Intestinal Blood Flow at Various Intraluminal Pressures in the Piglet with Closed Abdomen

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The influence of intraluminal pressure on intestinal blood flow was studied in two segments of the small intestine and two of large intestine ligated after insertion of intraluminal catheters in ten piglets. Intestinal segments were inflated in stepwise increments in intraluminal pressures of 15, 30, 45 and 60 mmHg and blood flow was measured with radioactive microspheres using four isotopes (Ce, Cr, Sr, Sc). Other segments were inflated to a pressure of 60 mmHg and then pressure decreased in a stepwise fashion to 30, then 0 mmHg for the last two injections. Small and large intestinal blood flow fell progressively with increasing intraluminal pressure. At 60 mmHg a forward flow of 25% of normal was still present. Furthermore, not only was there an absolute decrease in blood flow with increasing intraluminal pressure but this decrease was disproportionately large in the intestinal mucosa. A hyperemic response lasting approximately 15 minutes was observed after complete decompression. The intestinal blood flow distal to the ligated segments was always moderately increased as compared to intestinal blood flow proximal to the segments. The results reported herein are at some variance from other reported studies performed with the abdomen open and on isolated segment preparations. The reasons for these variations are discussed.

THE PATHOPHYSIOLOGY of intestinal obstruction involves mechanical obstruction to passage of air and feces accompanied by imbalance between intestinal secretion and resorption resulting in progressive bowel distention and increasing intraluminal pressure. This elevated pressure and distention of the bowel wall progressively compromises the microcirculation first by obstructing venous outflow, resulting in edema and further increase in intraluminal pressures and ultimately compromise in arteriolar blood flow. Finally, the bowel wall ischemia coupled with detrimental effects of absorbed bacterial toxins leads to necrosis and death of the bowel wall. A number of experimental studies have documented this sequence of events and have related the influence of incremental intraluminal pressure increase on intestinal blood flow.[3,5,7,8,11] To date, all observations on intraluminal enteric pressures and blood flow have been performed under relatively unphysiologic circumstances with an open abdomen and an isolated loop preparation. The latter preparation denervates the intestine and interrupts the continuity of the mesenteric vessels. Little is known about intestinal blood flow, particularly with intestinal obstruction in the intact animal with the abdomen closed. The purpose of this study was to investigate the influence of changes in intraluminal intestinal pressures on intestinal blood flow measured with radioactively labeled microspheres.

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Material and Method

Ten piglets of approximately 15 kg body weight fasted for 18 hours, were initially anesthetized with 6 cc Sernylan and subsequently pentobarbital was given intravenously as necessary. Equal sized catheters were inserted into both femoral arteries for arterial pressure monitoring and reference sampling for the microsphere blood flow studies. A catheter was placed in a femoral vein as an IV line.

All animals underwent tracheotomy and were ventilated with a Harvard volume cycle respirator. Blood gases were monitored and maintained in a physiological range. A left atrial cannula was placed for injection of microspheres and pressure monitoring. After inducing complete heart block as described by Steiner and Kovalik[13] the heart rate was kept constant by electrical pacing at 110/minute. Via a midline abdominal incision two segments of small intestine and two of large intestine (Fig. 1) of about 30 cm length were encircled at both ends with umbilical tape and the proximal tape of each segment tied. Prior to ligation of the distal tapes a catheter was introduced into the study segment 2 cm below the distal tape, threaded

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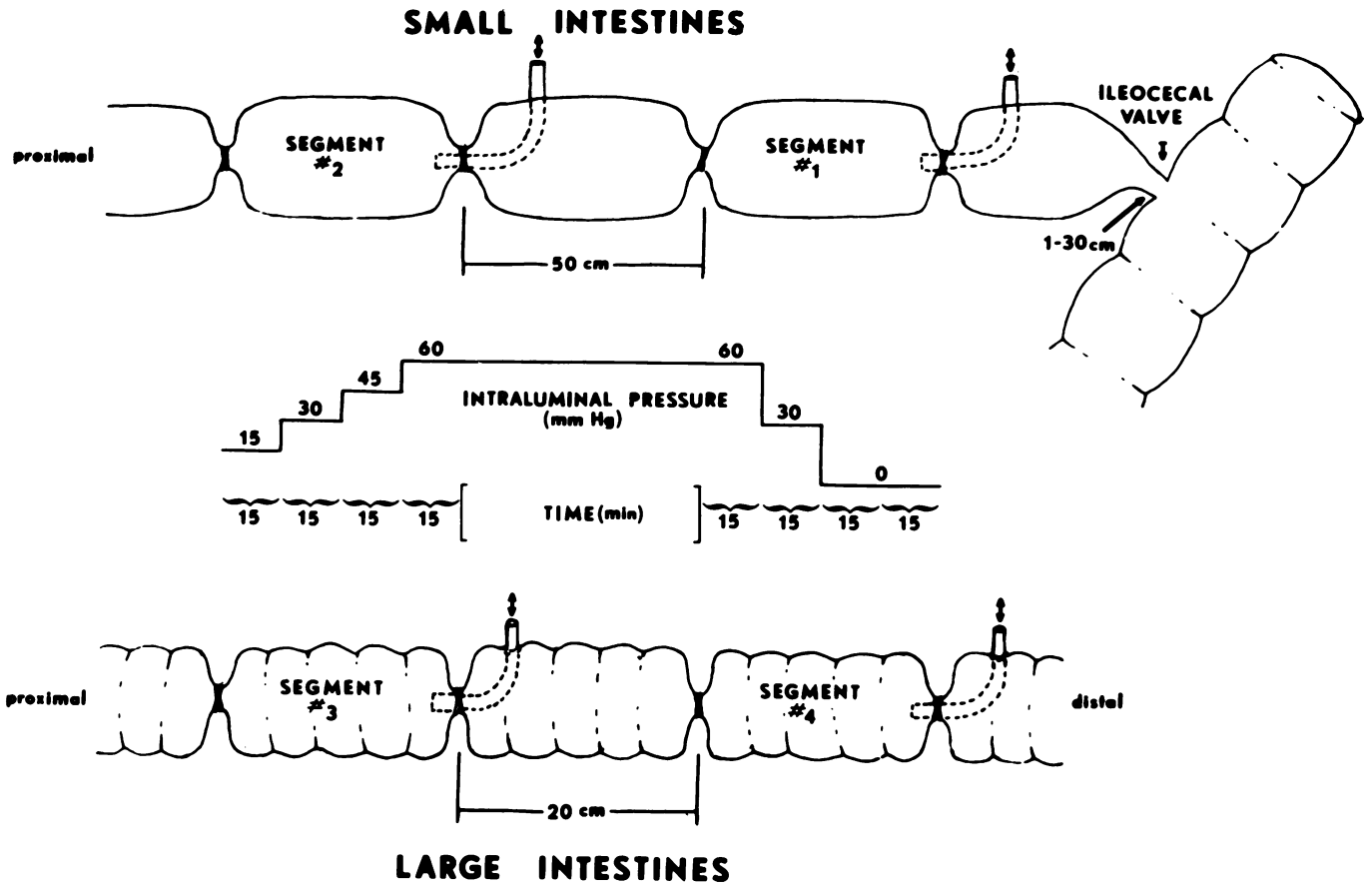

FIG. 1. Experimental design of the four ligated segments. Each segment had a length of approximately 30 cm.

into the segment, secured with a purse string suture and kept in place by tying down the distal umbilical tape. After closure of the abdomen a test inflation was done to prove air tightness. To assure comparable anatomic position of the ligated segments of small bowel the distal ligature of segment 1 was placed 30 cm proximal to the ileocecal valve and the distal ligature of segment 2 approximately 50 cm proximal to the proximal ligation of segment 1 (Fig. 1). The proximal ligation in the large bowel of segment 3 was placed 10 cm apart from the hepatic flexure and segment 4 was located about 20 cm distal to the distal ligation of the first segment.

Segments 2 and 3 of the small and large intestine were inflated with air in increments of 15, 30, 45 and 60 mmHg. Simultaneously in the other two large and small intestinal segments (1 and 4) an initial intraluminal pressure of 60 mmHg was established and then reduced to 30 mmHg and the bowel then completely decompressed in order to assess the behavior of intestinal blood flow in the recovering gut after decompression. The intraluminal pressure was measured individually for each segment with aneroid manometers (Tycos, calibrated in mmHg). After each increment, intestinal blood flow was measured as described below. Each pressure was maintained for approximately 15 minutes. In order to keep the pressures at the level desired, additional air had to be injected over time.

Microspheres Method

Intestinal blood flow was measured on the aforementioned four intraluminal pressure increments by injecting carbonized plastic microspheres at the end of each 15 minute period at a new pressure level into the left atrium. Microspheres were 15 ± 5μ in diameter labeled with ^{141}Ce, ^{51}Cr, ^{85}Sr and ^{0}Sc gamma emitting nuclides (3 M Company, Minneapolis, MN). Arterial blood (reference blood samples) was withdrawn from both femoral arteries at 4 ml/minute over two minutes with a Harvard pump. Withdrawal was started five seconds after the injection of microspheres was begun. The catheters were tied into the vessel not farther than 2 mm away from the tip in order to insure cross sectional sampling of arterial blood during the collecting period. In no instance did the radioactivity in two corresponding blood samples differ more than 10%. The sequence of the isotopes injection was such that the Ce spheres were injected first, followed by Cr, Sr and Sc.

After the last injection, the animal was sacrificed with hypertonic KCl solution, the intestinal segments checked for air tightness and macroscopic appearance. During subsequent excision, the mesentery was carefully cut as close as possible to the intestinal wall. The segments were divided into four quarters of approximately 7–8 cm length, mechanically cleaned and blotted dry. The mucosa was divided from muscle and serosa using a scraping technique. The specimens were finally put into preweighed glass test tubes. For each segment, the flow values were averaged over the four quarters. Specimens of about 7 cm length proximal and distal to the ligated segments were excised in order to determine blood flow in the adjacent bowel. Six to 18 specimens of normal intestine were taken from the proximal small bowel and distal large bowel and these served as reference samples. Counts in these areas were considered normal or 100% blood flow and other blood flow values were expressed as a per cent of these values. This method of expressing blood flow was essential to allow interanimal comparisons in that it eliminated the problem created by the wide variation in normal blood flow in the animals studied.

After weighing of the specimens the test tubes were placed into a Beckman 2-channel well-type scintillation counter. For each specimen, the radioactivity was measured in a window corresponding to the peak activity of the isotopes and the spectrum counts were determined using the method described by Rudolph and Heyman.[12]

From the radioactivity counts, intestinal blood flow could be calculated with the formula: $F_u = F_k/Q_k \times Q_u$, where F_u = unknown flow in the specimen to be assessed, F_k = blood flow in the reference sample, Q_k = radioactivity of the reference sample and Q_u = radioactivity of the specimen to be assessed.

The reference method implies that the blood flow to any organ is closely related to the radioactivity contained in this organ after microsphere injection into the left atrium since the spherules have a specific density (1.3 g/cm^3) similar to that of blood. When injected into the blood stream, they have approximately the same flow properties as the corpuscular components of the whole blood and are distributed evenly over the organism.

By means of a computer program the final flow values were printed out as ml/min × g^{-1} and expressed as percent of normal blood flow. In order to obtain total wall blood flow values the cpm and weights of the mucosal and muscular and serosal layer were added up and underwent the aforementioned calculation. Student t-test adapted for unpaired comparisons was used to determine the statistical significance of differences.

Results

Intestinal Blood Flow After Increasing Intraluminal Pressure in Increments

Figure 2 shows the influence of increasing intraluminal pressure in increments of 15, 30, 45 and 60 mmHg on total wall blood flow in the small and large intestinal segments. A pressure related decrease in blood flow can be observed in the small intestine. The large intestine maintains a relatively higher flow up to an intraluminal pressure of 45 mmHg than the small intestine. The difference in blood flow between large and small bowel is statistically significant for the intraluminal pressure of 30 mmHg ($p < 0.002$) and 45 mmHg ($p < 0.05$). At 60 mmHg intraluminal pressure the intestinal blood flow in both parts of the intestine is reduced to 23 ± 6% (small intestine) and 25 ± 5% (large intestine), respectively. Mucosal and muscular blood flows are listed (per cent of normal) in Table 1. Whereas at an intraluminal pressure of 15 mmHg in the small intestine segment 2, mucosal blood flow is reduced to less than half of its normal value, (45 ± 2%) intestinal blood flow in the muscular layer is greatly increased (218 ± 12%).

After stepwise increase of intraluminal pressure up to 60 mmHg, blood flow in the mucosa had waned to 18 ± 6%, whereas blood flow to the rest of the wall is still 74 ± 8%.

Intestinal Blood Flow After Decreasing *Intraluminal Pressure in Increments*

In two other segments of approximately the same length of the small intestine and large intestine an initially high intraluminal pressure (60 mmHg) was decreased stepwise in order to obtain information about intestinal microcirculation after removal of an obstruction. The results for total wall blood flow are depicted in Figure 3 and expressed as a per cent of normal. Again, a pressure dependent reduction of intestinal blood flow is noted. At an initial intraluminal pressure of 60 mmHg the small intestine and large intestine maintain an intestinal blood flow of 31 ± 5% and 32 ± 4% of normal, respectively. This seems to be slightly higher than intestinal blood flow at the same intraluminal pressure after stepwise increase of intraluminal pressure, however, the difference is not statistically significant ($p > 0.05$).

The reduction of intraluminal pressure to 30 mmHg results in an amelioration of intestinal blood flow to 81 ± 15% (small intestine) and 86 ± 18% (large intestine) and after complete decompression with no measurable intraluminal pressure an hyperemic response (114 ± 16% for small intestine and 118 ± 3% for large intestine) is observed. After another

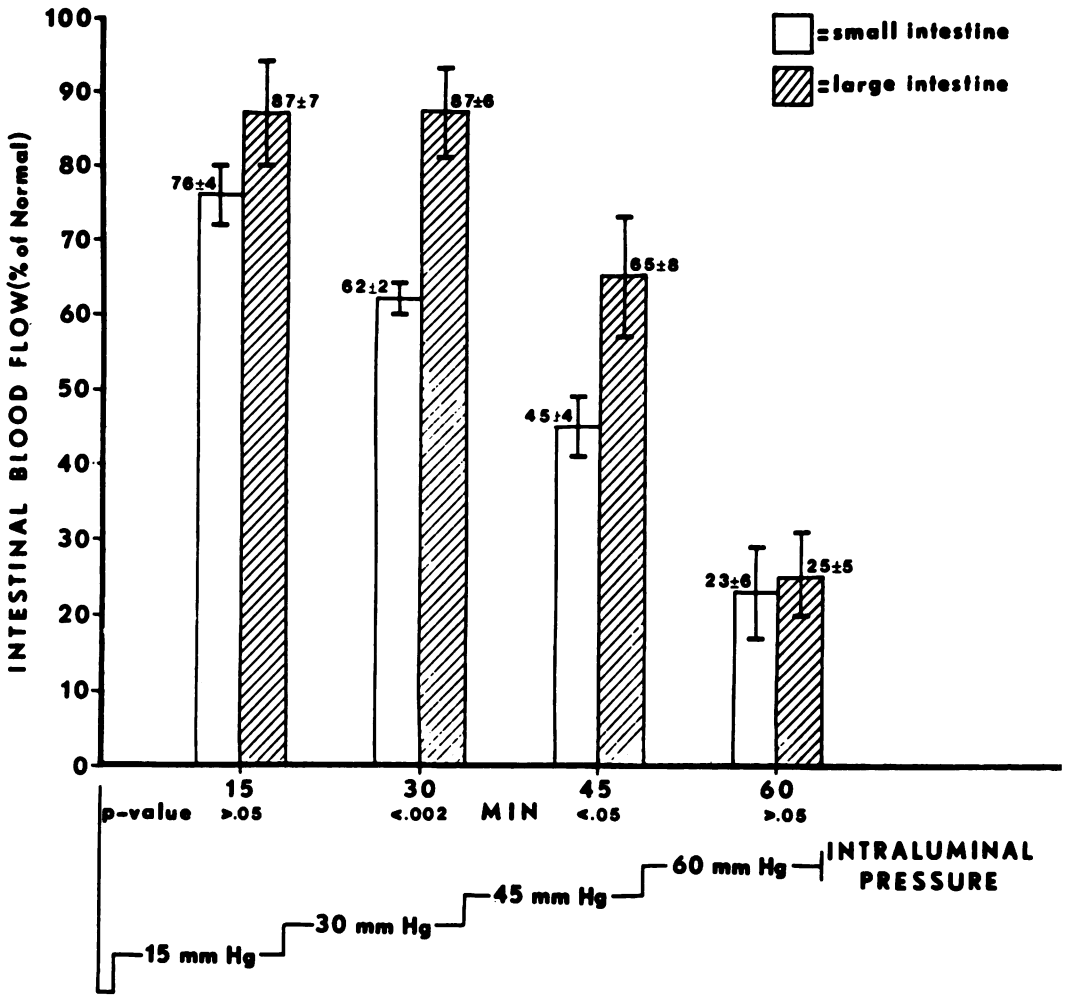

FIG. 2. Intestinal blood flow for the total wall (expressed as per cent of normal with standard deviations) in the segments with step-wise increase of intraluminal pressure (2). There is a significantly severer reduction of intestinal blood flow at intraluminal pressures of 30 and 45 mmHg in the small intestine than in the large intestine.

15 minutes under the same circumstances total wall blood flow has returned to levels slightly below normal (96 ± 5% for small intestine and 83 ± 12% for large intestine).

In the small intestine segment 1 (incremental decrease of intraluminal pressure) (Table 1) blood flow increases relatively more in the muscle than the mucosa and the hyperemic response persists for the period measured whereas in the mucosa, blood flow decreases to 68 ± 7% after a hyperemic period of about 15 minutes (110 ± 12%). Again, muscularis blood flow is much higher than in the mucosa for any period measured. Thirty minutes after the segment has been deflated completely, muscle blood flow is still 196 ± 12% of normal.

Looking at the blood flow values of large intestine

TABLE 1. *Blood Flows (Expressed as Per Cent of Normal ± SEM) for Mucosa, Muscle and Total Wall. Segments 1 through 4.*

Small Intestine	Segment 2					Segment 1			
IP (mmHg)	15	30	45	60	IP (mmHg)	60	30	0	0
BF Mucosa	45 ± 2	40 ± 4	28 ± 3	18 ± 6		20 ± 6	31 ± 4	110 ± 12	68 ± 7
BF Muscle	218 ± 12	183 ± 14	122 ± 9	74 ± 8		82 ± 7	141 ± 8	185 ± 9	196 ± 12
BF Total Wall	76 ± 4	62 ± 2	45 ± 4	23 ± 6		31 ± 5	81 ± 15	114 ± 16	96 ± 5
Large Intestine	**Segment 3**					**Segment 4**			
IP (mmHg)	15	30	45	60	IP (mmHg)	60	30	0	0
BF Mucosa	45 ± 4	36 ± 7	31 ± 4	20 ± 6		25 ± 6	32 ± 4	104 ± 6	68 ± 7
BF Muscle	261 ± 17	249 ± 14	165 ± 14	82 ± 8		90 ± 7	180 ± 17	204 ± 12	176 ± 14
BF Total Wall	87 ± 7	87 ± 6	65 ± 8	25 ± 5		32 ± 4	86 ± 18	118 ± 3	83 ± 12

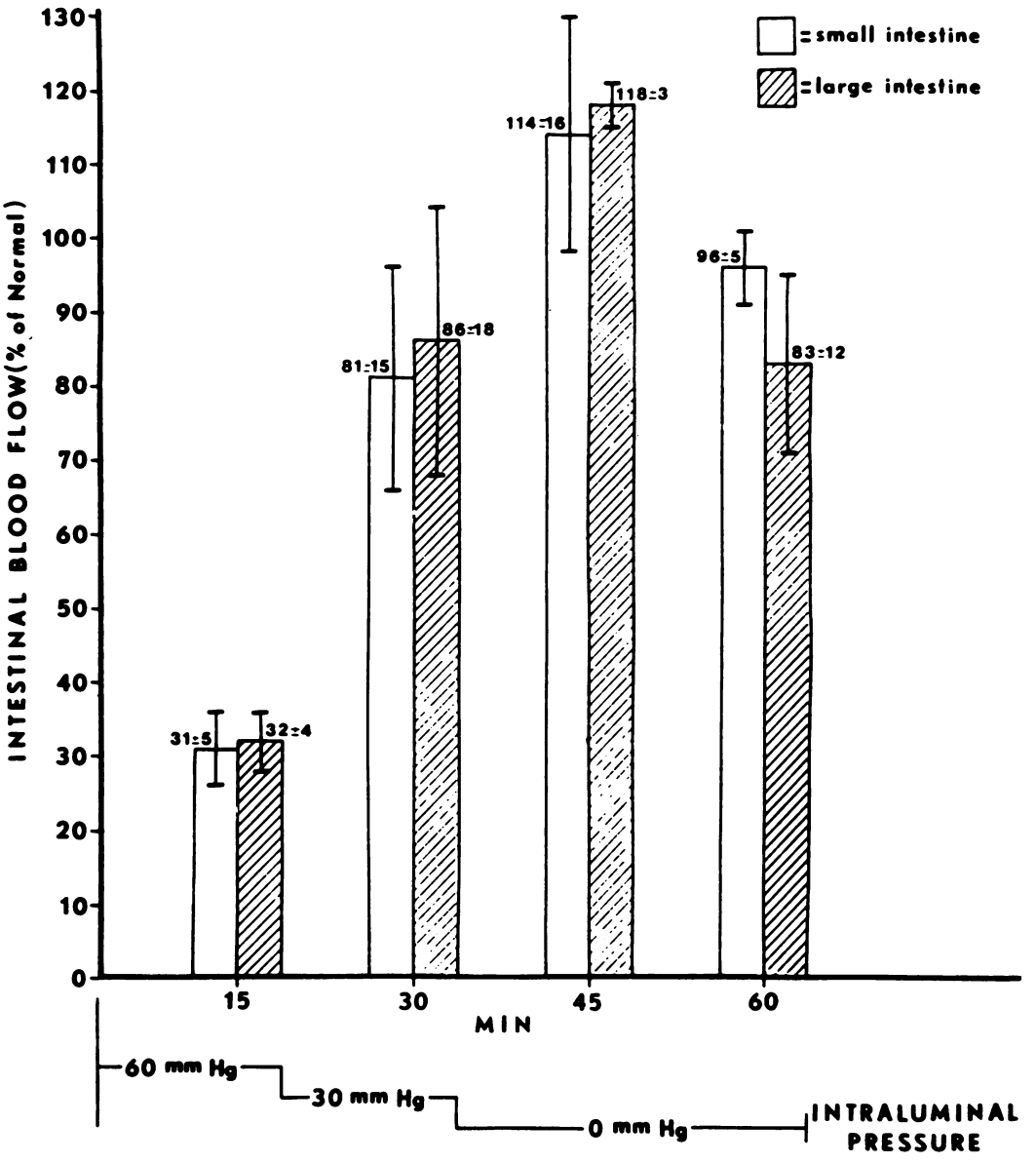

FIG. 3. Intestinal blood flow for the total wall (expressed as per cent of normal with standard deviations) in the segments with step-wise decrease of intraluminal pressure (1). After complete decompression, a hyperemic response lasting about 15 minutes can be observed for both parts of the intestine.

segment 3 (Table 1) mucosal flow is severely reduced at intraluminal pressure 15 mmHg and declines to 20 ± 6% at intraluminal pressure 60 mmHg. A marked increase in muscular blood flow occurs at intraluminal pressure 15 mmHg (261 ± 17%) which is maintained almost at the same level at intraluminal pressure 30 mmHg and then declines to 82 ± 8% at intraluminal pressure 60 mmHg. Similar response of intestinal blood flow in the inverse direction is noted for large intestine segment 4. Muscular blood flow increases relatively much more than mucosal flow as intraluminal pressure is reduced.

Intestinal Blood Flow Proximal and Distal to the Segments

Intestinal blood flow close to the ligated segments would be of interest in terms of local blood flow regulation induced by changes in intraluminal pressure.

In Table 2 the intestinal blood flow (expressed as per cent of normal) proximal and distal to the segments is listed for the small intestine. The specimen proximal to the segment has a moderately reduced intestinal blood flow between 70 and 79% and distally the intestinal blood flow is slightly higher than in the normal intestine. These differences are highly significant and independent of the applied segmental pressure.

The large intestine (Table 3) shows a similar tendency to that seen in the small intestine with only slightly reduced blood flow in the specimen proximal to the first ligature and marked hyperemia in the segment distal to the last ligature. Again, these values are independent of the intraluminal pressure applied to the segment, whether intraluminal pressure is stepwise increased or decreased and are maintained even at a zero intraluminal pressure in the segments where intra-

TABLE 2. *Intestinal Blood Flow (Expressed as Per Cent of Normal ± SEM) in the Small Intestine Proximal and Distal to the Ligated Segments*

Segment 2				Segment 1			
IP (mmHg)	Proximal	Distal	p Value	IP (mmHg)	Proximal	Distal	p Value
15	70 ± 4.1	116 ± 7.3	<0.001	60	77 ± 6	125 ± 9	<0.01
30	75 ± 2.9	106 ± 5.6	<0.001	30	76 ± 2	112 ± 6	<0.05
45	79 ± 2.8	108 ± 7.2	<0.01	0	77 ± 8	109 ± 9	<0.03
60	76 ± 7	116 ± 6.5	<0.01	0	75 ± 5	109 ± 8	<0.05

luminal pressure has been decreased stepwise, at least for the time period measured.

Macroscopic observation of the segments always demonstrated patchy submucosal hemorrhage in the small intestine with moderate edema of the intestinal wall. In two animals an 8 cm serosal tear was noted in the large intestine. This occurred in segments where the intraluminal pressure had stepwise been increased. Small serosal tears of the large intestine with scattered areas of mucosal bleeding occurred frequently. The large intestine also was edematous, usually to a greater degree than noted in the small intestine.

Discussion

An intestinal pressure dependent deterioration in small and large intestinal blood flow was demonstrated in piglets with closed abdomen. The most severe reductions in flow occurred in mucosa. At an intraluminal pressure of 60 mmHg intestinal blood flow, although reduced to 23 and 25% of normal respectively was still present.

The large bowel maintained fairly normal blood flow up to 30 mmHg intraluminal pressure, whereas the small intestine seems to be more sensitive to an intraluminal pressure increase. This behavior of the large intestine is supported by clinical observations of enormous colonic dilation with large bowel obstruction. Wangensteen[15] found intraluminal pressures as high as 52 cm of water above colonic obstructions in man, whereas intraluminal pressure in the small intestine after experimental occlusion is reportedly much lower at 8–10 mmHg.[9,10] These latter observations are consistent with the present observations showing more rapid fall off in flow in the small intestine with intraluminal pressure up to 30 mmHg. A close relationship between intraluminal pressure or bowel distention and blood flow has been reported earlier by authors using optical methods.[7,8,11] In contrast to our results they did not observe reduction of intestinal blood flow at low intraluminal pressure and they reported ceasing of blood flow at 60 mmHg intraluminal pressure whereas in the experiments described herein, intestinal blood flow was still 25% at the pressure mentioned. Apparently, microscopic capillary flow observation does not enable quantitative statements about intestinal blood flow. Other investigators, measuring intestinal blood flow by collecting venous out-flow in the isolated, denervated intestinal loop preparation,[2–4,9,10] reported severely restricted intestinal blood flow at a much higher intraluminal pressure of 100–120 mmHg. However, at these and even higher intraluminal pressure, intestinal blood flow did not decrease further below about 20% of normal.[1] It is evident from our data that the 20% level of intestinal blood flow is reached much earlier in the closed abdomen, with the blood vessels and nerval supply still intact. Also, the intra-abdominal pressure may play an important role by compressing the intestines from the outside and limiting distention. Lawson and Chumley[6] described only transient diminutions of intestinal blood flow with intraluminal pressure below 60 mmHg. This could neither be confirmed by other authors nor by us and may be due to inaccuracies in their method of measuring intestinal blood flow using differential manometry.

When the intraluminal pressure is decreased stepwise, the intestinal blood flow in the small intestine is higher (81 ± 15%) at 30 mmHg intraluminal pressure than that noted at the same pressure with step-

TABLE 3. *Intestinal Blood Flow (Expressed as Per Cent of Normal ± SEM) in the Large Intestine Proximal and Distal to the Ligated Segments*

Segment 2				Segment 1			
IP (mmHg)	Proximal	Distal	p Value	IP (mmHg)	Proximal	Distal	p Value
15	90 ± 6	129 ± 7	<0.001	60	88 ± 8	119 ± 9	<0.05
30	97 ± 7	121 ± 7	<0.05	30	91 ± 9	117 ± 5	<0.05
45	93 ± 6.4	125 ± 6	<0.01	0	89 ± 10	112 ± 9	<0.05
60	96 ± 5	119 ± 5	<0.01	0	95 ± 7	115 ± 6	<0.05

wise increase (62 ± 2%) though this difference does not reach significance ($p > 0.05$).

Reducing intraluminal pressure further to zero results in an hyperemic response in both the small and large intestinal segments lasting for approximately 15 minutes. Thereafter, intestinal blood flow is slightly below normal. This is in contrast to the results reported by Ohman using an isolated intestinal segment preparation.[9,10] He described a slight flow increase upon deflation, however, flow rate did not attain preinflation level, and vascular resistance remained above control. This may represent a basic difference in behavior of the intact intestine as compared to the denervated gut in that it is not deprived of its autoregulatory capabilities.

Analyzing behavior of the blood flow in the different layers of the intestinal wall—mucosa and muscularis—shows that mucosal blood flow is severely diminished at an intraluminal pressure of 15 mmHg in segments 2 and 3 whereas the muscularis blood flow is increased (Table 1). The mucosa–muscle blood flow relation of about 2:1 in the unaffected intestine is inversed to 1:4 in a situation with elevated intraluminal pressure. Thus, blood flows measured for total wall in any instance show that mucosal blood flow may be severely reduced whereas muscular flow is significantly increased.

This observation is consistent with the findings of Gatch and Gulbertson[3] who described a greater blood flow affect of gut-distention on the mucosa than on the muscle. However, with their method of microscopic capillary blood flow observation they were unable to make quantitative assessments. To our knowledge this significant increase in muscular blood flow at low intraluminal pressures has not been described before.

The occurrence of slightly to moderately reduced intestinal blood flow proximal to the occluded segments and moderate hyperemia distal to the occluded segment may be explained by intramural peristaltic reflex mechanisms resulting in enhanced blood flow distal to the site of obstruction. This remains speculative, however, since measurements of bowel mobility have been omitted in order to reduce trauma to the intestines. The ischemic ulcerative mucosal lesions[14] proximal to intestinal stenoses are similarly consistent with the reduced intestinal blood flow noted proximal to the ligated segment.

The peak intraluminal pressure created in this experimental situation are higher than intraluminal pressures occurring in clinical and experimental acute and chronic small bowel obstruction.[8,10] This suggests that progressive increase in intestinal pressure particularly with small bowel obstruction are not great enough to reduce intestinal blood flow to a point of critical ischemia. Thus, bowel wall necrosis occurring late in intestinal obstruction is probably due to a variety of other factors. Certainly, the intestinal wall is able to maintain adequate blood flow at intraluminal pressure far above capillary pressure of 15 mmHg.

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