## THE EFFECT OF ACUTE INTESTINAL OBSTRUCTION ON THE BLOOD AND PLASMA VOLUMES

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FROM A GROUP of studies on intestinal obstruction already completed,<sup>1, 2, 3, 4</sup> and from experiments still in progress, we have made the following observations: (1) Ligation of the cardia and ileocecal valve (*i.e.*, closed-loop obstruction of the entire stomach and small intestine) in the cat, the gastro-intestinal tract of which has been rendered free of food, fluid and gas by a preliminary 24-hour period of starvation, does not cause notable disturbances in the gastro-intestinal tract. Death results in a few days primarily because of dehydration and starvation. (2) The introduction of various types of food into such closed loops, depending on the kind of food used, may result either in rapid death from the accumulation of gas and fluid under great tension or slow death with only moderate or insignificant quantities of gas and fluid. (3) The survival time of cats dying from gaseous distention is inversely proportional to the intra-intestinal pressure. (4) The inhalation of 100 per cent oxygen will reduce the intra-intestinal pressure in gaseous (nitrogen) distention to normal, or nearly normal, and substantially prolong the life of the animal. (5) Gaseous distention, at or above the pressure levels observed in obstruction in man and animals, does not notably increase the volume of intra-intestinal fluid, the weight of the bowel wall, or the fluid in the peritoneal cavity above the normal. (6) Dehydration alone does not account for the rapid death of such animals. (7) Denervation of the extrinsic nerve supply to the intestine does not influence the survival time of these animals. (8) We have further observed that high grade intestinal distention increases the femoral venous pressure without affecting the jugular venous pressure. Studies now in progress by the plethysmograph and by assays of water content of muscle tissue of the lower extremities suggest that distention may, by compression of the abdominal vessels, cause a loss of plasma into the tissues distal to the site of compression.

We present in this communication a study of the effects of distention, at levels of pressure observed clinically, on the volume of the plasma and on the total blood volume in dogs.

*Method.*—The plasma volume of 18 dogs was determined by the method of Gibson and Evans,<sup>5</sup> who used a blue dye (T-1824 or "Evans Blue"), the concentration of which in the blood was measured by the photo-electric microcolorimeter (Gibson and Evelyn<sup>6</sup>). This dye is nontoxic in the dosage used and very slowly diffusible. The error of other methods, arising from

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variable degrees of mixing of dye with the blood, is eliminated by taking multiple blood samples at accurately known intervals. By extrapolating the disappearance slope of the dye from the blood to the time of injection of the dye, the plasma volume can be calculated with variations not exceeding 2 per cent in duplicate samples. Since 30 to 35 cc. of blood are required for each determination, this volume was duly considered in the calculations. With the plasma volume known, the total blood volume was calculated from the measured plasma volume and hematocrit.

The normal values were determined in all but several large dogs a week before the day of experimental obstruction. In these exceptional instances this was done on the same day. All measurements were made under intraperitoneal nembutal anesthesia.

Four groups of dogs were studied (Table I). Two dogs comprise the first or control group. Nothing was done to them except to keep them under intraperitoneal nembutal anesthesia and to make plasma volume determinations every 24 hours until they died; one after 60 hours, the other after more than 72 hours. One of the two dogs (Dog 18), received 500 cc. of 5 per cent glucose in physiologic saline each day following the plasma volume determination. Two dogs comprise the second group. They were prepared as follows: After 24 hours, during which time only water was allowed so that the small intestine would be empty and collapsed, intraperitoneal nembutal anesthesia was administered and an occluding ligature placed around the pylorus. The terminal ileum was divided, the distal end inverted, a cannula was inserted into the proximal end, brought out through a stab wound, clamped off, and the incision closed. Plasma volume determinations were made after four hours and again after 23 hours. Death occurred in one after 31 hours, in the other after 34 hours.

The third group included 11 dogs. They were prepared similarly to those of Group II except that after dividing the ileum and closing the distal end a cannula was inserted into the proximal end and connected, after being brought out through a stab wound, to a Perusse pressure bottle. The entire small intestine was then continuously inflated with air at a constant level of pressure. Fifteen cm. of water pressure was used in six dogs, 20 in four others, and 30 in one. Plasma volume studies were made after four hours in nine dogs, after 13 hours in two and after 18 to 23 hours in five. The average survival time was 20.8 hours.

Three dogs treated in exactly the same manner as those in Group III, and subjected to pressure of 40, 30, and 20 cm. of water respectively, died after 10, 12 and 18 hours, with an average survival time of 13 hours. Their more rapid death was due to the unanticipated finding at autopsy of extensive venous congestion, mucosal degeneration and extravasation of blood and plasma into the intestinal lumen, mesentery and peritoneal cavity. They are, therefore, classified as Group IV, *i.e.*, as dogs with obstruction, distention and strangulation. Their short survival time permitted plasma volume determinations only once, after four to four and one-half hours. From this and previous investigations, we learned that the resistance of the dog's intestine to increased pressure is notoriously poorer than that of the cat. Strangulation almost never occurs in the cat even at pressure levels of 80 cm. of water, whereas in five dogs, subjected to 40 cm. of water pressure, death occurred so quickly from strangulation and shock that no plasma volume determinations were possible.

The distention pressure levels used in the dogs of Groups III and IV are reasonably close to those found in various types of obstruction in man and in experimental obstruction (without artificial distention) in  $dogs.^7$ 

The dogs were kept under intraperitoneal nembutal anesthesia until death occurred. In previous studies no substantial difference had been observed in the survival time of two groups of cats similarly prepared, one under anesthesia, the other awake, subjected to the same levels of distention and pressure.

*Results.*—Table I shows that the average normal plasma and whole blood volumes of the 18 dogs studied were 5.0 and 8.8 per cent of the body weight respectively and that the average normal plasma volume was 56.8 per cent of the whole blood volume. These results are reasonably close to those of Gibson, Keeley, and Pijoan<sup>8</sup> and of Gasser, Erlanger, and Meek.<sup>9</sup> The former, using the method of Gibson and Evans, found that the normal blood volume varied between 8.4 and 9.7 per cent of the body weight. The latter (by a method probably less accurate than that of Gibson and Evans) found the average blood volume in a large series of dogs to be 9.7 per cent of the body weight and the plasma volume 60 per cent of the whole blood volume.

Part of the changes in plasma volume in these various groups of dogs are presumably due to the dehydration and perhaps pooling of capillary filtrate, especially in the dependent tissues, owing to muscular inactivity. Almost none of the dogs in the entire series discharged urine or showed a distended bladder at autopsy, so that it is not necessary to attribute any substantial part of the plasma volume changes to loss of fluid in the urine.

In control Group I, the plasma volume after 24 hours decreased 22.4 per cent in the dog which received no fluid and 18.6 per cent in the one which did, the average being 20.5 per cent. The loss of plasma for the same period in the two dogs of Group II (obstruction without distention) was 8.8 and 20 per cent, respectively, averaging 14.4 per cent. In contrast to these figures, the average plasma loss in five dogs of Group III (obstruction with distention) after 18 to 23 hours was 55.0 per cent (Table II and Chart 1).

The significance of these figures becomes impressive when translated into terms of the percentage of body weight which these losses of plasma represent; *viz.*, 0.85, 0.7, and 3.1, respectively, in the three groups (Table II and Chart 2). Johnson and Blalock<sup>10</sup> caused death in dogs when blood plasma equivalent to 2.4 per cent of the body weight was removed in 0.5 per cent fractions every six hours. The conditions prevailing in our experiments are comparable to those of Johnson and Blalock, who obtained their results by the removal of whole blood and the immediate reinjection of the red cells.

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Change Plasma Total Red in .... Blood Cell COMPARATIVE CHANGES IN PLASMA, WHOLE BLOOD, AND RED CELL VOLUMES AND IN HEMATOCRIT IN FOUR GROUPS OF DOGS Change in Red Reduc-tion in Reduc-tion in Intra-intesti-

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Bog			4.3	3.4	3.I	4.3	3.5	3.4			4.0	4.06	3.7	4.6	3.9	3.6			5.2	3.3	2.8
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4.9	3.9	2.6	5.4	3.3	5.8	3.8	6.0	4.7	3.1	5.1	3.1	2.0	5.6	3.2	4.8	2.I	I.8	4.1	2.8	4.6	3.0	5.9	3.2			4.7	I.6	5.4	2.6	4.5	3.1
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The hematocrit in the dogs of Group III showed a significant increase within four hours of the onset of distention. This increase averaged 42.5 per cent after 18 to 23 hours, while the undistended, obstructed dogs (Group II)

#### CHART I

#### AVERAGE REDUCTION IN PLASMA VOLUME

Reduction in P.V of intact DOG after 24 hours under nembutal  $\bigcirc$ 2 Reduction in P.V of obstructed DOG after 24 hours under nembutal

Reduction in P.V of obstructed and distended DOG after 24 hours under nembutal 3

Reduction in PV of obstructed and distended DOG after 4 hours under nembutal (4)

Reduction in P.V of obstructed and distended and strangulated DOG after 4 hours under nembutai (5)



showed a drop of 9 per cent and the intact, anesthetized dogs (Group I) an average rise of 8 per cent after the same interval. Table II shows the relatively small proportion of the average total blood volume loss that can be accounted for by the average loss in red cell volume when these losses are expressed in terms of percentage loss of body weight. For example, in

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		REDUCTION IN	THE PLASMA, W	HOLE BLOOD ANI	) RED BLOOD CEL	L VOLUMES		
	Aver Plast	age Loss of na Volume	Average Total Blo	e Loss of od Volume	Average Red Cell	Loss of I Volume	Average Change in Hematocrit	Average Survival
	In Per Cen	In Per Cent t of Body Weight	In Per Cent	In Per Cent of Body Weight	In Per Cent	In Per Cent of Body Weight	In Per Cent	Period in Hours
	With- Wit out Fluid	h With- With d Fluid Fluid	With- With out Fluid Fluid	With- With out Fluid Fluid	With- out With Fluid Fluid	With- out Fluid Fluid	With- out Fluid Fluid	With- With out Fluid Fluid
Intact, anesthetized			•					
dogs 24 hrs	22.4 18.	6 0.9 0.8	6.6 18.0	0.5 1.6	+8.2 20	+0.4 0.8	+ I6 0	60 72
48 hrs	27.5 19.	п.2 0 0.9	I3.I 28.0	I.I 2.4	0 37	0 I . 5	+16 -12	31
Obstruction; with- out distention								
4 hrs	5.6 14.4	0.25 0.68	6.6 12.8	1 1 9 0	4.6 10.9	0.25 0.90	+1.0 -9.0	32.5
Obstruction; with distention							·	
4–6 hrs	36.4	2.3 2	17.2 26 0	л. 1.7	1.6 16.4	0.00	+37.8	
18–23 hrs	55.0	3. I	40.0	3.2	17.0	0.50	+42.5	20.8
Obstruction; with distention and strangulation	<b>x</b> 0.	بر م	2 1 2	ى 2	-	5	+ 20 0	1 2 л
4-4½ hrs.	48.ó	2.6	27.4	2.4	I.I	0.0	+39.0	13.5

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TABLE II

INTESTINAL OBSTRUCTION

Volume 110 Number 1 the obstructed and distended dogs, after 18 to 23 hours, the loss in whole blood volume is 3.2 per cent of the body weight. Of this amount only 0.5 per cent is due to loss of red cells.

Dehydration cannot be held responsible for the greater loss of plasma volume in the Group III dogs, since there was no noticeable loss of fluid into the intestinal lumen, bowel wall, or peritoneal cavity in any of the first three groups, while the dehydration due to lack of fluid intake, water of perspiration, and expiratory air was presumably the same in all groups. Moreover, although Dogs 10 and 11 of Group III received 500 cc. of 5 per cent glucose in physiologic saline during the course of their distention, their loss of plasma volume was as great after the same interval as in any of those in the same group which did not receive fluid.

It is consequently obvious that the plasma volume loss is due, at least in large part, to capillary leakage of plasma in a manner similar to that occurring in traumatic shock. Therefore, death from acute intestinal obstruction may be properly attributed to crucial changes in plasma volume due to the factor of distention alone.

In the fourth group of three experiments in which spontaneous venous strangulation occurred after obstruction and distention, the average plasma loss after four and one-half hours was 48.6 per cent in comparison with an average loss, after the same interval, of 36.4 per cent in nine distended dogs of Group III without strangulation, and of 5.7 per cent in two obstructed dogs without strangulation or distention (Chart I). Practically all of the loss of whole blood can, in these dogs, as in the Group III dogs, be accounted for by the loss of plasma. This suggests that the more rapid death of the strangulation obstruction dogs is due entirely to the more rapid loss of plasma. It is, therefore, probable that the clinical condition of strangulation obstruction (before the stage of peritonitis) constitutes a greater emergency than simple obstruction, not because of a fundamental difference in the pathologic physiology (*e.g.*, "toxic proteoses"), but merely because of a quantitative difference in the rate of loss of plasma.

*Discussion.*—The experimental contributions to the pathologic physiology of acute intestinal obstruction have been significant and useful, but it is all too clear in clinical practice that some vital factor still awaits clarification. Confirmation of the intoxication theory seems remote. The importance of noxious nervous stimulation cannot be ignored,<sup>11, 12</sup> but the available evidence regarding its rôle is conflicting.<sup>4</sup> If the complicating features of strangulation and peritonitis are excluded from consideration, unrelieved obstruction remains a lethal disease in spite of the effective control of electrolytic imbalance and dehydration.

There is universal agreement that the central disturbing agent in simple acute intestinal obstruction is the increase in intra-intestinal pressure and that restoration of normal tension, whether by enterostomy, intubation and suction or inhalation of 100 per cent oxygen, will restore the patient to normal, provided the clinical condition has not reached an irreversible stage, and the deficiency in water and electrolytes is corrected.

It is important to note that most of the experimental analyses of the effects of intra-intestinal tension are based on pressure levels which are far in excess of the values observed in clinical mechanical obstruction.<sup>7</sup> Furthermore, it is somewhat surprising that these investigations have largely ignored the possible lethal effects of distention *per se* on the other organs of the peritoneal cavity, their lymphatics and blood supply, and on the dynamics of the general circulation.

It is a commonplace experience in the clinic and the experimental laboratory that uncomplicated intestinal obstruction (*i.e.*, without strangulation or peritonitis) is compatible with health so long as distention is prevented and the alimentary requirements are satisfied. A significant loss in plasma volume would not be expected and does in fact not occur in these circumstances. Two dogs with obstruction in the absence of distention showed, after 24 hours, an average plasma volume loss of 14.4 per cent, which is 0.7 per cent of the body weight. Two intact dogs, under light anesthesia, lost an average of 0.85 per cent of the body weight in plasma in the same interval.

But as soon as distention is produced, a rapid and extensive loss of plasma occurs. In four to six hours' time this averages 36.4 per cent of the normal plasma volume and in 18 to 23 hours 55 per cent, which is equivalent to 3.1 per cent of the body weight (Table II).

The marked difference induced by the distention factor alone is not due to a greater loss of water and electrolytes into the intestinal lumen, bowel wall, or peritoneal cavity, since the volume of fluid in these areas at autopsy was very small in all the dogs of this series except those with strangulation. Experiments now in progress to locate the site of the lost plasma and the mechanism by which distention causes the loss of plasma indicate that some of it, at least, may be incarcerated in the lower portion of the trunk and lower extremities as a result of mechanical obstruction to venous return, with resultant slow blood flow and capillary anoxemia, occasioned by the distended gut.

In two previous papers,<sup>2, 4</sup> evidence was given that the survival time of cats exposed to varying degrees of intra-intestinal pressure was inversely proportional to the height of pressure. It is apparent from Table II that the survival time of the dogs in the four groups is inversely proportional to the extent of the loss of plasma. This suggests a probable correlation between the volume of plasma loss and the height of intra-intestinal pressure, although we did not observe such a correlation within the limited range of pressures used (15–30 cm.).

Aird,<sup>13</sup> by the vital red method of Brown and Rowntree,<sup>14</sup> found a plasma loss of 31 and 50 per cent respectively in two of four dogs after several days of low small bowel obstruction. In the other two no significant change in plasma volume was noted. Those showing plasma loss had "gross dilatation and venous congestion" at autopsy, while the other two showed "moderate

Volume 110 Number 1 dilatation." In the light of our experimental data, we would conclude from these statements that the degree of distention determined the extent of plasma loss. Aird's method of plasma volume determination is, however, open to the objection that the reliability of the method is questionable.

That the loss of plasma due solely to distention is of sufficient magnitude  $(2.34 \text{ per cent of the body weight* after 24 hours at a pressure of 15 to 20 cm. of water) to cause death is clear from the work not only of Johnson and Blalock on dogs, but also of Elman and Cole,<sup>15</sup> who found that cats die after a loss of plasma equivalent to 2.7 per cent of the body weight. Boyce, McFetridge, and Lampert<sup>16</sup> found that death occurred in dogs after removal of an amount of whole blood equivalent to 4.56 per cent of body weight. Roome, Keith, and Phemister<sup>17</sup> obtained nearly the same result,$ *i.e.*, 4.51 per cent. Harkins and Harmon<sup>18</sup> and others have shown that much less loss of plasma than of whole blood can be tolerated by the experimental animal. A loss of red cells is better endured than an equivalent loss of plasma.

The marked loss of plasma in the distended animals is in conformity with the rise in hematocrit which, as early as four hours after the onset of distention, averages 37.8 per cent and, after 24 hours, averages 42.5 per cent. Since the loss of red cells is negligible (Table II), the hemoconcentration is due almost entirely to the loss of plasma. The implications of this observation in clinical therapy of obstruction is clearly that the use of whole blood for transfusion purposes is not only inferior to an equivalent volume of plasma, but has the disadvantage of adding red cells, which are not only not needed, but also increase the viscosity of the blood which is already too high. In determining whether the distended patient needs whole blood or merely plasma, the hematocrit should be the determining factor.

That the loss of plasma is an early and basic process in the syndrome of intestinal obstruction is evident from the extent of the plasma loss as early as the fourth hour after the onset of distention. It is, consequently, proper to conclude that the replacement of plasma is as essential as any other therapeutic measure, with the exception of the all important necessity of relieving the intra-intestinal pressure. If effective decompression cannot be achieved within a short time, the patient may die from lack of sufficient plasma volume.

The extent of the plasma loss after only four hours of distention in dogs provides a rough index of the amount of plasma which may be needed by a patient with obstruction who is on the verge of, or in the state of shock, *e.g.*, the average loss of plasma in dogs with obstruction and distention after four hours, while the animal is still in good condition, is 36.5 per cent. This percentage loss of plasma in an average individual weighing 70 Kg. is approximately 1,000 cc. If restored in the form of whole blood, 1,800 cc. would be required. The deficiency of current medical practice in this connection is therefore sufficiently obvious.

<sup>\*</sup> This figure is derived by subtracting the average 24-hour plasma loss in Groups I and II from that of Group III.

Experiments are now in progress to determine the value of plasma transfusions in intestinal obstruction.

Correcting dehydration, though useful and necessary, would seem to be a less vital matter at a critical stage in the process than the correction of the plasma deficiency.

The least reliable guide to impending shock in animals with obstruction is the blood pressure curve which fails to show a shock level until just before death. Since a significant fall in plasma volume is demonstrable long before the blood pressure reaches shock level, reliance on the blood pressure is misleading.

#### CONCLUSIONS

(1) Dogs with intestinal obstruction die more rapidly if distended than if not distended. If strangulation is superimposed on the distention, death occurs even more rapidly.

(2) Distention of the obstructed intestine in dogs causes an early and progressive loss of blood plasma. The average loss of plasma volume reaches 36.4 per cent within four to six hours and 55 per cent within 24 hours. A 55 per cent loss of plasma is equivalent to 3.1 per cent of the body weight. Of this amount, 0.7 per cent can be attributed to dehydration; the remainder, or 2.38 per cent, is due solely to the deleterious influence of the distention on the general circulation. A loss of 2.38 per cent of the body weight in terms of plasma is sufficient to cause death.

(3) Distention *per se* does not cause a loss of fluids into the intestinal lumen, bowel wall, or peritoneal cavity.

(4) When strangulation is added to obstruction and distention, a 48 per cent loss of plasma occurs within four hours. It is suggested that strangulation obstruction in the absence of peritonitis causes death sooner than simple obstruction not because of a fundamental difference in the basic phenomena involved so much as because of a quantitative difference in the rate of loss of plasma.

(5) The magnitude of the plasma loss due to distention alone is sufficient to indicate that the all important need for immediate decompression of the gut must be accompanied by a simultaneous administration of adequate quantities of plasma. The volume of plasma necessary to restore the normal plasma volume is far in excess of the amount commonly given to obstructed patients in clinical practice. The use of whole blood has disadvantages which make the use of plasma preferable.

(6) The administration of plasma is necessary long before evidence of shock is indicated by the level of the blood pressure. The blood pressure curve is a misleading guide to the patient's condition.

(7) The use of intravenous fluids and electrolytes is necessary but not so vital as that of plasma.

(8) Distention is the central disturbing agent in uncomplicated obstruction. The mechanism by which it causes the loss of plasma is not clear. That

Volume 110 Number 1 it is not because of a loss of fluids into the intestine and peritoneum (unless strangulation supervenes) is certain.

(9) In evaluating the need for plasma or whole blood for the correction of the blood volume changes, the hematocrit should serve as a useful guide.

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