment of Induced Mesenteric Venous Thrombosis. Ann. Surg., 163:432, 1966.
16. Williams, Lester F., Anastasia, Louis F., Hasiotis, Christos A., Bosniak, Morton A. and Byrne, John J.: Experimental Nonocclusive Mesenteric Ischemia: Physiologic and Anatomic Observations. Arch. Surg., 96:987, 1968.
17. Williams, Lester F., Anastasia, Louis F., Hasiotis, Christos A., Bosniak, Morton A. and Byrne, John J.: Experimental Nonocclusive Mesenteric Ischemia: Therapeutic Observations. Amer. J. Surg., 115:82, 1868.

Discussion

Dr. Wishard S. Lorimer, Jr. (Fort Worth): It is so rarely that scout film of the abdomen is of any value in diagnosing the acute abdomen that I felt it worth while to show an instance of nonocclusive mesenteric vascular disease in which it was of extreme value.

This is a pathognomonic finding which enables you to differentiate preoperatively between mesenteric vascular occlusion disease and other disorders. The case in point is that of a 66-year-old woman who had been complaining of nonspecific abdominal pain. Gastrointestinal x-rays proved to be negative; she had been bitterly complaining of pain over a period of 3 months and lost about 30 pounds. She developed sitophobia, weakness, and so forth, before she came in.

When she came into the hospital, the pain had become worse, but still it was not a specific type of pain and was difficult to diagnose.

She developed severe generalized tenderness and rigidity in the first 12 hours after admission, and we took an abdominal roentgenogram which we will show.

[Slide] I don't know whether you can make this out or not, but notice the branching gas pattern in the right upper quadrant of the liver. This is gas in the portal system.

[Slide] This is a better view, notice the fine texture of this, and the fact that the gas goes to the periphery of the liver, as opposed to the gas pattern which one sees in the intestinal biliary fistula, where only the main branches are seen.

This x-ray enabled us to diagnose beforehand intestinal necrosis, to advise the family of this ominous sign, and the very grave prognosis which it carries. The pathogenesis of this entity is probably intestinal necrosis—mucosal necrosis—large amounts of gas entering the venous circulation, and large numbers of gas-forming organisms produce gas in the entire portal system. This, of course, does not occur as the usual cause of intestinal necrosis; namely, mechanical obstruction, because the interluminal pressure is increased prior to necrosis, and the venous channels are closed.

Dr. Richard C. Cheek (Closing): We have not observed portal gas embolus in our cases of nonocclusive disease. However, we have seen one patient with superior mesenteric artery embolus who had portal gas embolism, and this has been described as an almost uniformly prognostic sign of fatal outcome.

I would like to add two other points from our experimental work which Dr. Britt did not have time to mention; namely, the changes which we found in the cardiac output and in the peripheral resistance.

Cardiac output was measured by the dye dilution technic in the groups of animals receiving the splanchnic and the epidural block. Atrial fibrillation was found to produce a 41 per cent decrease in cardiac output below the baseline level. Epidural block produced a further 40 per cent decrease, while splanchnic block produced no significant change in cardiac output.

The resistance of the mesenteric circulation was calculated by dividing the superior mesenteric artery blood pressure by the mesenteric artery flow, and expressed as peripheral resistance units. Atrial fibrillation produced a 20 per cent mean increase in mesenteric resistance above our baseline rate of 0.89 peripheral resistance units.

(Slide) This slide shows the changes which we observed after the various blocks, before and after volume support. Notice that epidural block alone was the only one which produced an increased resistance, while all of the other blocks produced a decrease. We attributed this to the relative hypovolemia due to loss of caudal vasomotor tone, and supported by the fact that the cardiac output and the mesenteric artery flow decreased also in the system.

After intravenous fluid support, all blocks showed a decrease in mesenteric resistance, with an average value of 66 per cent less than the control animals receiving intravenous fluid, but no blocks.