Serum Oncotic Pressure and Protein Changes After Hemorrhage in Man[1] (35775)

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Complete transcapillary refilling of the blood volume after hemorrhage in man occurs within 48 hr (1, 2). Starling's classic studies showed that fluid absorption and filtration across the capillary wall depend on the balance between oncotic pressure exerted by plasma proteins and capillary hydrostatic pressure (3). The present studies investigate the relationship between serum oncotic pressure and protein concentration after acute nonshocking hemorrhage in 14 fasting, resting normal healthy male subjects.

Methods. Fourteen normal healthy males, ages 21 to 28 years, were studied during separate 3-day hospital admissions. A preliminary physical examination, blood count, urinalysis, electrocardiogram, and chest film were made to exclude the presence of disease. The blood volume was measured by summation (4), using autologous red cells labeled with chromium 51 and Evans blue dye. Serum oncotic pressure (π_s) was measured by placing 2 ml of serum in a brass chamber (5) which was separated from a small displacement arterial strain gauge (P 23 Dd) by a synthetic hydrated polymer semipermeable membrane (Amicon UM 10) supported by a plastic perforated disc. The strain gauge and connecting polyethylene tubing were filled with isotonic sodium chloride having no colloid osmotic pressure and were in fluid continuity with the chamber by the perforation in the supporting plastic disc. Measurements of π_s were recorded by a Brush 240 recorder. Equilibration times of at least 1 hr were used for each determination. All serum oncotic pressure measurements were corrected to 37° (6). Serum oncotic pressure measurements on 16 duplicate plasma samples varied by an average of 3.1%. The pH of the serum samples varied from 6.9 to 7.2. These differences are not sufficient to produce a significant change in π_s (6). Total proteins were measured by a modification of the biuret reaction (7). Albumin and globulin concentrations were determined by electrophoresis with cellulose acetate strips.

Samples of blood were taken without a tourniquet from the fasting and thirsting subjects for π_s and protein concentration measurements 2 hr pre-, 15 min pre-, 15 min post-, 2, 6, and 24 hr post-bleeding or exchange transfusion. Ten subjects were bled 15% of the measured blood volume (av hemorrhage vol = 786 ml in 15 min), and 4 subjects underwent simultaneous bleeding and exchange transfusion of a similar percentage of autologous blood (av exchange transfusion vol = 932 ml), 500 ml of which was drawn 7–10 days in advance so that no net blood volume change occurred. Previous studies of hemorrhage in normal man have shown that 100% transcapillary refilling of the measured blood volume occurs by 48 hr after acute blood loss (1). Statistical analyses were performed by paired and unpaired t tests.

Results. Within 15 min after hemorrhage, there was a drop in mean π_s in comparison to the measurements immediately before hemorrhage (—0.25 hr sample), but this drop was not significant until 6 hr after hemorrhage ($p<0.025$) (Table I, Fig. 1). An even greater drop in π_s occurred at 24 hr after

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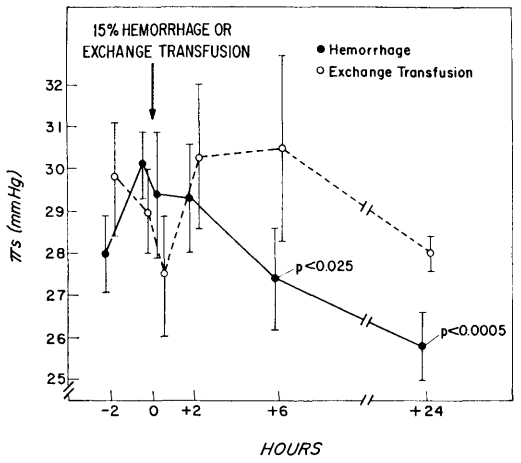

FIG. 1. Serum oncotic pressure after hemorrhage or exchange transfusion in normal man: A significant decrease in π_s occurred at 6 and 24 hr after hemorrhage, but not after exchange transfusion (control). All values mean ± SEM.

blood loss ($p<0.0005$). No significant changes in π_s occurred in control subjects undergoing exchange transfusion. Unpaired t testing did not demonstrate significant intergroup differences between those subjects who were bled and those subjects who underwent exchange transfusion. Serum oncotic pressure is plotted as a function of total protein concentration in Fig. 2. The nonlinear relationship between serial dilutions of normal serum total protein concentration at higher protein concentrations (6 to 8 mg/100 ml) and π_s is noted in Fig. 2. All of the serum samples from subjects who underwent bleeding or exchange transfusion fall on this curve.

Changes in total proteins, albumin, and total globulins are shown in Fig. 3. Only at 2 and 6 hr after hemorrhage was there a significant decrease of the concentration of total proteins ($p<0.05$ and $p<0.0025$, respectively). A significant increase in total proteins occurred at 6 hr after exchange transfusion ($p<0.01$). Albumin concentration did not significantly change after hemorrhage, but was significantly increased at 6 hr after exchange transfusion ($p<0.025$). A significant decrease in total globulins was observed at 24 hr after hemorrhage ($p<0.01$).

Discussion. The present studies are the first to demonstrate a significant decrease of serum oncotic pressure after hemorrhage in normal man. Albumin is the major osmotically active protein in mammalian serum and contributes about 65% of the protein pressure (8). In the present experiments, albumin concentration did not significantly decrease after hemorrhage, but there was a significant decrease in the concentration of total globu-

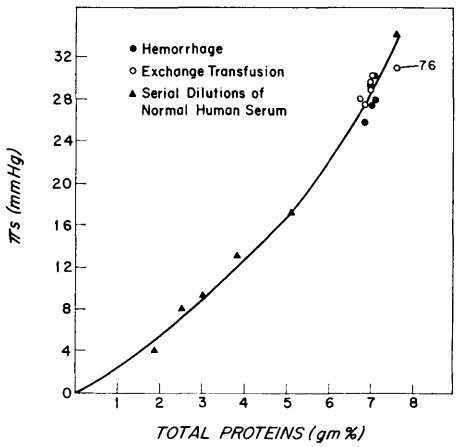

FIG. 2. Serum oncotic pressure as a function of total protein concentration: Serial dilutions of normal human serum (▲) indicate the typical nonlinear curve. Mean values for 10 hemorrhage and 4 exchange transfusion subjects are shown at each of the six time periods before and after hemorrhage or exchange transfusion.

TABLE I. Serum Oncotic Pressure After Hemorrhage or Exchange Transfusion in Normal Man.[a]

Group	No. of subjects	Serum oncotic pressure (mm Hg); time after hemorrhage or exchange transfusion (hr)					
		−2	−0.25	+0.25	+2	+6	+24
Hemorrhage	10	28.0 ± 0.8	30.1 ± 0.8	29.4 ± 1.4	29.3 ± 1.4	27.4 ± 1.2	25.8 ± 0.8
Exchange transfusion	4	29.8 ± 1.4	29.0 ± 1.1	27.5 ± 1.4	30.3 ± 1.7	30.5 ± 2.2	28.0 ± 0.4

[a] All values are mean ± SEM; all serum oncotic pressure measurements corrected to 37°.

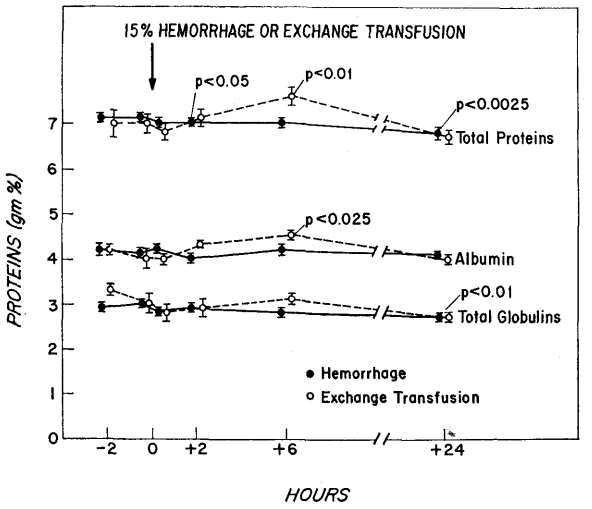

FIG. 3. Total protein, albumin, and total globulin concentrations after hemorrhage or exchange transfusion: A significant decrease in total protein concentration and total globulin concentration occurred by 24 hr after hemorrhage. These changes were not seen after exchange transfusion. Albumin concentration did not decrease significantly after blood loss.

lins. Globulins comprise a spectrum of components whose molecular weights vary from 45,000 to 1,000,000 (8). It has been pointed out that the osmotic activities of the various globulin components vary greatly, and no simple physiochemical meaning can be predicted from crude, heterogeneous globulin fractions (8). Although specific concentrations of the various globulin fractions were not determined in the present experiments, a previous study of acute blood loss in man showed decreases in the concentration of alpha 2, beta, and gamma globulin, fractions at 24 hr after hemorrhage (1). It seems likely that changes in these globulin fractions are responsible in part for the decrease in mean serum oncotic pressure from 30.1 ± 0.8 (SEM) to 25.8 ± 0.8 by 24 hr after blood loss. Fifteen percent of the total protein pressure of human plasma is contributed by known globulin components and another 20% of the protein pressure is contributed by unidentified components, whose concentration in normal plasma is estimated at 1.0 g/100 ml (8). It seems possible that changes in this unidentified protein component of oncotic pressure may also contribute to the decrease of oncotic pressure seen after bleeding, a decrease which was absent in the control subjects who underwent exchange transfusion.

The nonlinear relationship between oncotic pressure and protein concentration shown in Fig. 2 is partly related to the Donnan effect, in which net charges on the protein molecules cause unequal distribution of electrolytes across a semipermeable membrane. Electrostatic interactions between protein molecules and between protein and salt may also contribute to this nonlinear effect (8).

Serum oncotic pressure may be reduced after extensive operations, particularly when noncolloid solutions have been the major source of fluid replacement (9). The present data indicate that blood loss alone will result in a decreased serum oncotic pressure. Increased filtration of fluid into the interstitial fluid space or a decreased absorption of fluid into the blood stream will be the result of a decrease in oncotic pressure, unless capillary hydrostatic pressure falls an equivalent amount. Previous studies of a similar magnitude of rapid venous hemorrhage in man showed that mean femoral arterial blood pressure fell 19% in comparison to a 25% decrease in central venous pressure (10). These previous data suggest that a decrease in capillary hydrostatic pressure occurs after hemorrhage which serves as a stimulus to

transcapillary refilling of the blood volume (1). The common clinical practice of restoring deficient circulating blood volume with noncolloid electrolyte solutions may increase net capillary filtration by maintaining intravascular capillary hydrostatic pressure and lower still further the serum oncotic pressure by dilution of serum proteins. A fall in serum oncotic pressure, therefore, may have undesirable effects for postoperative patients in whom maintenance of circulating blood volume is critical to cellular perfusion.

Summary. Serum oncotic pressure, total protein, albumin, and total globulin concentration were studied after 15% hemorrhage or exchange transfusion (controls) in 14 normal healthy males. Significant decreases in serum oncotic pressure occurred at 6 and 24 hr after hemorrhage, but not after exchange transfusion. The decrease in serum oncotic pressure was associated with a significant fall in total globulin concentration, but not in albumin concentration.

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