Splanchnic Contribution to Transcapillary Refill after Hemorrhagic Shock

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IN most analyses of the seemingly irretrievable course of hemorrhagic shock, the gastrointestinal tract is depicted as a villain. The progressive sequestration of blood within the abdominal viscera is believed to be a prime cause of the irreversible phase of experimental hemorrhagic shock.[5, 15] In contrast, the results of this study indicate that the splenchnic bed represents a major site for transcapillary refill during the early phase of hemorrhagic shock. As transcapillary refill is the principal mechanism tending to restore blood volume following blood loss in man and animals, it is proposed that a more positive role should be assigned to the gastrointestinal tract in the readjustment to the shock syndrome.

Materials and Methods

Part I. Rabbits

Two groups of rabbits were subjected to hemorrhage: 1) nine normal controls, and 2) seven partially eviscerated animals (involving removal of the stomach, small and large intestines, pancreas, spleen, and ligating the hepatic artery). To add a component of surgical trauma prior to producing shock in some control animals, four additional rabbits were subjected to guillotine amputation of their left hind legs prior to the production of shock.

A cannula was inserted into the carotid artery of all animals prior to hemorrhage. Seven animals were selected at random and subjected to evisceration prior to shock. The bowel was separated at the rectum and reflected back. The inferior and superior mesenteric and celiac arteries were ligated and divided serially. The mesenteric and portal veins, and the hepatic artery and common bile duct were then ligated, as was the esophagus. The entire visceral mass with the exception of the liver was then removed and weighed. Peritoneal contamination and hemorrhage were avoided. The abdomen was then closed. Each operative procedure (evisceration or amputation) required from 10 to 18 minutes.

After an initial dose of diabutol (30–35 mg./Kg. intravenously), no further anesthesia was given. Before bleeding, all rabbits had partially recovered from anesthesia following cannulation, evisceration or amputation; that is, they were all able to react to painful stimuli. The entire shock experiment encompassed 3 to 4 hours.

Hemorrhage was begun 10 to 20 minutes after evisceration or amputation, or one hour after cannulation in the case of intact animals. Arterial blood was removed rapidly, within 10 minutes, until a mean arterial blood pressure of 45 mm. Hg resulted. In many instances, more blood was removed later to maintain the blood pressure between 30 and 45 mm. Hg. No blood

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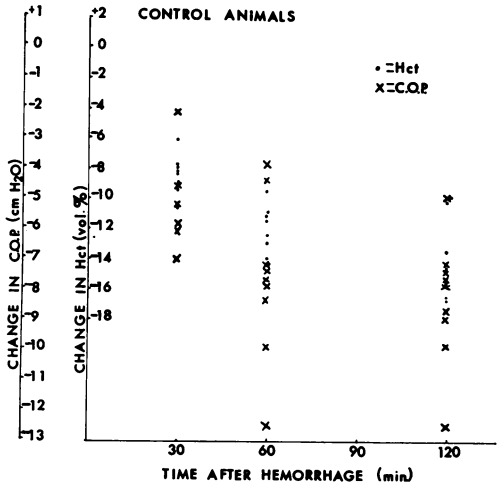

FIG. 1. The hemodilution that occurs after severe hemorrhagic hypotension in intact rabbits.

was replaced, and the only fluid given to the animals was heparin-saline in amounts just sufficient to clear the arterial catheters. Two ml. heparinized blood samples were taken just before and after hemorrhage, and then at about one half hour intervals.

Hematocrits were recorded in duplicate; plasma colloid osmotic pressures were determined using an electronic membrane osmometer.[13] Blood pressure was measured using a mercury manometer.

Part II. Dogs

Two group of mongrel dogs, weighing between 12 and 19 Kg., were subjected to hemorrhage: 1) five splenectomized controls, and 2) seven eviscerated dogs. All dogs were treated for worm and ectoparasite infestation, immunized for rabies, distemper, and hepatitis, quarantined for three weeks, and fed a balanced diet of Purina dog meal. Twelve hours prior to the study, food was withheld, but water was provided ad lib.

Three dogs were splenectomized a month prior to the study. Two dogs were splenectomized just prior to the hemorrhage. The femoral arteries were catheterized in all animals. At first, two dogs were eviscerated using the same technic as described in Part I. These dogs tolerated hemorrhagic shock poorly, and died in metabolic acidosis about 1 hour after hemorrhage. The five remaining dogs in Group II were subjected to partial evisceration with preservation of the hepatic artery. These dogs tolerated protracted hypotension from 2½ to 4 hours; two of these animals had to be sacrificed after 4 hours of shock.

Except as noted above, the shock protocol, anesthesia, hematocrit, and colloid osmotic pressure determinations were as described in Part I. Mean arterial blood pressures of 45 mm. Hg were reached after 5 to 15 minutes of hemorrhage. In addition, 1 ml. heparinized arterial blood samples were collected anaerobically and cooled in ice for pH measurements using a Radiometer pH meter.

Results

Part I. Rabbits

Blood pressure readings averaged 98 mm. Hg prior to operation or hemorrhage in control rabbits. Just after evisceration, the average mean arterial blood pressure was

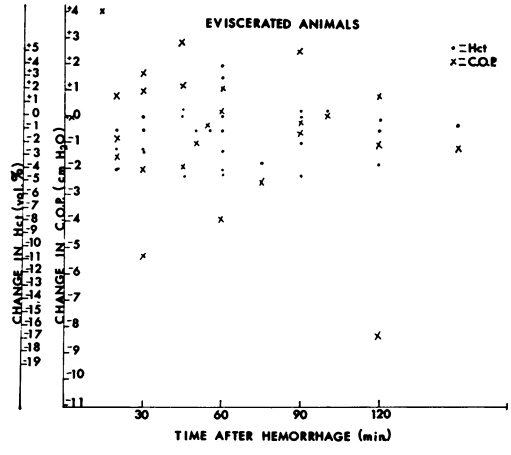

FIG. 2. Absence of hemodilution occurring after hemorrhagic hypotension in eviscerated rabbits.

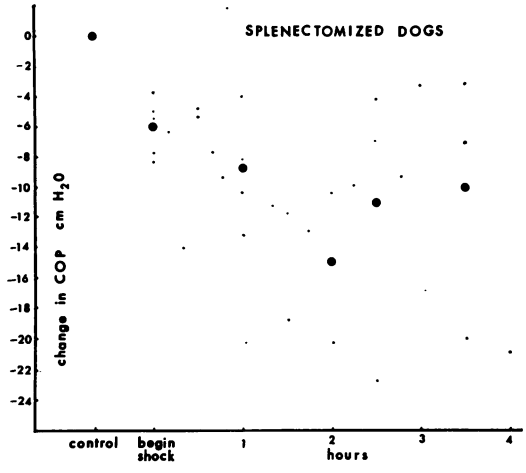

FIG. 3. The large drop in colloid osmotic pressure occurring in splenectomized dogs subjected to hemorrhage hypotension.

77 mm. Hg. In the nine intact control rabbits, hematocrits dropped after bleeding an average of 14 vol. % (40%) and colloid osmotic pressure fell 7 cm. H_2O (30%) within 1 hour. Subsequently, as Figure 1 shows, little change in hematocrit or colloid osmotic pressure occurred. The four rabbits subjected to hind leg amputation prior to shock hemodiluted to the same extent as the intact controls.

In contrast, essentially no hemodilution developed during hemorrhagic shock in the seven eviscerated rabbits, even though the same degree of hypotension was maintained for several hours (Fig. 2). As in the case of intact animals, blood loss of 2.4% per Kg. body weight served to maintain arterial pressure at shock levels when allowance was made for the weight of the removed viscera. However, mean survival time for eviscerated animals subjected to hemorrhagic hypotension was definitely reduced 2.4 hours) when compared to intact shocked animals, many of which had to be sacrificed after 4 hours of shock.

Part II. Dogs

Control pressures in anesthetized, splenectomized dogs averaged 118 mm. Hg prior to hemorrhage. Within one hour after the mean arterial blood pressure had been lowered to 45 mm. Hg by hemorrhage, the hematocrit was reduced by 10 vol. % (a 25% change from control values) and colloid osmotic pressures fell 9 cm. H_2O (a 33% change). The colloid osmotic pressure fell only slightly thereafter while hematocrits remained relatively unchanged (Fig. 3 and Fig. 4). The total amount of blood removed averaged 4% of Kg. body weight.

In Group II, mean arterial blood pressure averaged 122 mm. Hg prior to and 180 mm. Hg just after evisceration. After one hour of hemorrhagic hypotension (45 mm. Hg), the hematocrit dropped only 4 vol. % (a 10% change) in eviscerated dogs. Colloid osmotic pressure dropped 3 cm. H_2O, about 10% change from control values. There was little further change in colloid osmotic pressure or hematocrit in subsequent hours of shock (Figs. 5 and 6). The total blood volume deficit needed to maintain the BP at 45 mm. Hg was 2.8% of Kg. body weight. This figure includes an average of 225 ml. of blood removed with the viscera, as calculated from the literature.[8] The average weight of the viscera removed from dogs equalled 9% of Kg. body weight, as compared with 25% of body weight for the rabbits.

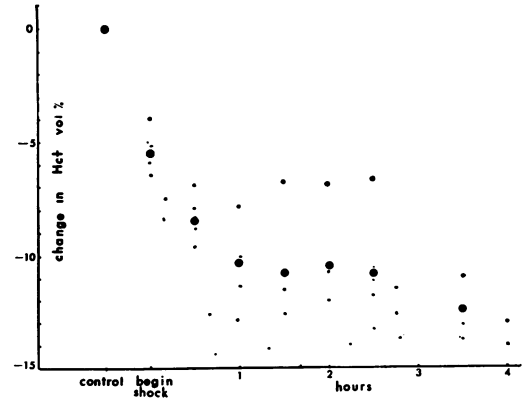

FIG. 4. The large drop in hematocrit that occurs in splenectomized dogs subjected to hemorrhagic hypotension.

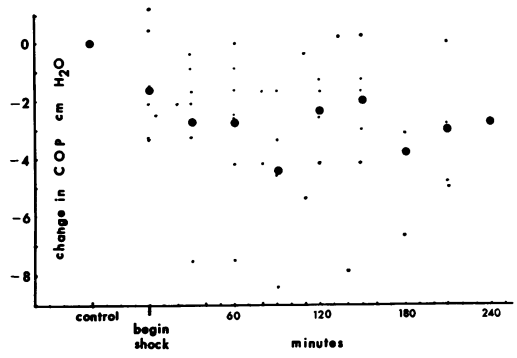

FIG. 5. The small drop in colloid osmotic pressure that occurs in eviscerated dogs subjected to hemorrhagic hypotension.

In Figures 5 and 6, the apparent declines in Hct and COP that occurred in one eviscerated dog were due in large part to the infusion of 70 ml. of $NaHCO_3$ (0.88 mEq./ml.) which was given in this one instance to counteract metabolic acidosis.

All data were analyzed using the student's "t" test; the difference between the means for control and eviscerated animals was found to be significant at the 5% level.

Discussion

In hemorrhage the balanced exchange of fluid between blood and tissues is disturbed. The hemodilution that occurs, often called transcapillary refill, can be monitored by observing progressive falls in hematocrit and plasma colloid osmotic pressure. When hemorrhage stimulates precapillary vasoconstriction, the resulting decrease in mean capillary hydrostatic pressure causes a net inward movement of extravascular fluid.[10] Later in hemorrhagic shock, preservation of the postcapillary resistance and loss of the precapillary vasoconstriction eventually results in a net outward movement of capillary fluid.[10]

Another component of the tendency toward hemoconcentration during the irreversible phase of shock has been suggested by Campion *et al.*[2] These workers proposed that failure of a cellular transport mechanism occurs late in shock. Their data indicate that a linear relationship exists between the severity of the hypotension and the loss of transmembrane potential. The resulting intracellular water accumulation might also deplete interstitial fluid stores, and thus contribute to the cessation of transcapillary refill.

The preceding discussion implies that transcapillary refill must be accomplished relatively quickly. We found that maximal hemodilution always occurred between 1 and 8 hours after shock. At first it may be difficult to relate these studies to man, for it is often stated that humans may take 12 to 36 hours to complete transcapillary refill.[12] Recent work on the early homeostatic adjustments after hemorrhage in man, however, indicates a biphasic dilutional response.[4] As in the intact rabbit and dog subjected to hemorrhage, the initial phase of dilution is extremely rapid.

Maximal dilution in human volunteers occurs 30 to 45 minutes after a 500 ml. phlebotomy. In the absence of hypotension, this fluid is soon lost in the urine.[4] Subsequently a protein-rich fluid then effects a more sustained volume restoration over the next 24 hours. In contrast, shocked animals are essentially anuric, so that hemodilution persists until the irreversible phase, at which time hemoconcentration may occur.

Turning to the early phase of hemorrhagic hypotension, our data indicate that the absorption of fluid after bleeding takes place mainly in the splanchnic bed. Others have done experiments which support this conclusion. For example, Johnson and Selkurt noted a decrease in intestinal weight during the early phase of hemorrhagic hypotension.[9] Glover and Shields[7] demonstrated that in dogs subjected to a reversible form of hemorrhagic shock, the ileum absorbed water and sodium more rapidly than in control, unbled dogs. In the jejunum no enhancement of absorption

was demonstrated. These authors also reported that in irreversible hemorrhagic shock in dogs, there was an almost complete cessation of absorption of water and electrolytes by the intestines,[11] and the oligemia was further aggravated by increased losses of fluid into the bowel. They concluded that the blood volume can be replenished by gastrointestinal fluids only during the early or reversible phase of shock.[7]

As might be expected, Gergely and Nagy [6] found that normovolemic dogs subjected to surgical exclusion of the small intestine one week prior to hemorrhagic shock were unable to tolerate severe hemorrhagic hypotension (30 mm. Hg). Most of their dogs died within 1 hour of hemorrhage. Although our eviscerated dogs tolerated hypotension for longer periods, less blood removal was required to precipitate circulatory collapse. These experiments suggest that the volume replenishment produced by transcapillary refill from the intestine during the initial stages of the syndrome may be a critical homeostatic mechanism in the face of blood loss.

A word should also be said about whether the lymphatic system replenishes intravascular volume to any great extent soon after hemorrhage. While some authors found that thoracic duct lymph flow increases slightly after hemorrhage,[3] others disagree.[1, 14] We have found that ligating the thoracic duct prior to producing hemorrhagic hypotension does not prevent hemodilution in rabbits (Marty, A. T., unpublished data). These observations support Starling's conclusion that a vascular, rather than a lymphatic mechanism replenishes blood volume after hemorrhage.[16]

Summary

Transcapillary refill is a major homeostatic mechanism tending to restore blood volume after blood loss in man and animals. When the balanced exchange of fluid between blood and tissue is disturbed by hemorrhagic shock, the hemodilution that occurs can be monitored by observing progressive falls in hematocrit and plasma colloid osmotic pressure (COP). For example, within one hour after severe hemorrhagic shock (BP 30–45 mm. Hg) was produced in nine rabbits and five splenectomized dogs, hematocrits dropped 25 to 40% and COP dropped 30 to 33%. After the first hour of hypotension, little change in COP or hct, occurred.

In a second series of experiments, evisceration of the intestinal tract, spleen, pancreas, and liver was performed prior to the production of the same level of hemorrhagic shock in seven rabbits and seven dogs. Comparatively very little hemodilution occurred with shock in these animals, even though the same degree of hypotension was maintained for several hours.

We conclude that the splanchnic bed represents an important site of early transcapillary refill associated with hemorrhagic shock in rabbits and dogs.

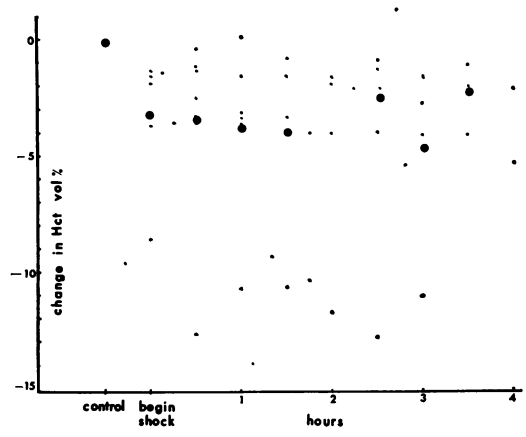

FIG. 6. The small drop in hematocrit that occurs in eviscerated dogs subjected to hemorrhagic hypotension.

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