BLOOD TEMPERATURE: A CRITICAL FACTOR IN MASSIVE TRANSFUSION

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Disturbances in cardiac function occur frequently during massive blood transfusions. Ventricular fibrillation and cardiac asystole have been the most serious complications.[1, 2] Various causes have been proposed but none has been incriminated as the single causative agent. The factors believed to be responsible for these derangements in cardiac function and the ones receiving the most discussion in the medical literature are citrate intoxication, depression of ionized plasma calcium[3-9] and increased plasma potassium.[10, 11] An additional factor is that of hypothermia produced by the infusion of cold bank blood.[1, 2, 13]

Rapid transfusion of cold blood will reduce the body temperature. Since the first organ exposed to the stream of cold blood, administered intravenously, is the heart, we decided to measure the change in temperature near the heart during rapid transfusion and to correlate this temperature with myocardial function.

Method and Results

Because of the impracticality of measuring the temperature of the heart directly, esophageal temperatures behind the heart were recorded. The average distance from the nostril to a point in the esophagus behind the cardiac atria was established by an esophageal electrocardiographic electrode. Measurements in many patients showed this distance to be 38 cm. in adults, with some variations due to body size. A thermocouple was introduced into the esophagus to this level in patients in whom blood loss was anticipated. The temperature was recorded at intervals and correlated with the amount of blood transfused. The blood loss was estimated gravimetrically, volumetrically and by serial hematocrits, and replaced by bank blood in an effort to maintain a normal blood volume. Cardiovascular function was assessed by the blood pressure, pulse and electrocardiogram.

The changes in these modalities in a patient who received 35 units (21,000 ml.) of cold blood during an operation can be seen in figure 1. Although during the first 110 minutes of operation the patient received 5 units (3,000 ml.) of stored citrated blood, the esophageal temperature dropped only from 37 to 36 C.; the blood pressure was maintained at preoperative levels and there was no change in the electrocardiogram. During the next 120 minutes profuse hemorrhage occurred necessitating transfusion of 18,000 ml. of cold bank blood at an average rate of 150 ml./minute. During this period there was a steady drop in esophageal temperature. At 31 C. the first ventricular premature contraction appeared and at 29 C. there was a marked prolongation of the ST segment followed by bradycardia and scattered ventricular extrasystoles. All cardiac function ceased at 27.5 C. At the time the esophageal temperature reached 29.8 C., the pulse and blood pressure which had remained throughout between 80 and 64 beats per minute and 112/60 ot 74/58 mm. of mercury, respectively, were unobtainable. From that point on, the only sign of cardiac function was the electrocardiogram and this deteriorated rapidly. At the time of cardiac arrest the estimated blood loss had been replaced. Hematocrit determinations taken at intervals throughout the procedure fluctuated between 30 and 36, further correlating adequate blood replacement.

In another patient who received 6,350 ml. of cold bank blood in 57 minutes (about 110 ml./minute) the esophageal temperature fell from 37.2 C to 32 C. The first sign of cardiac disaster occurred at 33 C. after the patient had received 5,000 ml. of cold blood. This was manifested by a prolongation of the ST

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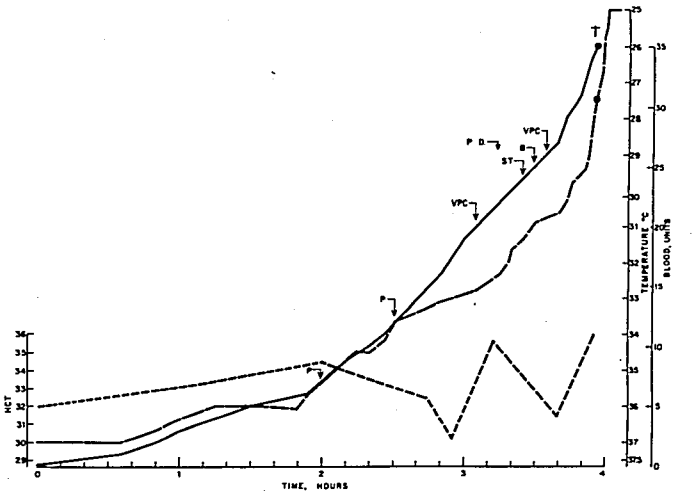

FIG. 1. Correlation between esophageal temperatures and the amount of cold bank blood transfused. — — — — — Esophageal temperature; ———— bank blood; ---------- hematocrit. (P) Unit of plasma; (VPC) ventricular premature contraction; (ST) ST segment of ECG; (B) bradycardia; (D) plasma expander—Dextran.

interval of the electrocardiogram followed by a pulse rate of 52 and a drop in blood pressure to 60 mm. of mercury. Up to this point the blood pressure had varied between 100/70 and 70/40 mm. of mercury and the pulse rate between 92 and 80. Shortly thereafter at 32 C. the heart stopped in asystole and could not be resuscitated. The measured blood loss correlated very closely with the 6,600 ml. of cold citrated blood the patient had received.

In several other instances a marked drop in esophageal temperature was demonstrated. One patient received 4,800 ml. of blood in 59 minutes (about 80 ml./minute) with the esophageal temperature falling to 31.5 C. Another patient had a transfusion of 9,000 ml. of stored blood in 150 minutes (60 ml./minute) with a resultant esophageal temperature of 30.5 C. These patients shivered, they were cold, with mottled skin, and in extreme vasoconstriction which prevented an accurate measure of the blood pressure.

In general, serial temperature recordings have shown that there is less than 1.5 C. change in esophageal temperature until after 1,800 ml. of stored blood has been administered. This generalization has to be correlated with body mass, speed of transfusion, temperature of the stored blood and the length of time the body cavities have been exposed to the relatively cold air in an air-conditioned operating room. We have observed that a three and a half hour exposure of the abdominal cavity to 20.5 C. room temperature without significant blood replacement can lower the esophageal temperature by 2.1 degrees centigrade.

Because of these observations we decided to transfuse warm blood to patients after the third unit of bank blood had been administered.

Originally, the cold bottles of bank blood were warmed in a water bath in anticipation of use. This was wasteful and uneconomical because many units of blood that had been warmed were not administered and could not

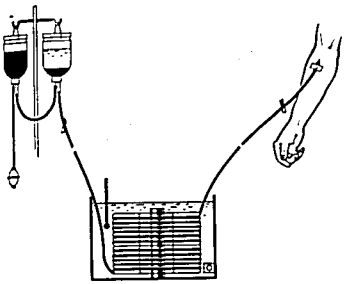

FIG. 2. Blood warmer apparatus consisting of a 20-liter plastic container; 24 feet disposable, sterile plastic tubing; bath thermometer, and a thermocouple with a red light set to flash at 37 C. This apparatus can be easily incorporated in a regular transfusion set-up.

be returned to the blood bank. In an effort to obviate this waste, an efficient, easy to operate, safe and inexpensive apparatus was devised which could warm cold blood rapidly. This apparatus, shown in figure 2, allows the blood to be warmed while being administered to the patient. It can be kept sterile and ready to be incorporated into the transfusion set-up.

The blood warmer consists of 24 feet of disposable sterile plastic tubing, 4.5 mm. in diameter, wrapped around a wire frame and immersed in a 20 liter water bath (fig. 2). The temperature of the bath is maintained at 37 C. (99 F.) by adding warm or cold water. A regular bath thermometer is sufficient to indicate the water temperature. As a safety measure a thermistor set at 37 C. is submerged in the warming bath. If the temperature of the water exceeds body temperature (37 C.), the thermocouple will activate a flashing red light. The efficiency of this apparatus with a water bath temperature of 37 C. was first tested in the laboratory. Bank blood at temperatures between 4 to 5.8 C. was run through the warmer at varying speeds and the resultant temperature of the blood upon exit from the warmer was measured. At rates of 50 ml./minute to 100 ml./minute the temperature of the warmed blood varied from 35 C. to 33 C. When the speed was increased to 120–150 ml./minute, which is equal to a transfusion rate of 600 ml. of citrated blood in 3–4 minutes, the temperature ranged between 32 C. and 30.6 C.

Initially the blood warmer was evaluated on a patient subjected to a hemipelvectomy during which he received 9,000 ml. of warmed bank blood of which 7,200 ml. was given in 120 minutes (60 ml./minute) (fig. 3). The esophageal temperature during this time varied within a degree centigrade (36.7 C.–

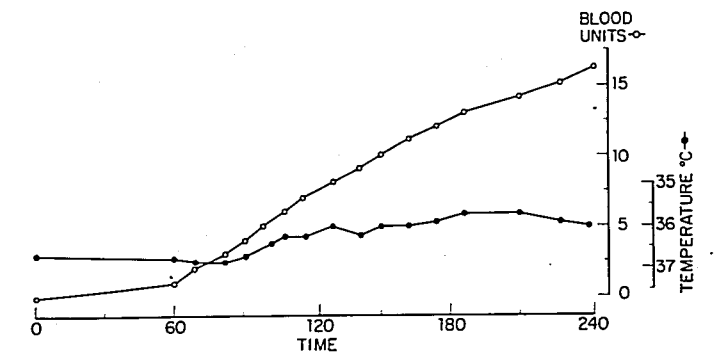

FIG. 3. Correlation between esophageal temperatures and the amount of warm blood transfused. —●—●—●— Esophageal temperatures; —o—o—o— blank blood (units).

35.7 C.); the electrocardiogram did not change and the blood pressure was well maintained. Another patient received 9,600 ml. of warmed bank blood of which 7,200 ml. was transfused in 115 minutes (about 60 ml./minute). His esophageal temperature remained at 36.2 C.–36.7 C. A third patient received 7,800 ml. warmed blood in 130 minutes (60 ml./minute). All three patients remained warm and pink; their electrocardiogram remained unchanged and the blood pressure was easily recordable, although at times at hypotensive levels. The contrast in clinical appearance between these patients and those who have received rapid transfusion of cold bank blood is striking. In other patients in whom a lowering in the esophageal temperature was observed during transfusion of cold bank blood before the blood warmer could be procured, further administration of warmed blood reversed this trend and brought the temperature to normal levels.

Discussion

A recently recognized facet of the massive transfusion problem, especially as related to cardiovascular disturbances, is that of hypothermia produced by cold blood. Bank blood is stored at a temperature of 4 C. and when given to the patient in the operating room has a temperature ranging between 6 and 10 C. During rapid blood transfusion the blood may stand at room temperature for only a short time and the infused blood will thus have a temperature closer to 4 C. This cold blood, administered under pressure, reaches the right heart rapidly without having been warmed to any significant degree by the body. As the hemorrhage increases the body loses still more heat. Further replacement by cold blood will gradually lower the temperature of the circulating blood and the whole body. In effect, this produces hypothermia by perfusion.

This has been substantiated by observation of esophageal temperatures taken behind the cardiac atria during massive blood transfusions. Additionally, this fall in temperature has been correlated with the amount of blood transfused and electrocardiographic manifestations of changes in the function of the heart.

It has been reported that during induced hypothermia the heart fibrillates more readily when the body temperature falls below 28 C.[12] McLean and associates have observed ventricular fibrillation in patients who were made hypothermic (as low as 29 C.) by transfusion of large quantities of cold bank blood.[13] Lowering of body temperature also affects the exchange of ions through the cell membrane creating adverse conditions interfering with the normal function of the heart.[14] Thus, a possible common factor resulting in cardiac difficulties during massive blood replacement, is the hypothermia of the heart. The effects of citrate excess, ionized calcium depression and increased potassium levels in the transfused bank blood may be augmented in the face of this hypothermia and play a contributory role in production of fatal cardiac arrest. Certainly none of these factors alone have been shown to cause the cardiac difficulties of massive transfusion.

Conclusions and Summary

The rapid administration of cold bank blood will result in a marked lowering of cardiac temperatures as measured by an esophageal thermocouple.

The hypothermia caused by the infusion of cold bank blood can be prevented by the use of a simple blood warmer.

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ANGIOTENSIN Angiotensin is a vasopressor polypeptide formed by the action of renin on renin substrate (hypertensinogen) normally found in the plasma. The active pressor portion of this substance (angiotensin II) has now been synthesized. Human studies prove that angiotensin is considerably more potent in raising blood pressure than is noradrenalin but is associated with a greater reduction of renal function. Venospasm was less of a problem with angiotensin than with noradrenalin. (*McQueen, E. G., and Morrison, R. B. I.: Effects of Synthetic Angiotensin and Noradrenalin on Blood Pressure and Renal Function, Brit. Heart J. 23: 1 (Jan.) 1961.*)

NEUROHORMONE FATE Electrical stimulation of the superior cervical ganglion produces a marked constriction of the blood vessels in the rabbit ear which rapidly disappears when the stimulation ceases, presumably because the neurohormone release has either been locally inactivated or washed out by the circulation. No evidence of a pressor substance was found in the perfusate after prolonged stimulation during recirculation of 4 ml. of perfusate even when inhibitors of amine oxidase and catechol-O-methyl transferase were used separately. In view of the negligible destruction of circulating adrenaline in the ear it is suggested that the neurohormone never accumulated in the perfusate above the threshold concentration of the preparation. (*Stinson, R. H.: Electrical Stimulation of Sympathetic Nerves of Isolated Rabbit Ear and Fate of Neurohormone Released, Canad. J. Biochem. Physiol. 39: 309 (Feb.) 1961.*)

ADRENAL-STEROID INHIBITOR A new chemical known as triparanol ethanol is an efficient inhibitor of cholesterol synthesis. Preliminary studies suggested that triparanol is an effective inhibitor of cortisol and aldosterone synthesis in man. A dose of 1,000 mg. of triparanol daily reduced the production of cortisol and aldosterone in healthy subjects. Adrenal secretory responsiveness to ACTH stimulation and to pyrogen stress was impaired during the administration of this drug. Adrenal responsiveness was completely restored one month after discontinuing the drug. (*Melby, J. C., St. Cyr, M., and Dale, S. L.: Reduction of Adrenal-Steroid Production by Inhibitor of Cholesterol Biosynthesis, New Engl. J. Med. 264: 583 (Mar. 23) 1961.*)