β-globulin, hemopexin. The observations provide support for the hypothesis that hemopexin depletion in hemolytic disease is due to its binding of heme and consequent shortened survival in the circulation.

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Effects of Intraluminal Pressure in the Colon on its Vascular Pressure-Flow Relationships* (33881)

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Distension of the small intestine has been shown to result in increased intraluminal pressure and resistance of blood flow (1). Welsh (2) concluded that mucosal blood flow in the colon is increased during periods of increased motility. Other studies showed that total colon blood flow is decreased during rhythmic contraction and by distension of the colon (3). Arterial pressure-flow studies have given evidence of autoregulation of blood flow in the small intestine (4) and colon (5). Elevation of venous pressure results in increased resistance in the intestine and the responses are abolished by the infusion of papaverine (5, 6). In the present paper data are given on the effects of distension of the colon on these vascular responses to changes in arterial or venous pressure.

Methods. Dogs weighing 20–25 kg were anesthetized with pentobarbital (30 mg/kg, iv). The colon was exposed and freed of its mesenteric attachments. Heparin (500 units /kg, iv) was given. Then a second dog to serve as a perfusion donor was anesthetized and heparinized. A femoral artery and vein were cannulated. The caudal mesenteric artery and colic vein of the exposed colon were then cannulated with PE tubing. The former was joined to the femoral artery cannula of the perfusion donor, the segment of gut quickly was excised and perfusion was started. Venous outflow was collected in a reservoir and returned by way of the femoral vein cannula. One-hole stoppers were tied into either end of the segment. Arterial perfusion, venous, and intraluminal pressures were recorded. Arterial inflow was measured with a Biotronex electromagnetic flowmeter. Arterial pressure was varied by means of an occlusive clamp on the perfusion tubing and venous pressure by changing the position of the outflow orifice. The preparations were distended with saline and intraluminal pressure was maintained at 50 mm Hg. Data are

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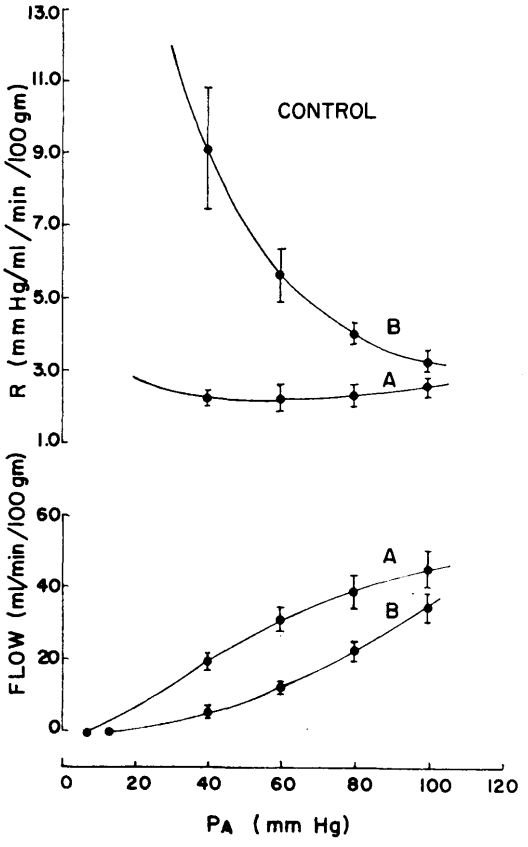

FIG. 1. Relationship of colon blood flow and resistance (R) to arterial perfusion pressure (P_A) in the undistended colon (A curves) and at an intraluminal pressure of 50 mm Hg (B curves). Data are the mean values (± SE) from 18 control experiments.

reported from 18 experiments in 11 of which the observations were repeated during papaverine infusion (0.4 mg/min).

Results. As arterial perfusion pressure was reduced some evidence of autoregulation was seen under control conditions in all 18 experiments. Over the pressure range of 100 down to 60 mm Hg the mean changes in flow and resistance were −30 ± 12 and −12 ± 2 (S.E.)%, respectively. Distension of the colon such that intraluminal pressure was held at 50 mm Hg resulted in dramatic changes in pressure-flow relationships (see Fig. 1). Evidence of autoregulation was absent in every case. Over the 100–60-mm Hg pressure range, mean changes in flow and resistance were −65 ± 4 and +77 ± 11 (SE)%, respectively. Papaverine infusion resulted in increased colon blood flow and also abolished autoregulation. Over the 100–60 mm Hg pressure range flow decreased 44 ± 4% and resistance increased 1 ± 4%. A significant ($p<0.01$) difference from the untreated group. Pressure-flow relationships in the distended, papaverinized colon did not differ significantly ($p>0.7$) from those seen in the control group at the same intraluminal pressure.

Elevation of venous pressure from 0 to 25 mm Hg resulted in a significant ($p<0.01$) decrease in colon blood flow and increase in resistance. The mean changes were −44 ± 3 and +52 ± 4%, respectively (see Fig. 2). When the colon was distended to a pressure of 50 mm Hg effects of elevated venous pressure (0–25 mm Hg) on flow and resistance were somewhat different as shown in Fig. 3. The mean 13 ± 2% decrease in flow and 14

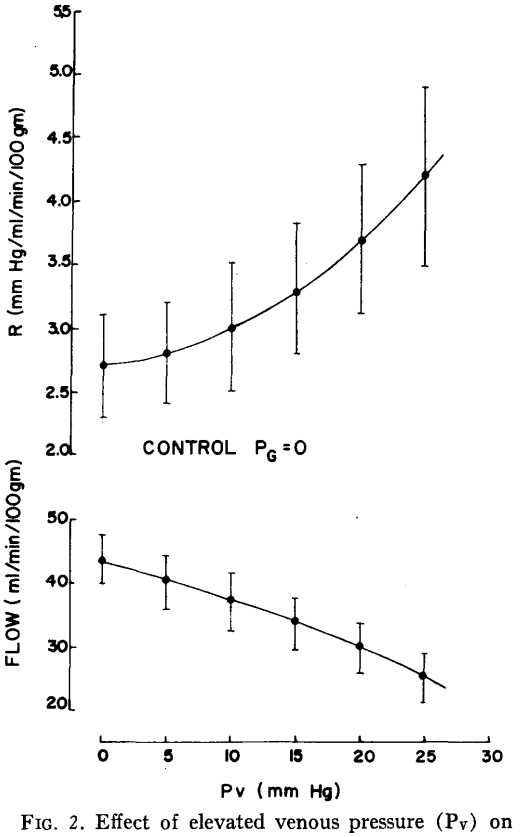

FIG. 2. Effect of elevated venous pressure (P_V) on blood flow and resistance (R) in the undistended colon. Data are the mean values (± SE) from 18 control experiments.

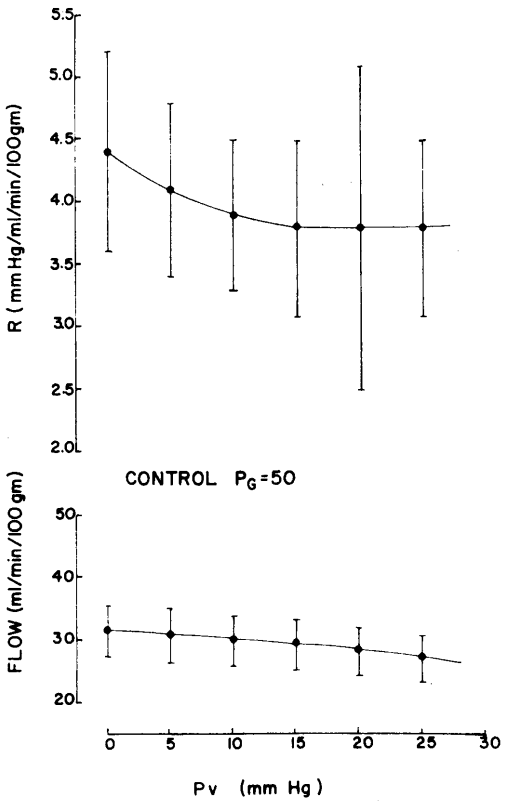

FIG. 3. Relationship of flow and resistance (R) to venous pressure (P_V) in the colon distended to an intraluminal pressure (P_G) of 50 mm Hg. Data are the mean values (± SE) from 18 control experiments.

± 2% decrease in resistance were not statistically significant ($p>0.5$). In the undistended colon treated with papaverine the same elevation in venous pressure resulted in a 27 ± 2% decrease in flow ($p<0.05$) while the resistance increase seen in control preparations was abolished. Elevation of venous pressure in drug-treated preparations during distension resulted in no significant change in either flow or resistance ($p>0.4$).

Discussion. The colon preparations showed a modest degree of autoregulation and an increased resistance in response to elevated venous pressure similar to results previously reported (5). Both are active responses blocked by papaverine and, as in the small intestine (7), are believed to be mediated by way of a myogenic response of the precapillary resistance vessels to changes in transmural pressure (5). Mesenteric arterioles have been observed to dilate as perfusion pressure and flow are reduced (8).

Intestinal blood flow is also greatly influenced by pressure in the lumen of the gut and degree of tension in its walls (1, 3). Distension of the colon to 50 mm Hg resulted in 34% flow reduction and 32% resistance increase reflecting effect of increased extravascular pressure. The effect of decreasing perfusion pressure on flow was twice that seen in the undistended state. Furthermore, autoregulation was abolished. The initial state of decreased transmural pressure resulted in collapse of the vasculature as arterial perfusion pressure was decreased below 100 mm Hg.

Microscopic observation of mesenteric vessels has revealed that the precapillary sphincters constrict in response to increased intravascular pressure, as occurs when large vein pressure is elevated (8). This vasoconstrictor response in the colon was blocked by papaverine; however, the decreased perfusion pressure gradient still resulted in a significant decrease in colon blood flow. Elevation of lumen pressure to 50 mm Hg resulted in an initial resistance at 0 mm Hg venous pressure which did not differ significantly ($p>0.8$) from the mean value which prevailed at a venous pressure of 25 mm Hg in the undistended colon (compare Fig. 2 and 3). Increased gut intraluminal pressure may have decreased blood vessel transmural pressure resulting in partial vascular collapse particularly in postcapillary elements. Apparently this nearly completely offset any influence that a large vein pressure of 25 mm Hg might ordinarily have on a myogenic response of precapillary vessels or on pressure gradient across the entire bed.

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Effects of Restraint-Stress on Enzymes Involved in DNA Synthesis* (33882)

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Recent investigations have shown that restraint-stress in rodents results in decreased cellular proliferation in the stomach (1, 2) and an inhibition of DNA[1] synthesis along the entire gastrointestinal tract (3). The synthesis of DNA is the result of several enzymatic steps which begins with the synthesis of DNA precursors and ends with their polymerization. The absence or inhibition of any of the enzymes involved in DNA synthesis would result in diminished synthesis. Certain of these enzymes are thought to play a more important role in the regulation of DNA synthesis because their activities have been shown to parallel closely the rate of cell proliferation in some tissues. Among these are TdR kinase (4) and TMP kinase (5) required for the synthesis of TTP, DNA nucleotidyltransferase (4) responsible for the polymerization of the deoxynucleoside triphosphates, and ATCase (6) which catalyzes the first step in the *de novo* synthesis of pyrimidines.

A reduction in the levels of any of these enzymes after restraint-stress but prior to the inhibition of DNA synthesis would indicate a possible site of action and lead to a better understanding of the factors involved. In the present study, the activities of these enzymes were measured in gastrointestinal tissues of restrained mice shortly before the observed inhibition of DNA synthesis. The results indicate that changes in the levels of these enzymes are not responsible for the decreased synthesis of DNA resulting from restraint-stress.

Materials and Methods. Male CFW mice weighing 25 g were restrained in a wire mesh screen (7) for 4 hr, injected intraperitoneally with 20 μCi of TdR-methyl-^{3}H (New England Nuclear, Boston; sp act 16.5 Ci/mmole) and killed 1 hr later. Control animals were kept individually in wire bottomed cages without food or water for the treatment period. The glandular stomach and jejunum were removed, homogenized in cold 0.01 *M* Tris–HCl (pH 7.5), washed free of acid-soluble material and assayed for DNA by the diphenylamine method. An aliquot of the DNA hydrolysate was used to measure the amount of acid-insoluble tritium by liquid scintillation counting. Details of this procedure have been reported (3).

Enzyme assays were performed on the 15,000*g* supernatant fraction of whole tissue homogenates, and the activities were expressed on a per unit DNA basis. The TdR kinase was assayed using the reaction mixture of Behki and Morgan (8) containing TdR-methyl-^{3}H with the addition of 1 μmole of NaF. After a 30-min incubation at 37°, the reaction tubes were immersed in boiling

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[1] Abbreviations: DNA, deoxyribonucleic acid; TdR, thymidine; TMP, thymidine-5′-monophosphate; TTP, thymidine-5′-triphosphates; ATCase, aspartate carbamoyltransferase; Tris, tris(hydroxymethyl) aminomethane; DEAE, diethylaminoethyl cellulose; ATP, adenosine-5′-triphosphate; dCMP, deoxycytidine-5′-monophosphate.