Current Issues in Fluid Resuscitation Following Trauma

Edward Crosby, MD, FRCPC

Department of Anaesthesia
Ottawa Hospital - General Site, University of Ottawa, Ottawa

Objectives

After this course, the participant should be able to:

1. Compare the body-compartment distribution of crystalloid and colloid resuscitation fluids in both trauma and non-trauma patients.
2. Discuss the rationale and the current evidence supporting the use of hypertonic saline as a resuscitation fluid.
3. Understand some of the arguments for delayed fluid resuscitation in selected groups of trauma victims and the dangers in generalizing to all patients in hemodynamic shock.
4. Explain some of the problems encountered in resuscitating the head-injured patient.
5. Discuss the development of a coagulopathy during fluid resuscitation for massive blood loss and the current recommendations or blood component therapy - when and with what.
6. Recognize the need for different protocols for urgent versus emergency transfusion situations along with the associated relative risks.

INTRODUCTION

There are a number of areas of controversy relating to fluid resuscitation following traumatic injury. There has, for example, been a recent re-expression of the possible benefit of delayed fluid resuscitation, especially in victims of penetrating injury. The resuscitation is delayed until the vascular breach has been definitively closed. Such a resuscitation scheme is contrary to the principles of conventional resuscitation as expressed in the ATLS regimen but growing evidence provides support for its application in select populations of trauma victims. The roles of hypertonic saline solutions and colloidal solutions in trauma resuscitation has yet to be defined. Finally, prophylactic administration of blood components during massive transfusion continues to be recommended by some authorities despite a paucity of evidence to support such a recommendation. These issues will be explored in the following paper.

RESUSCITATION FLUIDS

Conventional crystalloids include both balanced salt solutions (BSS) and hypotonic salt solutions. Balanced salt solutions include 0.9% NaCl (normal saline), Ringer's solutions, Plasma-lyte and Normosol and are characterized by having an electrolyte composition or calculated osmolality approximating that of plasma. Balanced salt solutions distribute to extracelluar space with about 1/4 of the administered volume remaining in the vascular space and the remaining 3/4 distributing to the extravascular (interstitial) space. With high volume crystalloid resuscitation, the extracellular space is expanded and the above ratio distorts to favour increased extracellular water, manifest in our patients as interstitial and peripheral edema.

Colloid solutions are solutions of proteins, starches, dextrans, and gelatins containing molecules sufficiently large that they do not normally cross capillary membranes. Under normal conditions most of the administered volume remains in the intravascular space. Distribution of fluids through the body (and across membranes) is determined by the Starling equation. A factor in the equation, the reflection coefficient, μ is a relative value expressing the ability of semi-permeable membranes to prevent movement of solute across

them. For colloids to work (ie. remain intravascular), μ must be large (approaching 1.0). An increased capillary permeability (a low μ) occurs at the site of traumatic injury and allows for colloidal movement across membranes, into the extravascular space. Once colloids have leaked into the interstitium, they must be removed by the lymphatic system or they will exert a reverse pressure gradient, drawing water from the vascular space. The removal of colloids from the interstitium is typically much slower than that of crystalloids. In patients undergoing elective procedures, the amount of capillary leak is limited to the surgical site and the use of colloids may be more effective in increasing intravascular volume. Following trauma, capillary leak may be extensive and may augment interstitial edema to the point of blood flow compromise. The role of colloids in acute fluid resuscitation following trauma is not yet established. In a meta-analysis comparing colloids versus crystalloids for resuscitation, Velanovich reviewed published reports comparing colloid and crystalloid resuscitation and included those studies that: 1) enrolled human subjects; 2) had random assignment to colloid or crystalloid group; 3) had as the only difference between subjects, group assignment; and 4) reported outcome (mortality).*(1)* With the pooled data, mortality favoured crystalloid resuscitation. However, when the data was separated into trauma versus non-trauma populations, the overall treatment effect for trauma trials favoured crystalloids, those for non-trauma studies favoured colloids.

Hypertonic saline (HS) solutions include 1.8%, 3%, 5%, 7.5%, and 10% sodium chloride solutions. Because the osmolality of the administered solutions exceeds that of intracellular water and because Na and Cl cannot freely cross membranes, a gradient is established that allows for water to pass from cells and into the extracelluar compartment. Intracellular fluid entering the extracelluar compartment is partitioned into extravascular and intravascular compartments in the ratio discussed previously. Hypertonic solutions thus increase the intravascular volume more than would the same volume of a balanced salt solution but at the expense of intracellular volume. Animal trials demonstrate an enhanced effect of HS solutions (alone and with dextran) in resuscitating shocked animals compared to balanced salt solutions. In animal studies, low volume resuscitation with hypertonic saline has been shown to restore cardiac output without returning blood pressure to normal. Hypertonic solutions reduce brain water, tending to

reduce ICP. In animals with raised ICP resuscitated from hemorrhagic shock, hypertonic resuscitation solutions are associated with significantly lower ICP solutions than are isotonic resuscitation solutions. Initial concerns were expressed regarding the potential for adverse neurological sequelae due to the hypernatremia caused by hypertonic solution resuscitation. These concerns appear not to be substantiated in clinical trials to date. The increment in serum sodium is less than was originally predicted and patients appear to tolerate the acute and transient increases in serum sodium. Central pontine myelinosis, which follows rapid correction of chronic hyponatremia has not been observed in clinical trials of hypertonic resuscitation. The value of hypertonic solutions in humans remains to be more fully elucidated although one major study documented fewer complications. A concern recently expressed is that, in experimental models of uncontrolled bleeding, hyperosmotic solutions may increase bleeding and adversely affect mortality. This finding will be more fully discussed in the following section.

RESTRAINED RESUSCITATION OF HEMORRHAGIC SHOCK AFTER PENETRATING TRAUMA

Conventional management of hemorrhagic shock involves aggressive fluid resuscitation using aliquots of crystalloid and colloid solutions followed by rapid blood transfusion. Present ATLS recommendations are to administer up to three 20 ml/kg aliquots of Ringer's lactate (or other balanced salt solution) to trauma victims presenting with hypotension in the emergency room. However, the aim of restoring a normal blood pressure in patients with uncontrolled hemorrhage at this phase has been questioned, with the concern being expressed that such aggressive fluid resuscitation may prejudice outcome. It has been proposed that a more judicious approach to fluid resuscitation is required in the face of continuing hemorrhage. Previous experimental studies used a controlled-hemorrhage shock (CHS) model, atraumatically withdrawing blood through a surgically implanted catheter until an arbitrarily predetermined blood pressure or volume

deficit was achieved. During the resuscitation phase (with intravenous crystalloid infusion), the catheter lumen was closed, so no further blood loss could occur. Although controlled hemorrhage was widely accepted as a method of studying hemorrhagic shock, this experimental condition has little clinical correlation with trauma. Trauma victims lose blood because of injury to a vascular circuit. Until that vascular interruption is definitively controlled, the possibility for further hemorrhage is present. CHS models, which fail to consider the interaction between the hemodynamic effects of the fluids administered and ongoing bleeding, are the basis for the recommendations integral to current trauma care. Newer animal models incorporate a vascular leak which continues to bleed throughout resuscitation and these models more accurately reflect the situation of the traumatized patient in the emergency room.

Kowalenko and Stern, employed an animal model of uncontrolled hemorrhage and hemorrhagic shock to test for outcome with varying intensity of fluid resuscitation.*(2,3)* They instrumented swine with a steel aortotomy wire in place, bled the swine to a mean arterial pressure of 30 mmHg and then pulled the aortomy wire to create a 4 mm aortic tear. The study groups included one which was not resuscitated and three others resuscitated to mean arterial pressures of 40, 60 and 80 mmHg, respectively. At one hour elapsed time, surviving animals were sacrificed and examined for intraperitoneal hemorrhage. The highest experimental mortality occurred in the non-resuscitated group. In the resuscitated groups, the highest mortality (and most intraperitoneal hemorrhage) occurred in the most aggressively resuscitated group and mortality decreased as the intensity of resuscitation diminished. The authors concluded that in the setting of severe, uncontrolled hemorrhage, maintenance of a controlled hypotensive state with judicious saline infusion causes less blood loss. Such restrained resuscitation may be preferable to aggressive fluid resuscitation before definitive surgical repair of bleeding sites has occurred. The authors further noted that aggressively resuscitated animals experienced a very early increase in pulse pressure and that this increment was delayed in less aggressively resuscitated animals. They advanced the hypothesis that this early increment in pulse pressure is sufficient to disrupt the tenuous initial clot and that as the clot matures it is better able to withstand later increases in pulse pressure.

In a similar animal model of uncontrolled arterial hemorrhage resulting from abdominal aortotomy, Bickell noted that rapidly administering lactated Ringer's solution intravenously significantly increases hemorrhage and death.*(4)* After crystalloid administration, mean arterial blood pressure, cardiac output, and stroke volume were significantly higher than those values for animals who were not resuscitated. As a result of the early (15 min) increase in cardiac output, tissue oxygen delivery was significantly increased over the control group. However, with the subsequent fall in cardiac output 30 min after aortotomy, oxygen delivery fell significantly below that of untreated control animals. At necropsy, the control group had a large firm extraluminal thrombus, which adhered to the aorta and the surrounding tissue while the thrombus observed in the crystalloid resuscitated group was of a more gelatinous consistency and was loosely overlying the aortotomy site. The increased volume of hemorrhage in the resuscitated group could have resulted from either accentuation of an ongoing hemorrhage of reinitiating the hemorrhage after spontaneous hemostasis had occurred. Bickell's model has been critcized for the sheer volume of administered fluid. If the fluid administration was extrapolated to a 70 kg human, they would have received 5600 ml in eight minutes. It has been argued that the uncontrolled hemorrhage may not have resulted from fluid resuscitation per se but rather the equally uncontrolled nature of fluid administration. A more judicious (and appropriate) restoration of circulating fluid volume may have resulted in less experimental mortality. Another criticism of the above studies has been the arbitrary end-points of the experiments. Even though the untreated animals survived to the experimental end-points of 60 and 120 mins, they remained hypotensive throughout. Longer term survival or even morbidity was not considered but it is estimated that at least 75% of the animals would have died as a result of their prolonged shock state.

Gross evaluated the role of timing of fluid administration on outcome in an animal model of uncontrolled hemorrhagic shock.*(5)* He reported that delayed resuscitation did not improve outcome compared to immediate resuscitation if the vascular injury remained unrepaired. Spontaneous clot formation could not be relied upon to prevent further hemorrhage once resuscitation occurred, even if resuscitation was delayed.

Martin carried out a prospective, randomized comparison of immediate versus delayed resuscitation in patients with penetrating trauma who were hypotensive (systolic blood pressure (< 90 MM HG) AT TIME OF FIRST CONTACT.*(6)* Three hundred patients were randomized although 123 were excluded with death at the scene or patients with minor injuries representing 95% of exclusions. Protocol variations (the most common being that the delayed resuscitation group received fluid resuscitation) resulted in further exclusions. 139 patient's records were assessed, 90 in the immediate resuscitation group and 49 in the delayed resuscitation group. There was a trend (not statistically significant) for decreased survival in the immediate resuscitation group. Although not statistically significant, there was a (clinically important) difference in the time delay pre-OR with the delayed resuscitation group entering OR at (mean) 71 min and immediate resuscitation group entering the OR at 120 mins. In later discussion, the author commented that there was pressure to get delayed resuscitation patients to OR more quickly than the immediate resuscitation group accounting for this difference. This is an important confounding variable as the management of the groups was clearly different, beyond the timing of fluid administration. Complications were higher in immediate resuscitation group and these included acute renal failure, ARDS, coagulopathy, sepsis, multiple organ failure, pneumonia, and wound infection.

Bickell reported the results of a randomized, prospective and blinded comparison of immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries.*(7)* Patients in the immediate resuscitation group received infusion of isotonic infusion of Ringer's acetate solution through two large bore iv catheters inserted at the scene. Patients in the delayed resuscitation group also had two large bore iv catheters inserted at the scene but these were then flushed and capped. After arrival in the operating room, iv crystalloid and packed red cells were given to all patients to maintain systolic blood pressure > 100 mm Hg, hematocrit > 25% and urine output > 50 ml per hour. 598 patients were enrolled in the study and 70 died before reaching the operating room. The rate of survival was higher in the delayed resuscitation group (70%) compared with that in the immediate resuscitation group (62%). The frequency of complications was similar in the two groups. The authors concluded that, in hypotensive patients with penetrating torso trauma, delay of fluid resuscitation until

operative intervention improves outcome.

Two solitudes are evolving regarding the optimum timing and scale of fluid administration after penetrating trauma. One view is that immediate fluid resuscitation should be avoided in victims of penetrating trauma, since restoration of the blood pressure may promote further hemorrhage. This may result in the need for massive blood transfusion with resultant dilutional coagulopathy, and technical surgical difficulties. The opposing (and more conventional) view is that fluid resuscitation should be started immediately since the longer the period of shock the greater the risk of developing multiple system organ failure. An argument against fluid restriction is that the blood pressure at presentation is an important factor influencing survival following trauma with the incidence of multisystem complications correlating with the duration and intensity of shock. An additional concern is that, should there be barriers to rapid surgical intervention, non-resuscitated patients may exsanguinate while awaiting operation. The majority of patients assessed by Bickell were in hospital within 30 min of reported injury and entered the operating room in less than one hour of hospital time. Finally, it must be recognized that the reviewed studies (animal and human) address models and clinical situations relating to penetrating injury and are not generalizable to the patient population with blunt traumatic injury.

We do not have agreement on goals for pre-definitive care of hemorrhagic shock, except for the need for prompt surgical hemostasis. Important is an early diagnosis of the type, magnitude, and context of injury. There may as well be competing goals in the predefinitive phase in patients with multiple injuries and there can be no global prescription for management. For example, a head-injured patient with a life-threatening hemorrhage may require a high cerebral perfusion pressure but may be harmed by further abdominal bleeding and worsening coagulopathy following aggressive fluid resuscitation. These situations can, in part, be resolved by attempting to stop bleeding as soon after injury as possible, with the minimum fluid being given for survival. Once surgical hemostasis has been achieved, vigorous optimization of circulation should commence and the goal is supranormal parameters. If surgery is not immediately available, there may be a place for low volume resuscitation, although hemodynamic

stability cannot be severely compromised for long periods. Patients requiring transport to another center for definitive care represent a dilemma with respect to devising an appropriate management regimen but again, hemodynamic compromise cannot be persistently severe.

FLUID RESUSCITATION IN HEAD-INJURED PATIENTS

Intravenous administration of large volumes of crystalloid solutions results in peripheral edema. This edema is caused by both the distributive pattern of balanced salt solutions in the extracellular space and the induced decrease in the colloid oncotic pressure. There is concern that a similar phenomena might occur in the brain during crystalloid resuscitation with the resultant production of cerebral edema and the development of intracranial hypertension. The use of colloids in trauma victims has been promoted by some who would argue that they preferentially target the intravascular space and more effectively restore haemodynamic stability in hypovolemic patients. Others have countered with concerns that colloid may cross the injured BBB, drawing fluid with them and actually worsen cerebral edema. However, the presence of the blood brain barrier (BBB) with its small pore size and limited permeability serves to enhance the role of osmolality and minimize the role of oncotic pressure in determining water movement from the vasculature into brain tissue.*(8)* An acute fall in oncotic pressure does not promote an increase in cerebral water content in the non-injured brain (intact BBB).

A consequence of brain injury is damage to the BBB. Following focal cerebral ischemia, hemodilution increases cerebral blood flow and reduces cerebral injury. By improving rheology, hemodilution is hypothesized to also reduce ischemia by increasing collateral circulation to and microcirculatory flow within ischemic areas of the brain. Increased blood flows through brain regions with disrupted BBB may also increase vasogenic edema and secondary brain injury. In an animal model of focal brain injury (temporary middle cerebral artery occlusion in the rat) pentastarch reduced BBB permeability, brain injury and edema.*(9)* In a rat model of temporary global ischaemia, the

effects of 0.9% saline, pentastarch and 1.5% saline on brain edema were compared.*(10)* No differences in brain edema were detected between the control group and the group hemodiluted with pentastarch. Brain water content was significantly decreased in the group treated with hypertonic saline. A canine model combining hemorrhagic shock and intracranial mass lesion was used to assess resuscitation with both hypotonic and hypertonic crystalloid solutions, each with and without colloid.*(11)* Cerebral blood flow (CBF) increased with resuscitation and then declined steadily in all groups. Fluids containing pentastarch were better able to support hemodynamic stability compared with crystalloid alone. However, if decreased intracranial compliance and hemorrhage are combined, ongoing resuscitation is associated with increased ICP and decreased CBF, independent of the tonicity and oncotic pressure of the infused fluid.

On balance, the data do not convincingly support or recommend against the use of colloid containing solutions in head-injured patients. The models used to assess the issue are largely deficient, many involving hemodiluting animals before exposing them to an ischemic injury. This does not correlate well with the hypovolemic, acidotic, hypoxemic head-injured victim who is hemodiluted as a result of fluid resuscitation after injury. Extrapolation of the results of these experiments to the clinical situation should be cautiously done. Models which more closely approximate the clinical situation do not demonstrate problems with the use of colloid containing solutions.

THE ROLE OF HYPERTONIC SOLUTIONS IN TRAUMA RESUSCITATION

The volume of standard resuscitation fluid (balanced salt solutions) capable of being delivered during the transport of injured patients is of little clinical benefit when evacuation time is short. Encouraging results after small volume infusions of HS solutions in animal models of hemorrhagic shock led to the recommendation for their use in the prehospital phase of fluid resuscitation of injured patients. Infusion of

HS solution restores arterial blood pressure, cardiac output and prevents mortality in models of controlled hemorrhagic shock. Unfortunately, much of the published work cited in support of the recommendation involves the controlled hemorrhagic shock model which does not accurately reflect the trauma scenario. Gross, using an animal model of uncontrolled hemorrhagic shock demonstrated that infusion of HS solution increased intra-abdominal bleeding, led to fall in systemic blood pressure and early mortality.*(4)* Delayed therapy (2 hours following injury) was as likely to cause this response as was therapy provided immediately after injury. Although there was adequate time for clot formation in the delayed resuscitation group it is possible that clot formation was compromised by the persistent shock state of the animal. Mattox reported the results of a multicenter randomized, double-blind study in which hypotensive (< 90 MM HG) TRAUMA VICTIMS WERE GIVEN EITHER 250 ML OF HYPERTONIC SALINE WITH DEXTRAN (HSD - 7.5% NACL IN 6% DEXTRAN 70) OR 250 ML BALANCED SALT SOLUTION (BSS) IN THE PRE-HOSPITAL PHASE OF CARE.*(12)* 422 patients were enrolled and 359 records were analyzed. 77% of patients had penetrating trauma. Survival with HSD was 83%, and 80% with BSS. Although more patients in the BSS group had complications, these were considered by investigators to be secondary to injuries. The authors concluded that infusion of HSD solution is as effective as standard resuscitation solutions in prehospital management and may be more effective at improving physiologic parameters but appear to have little overall effect on survival. However, there appears to be less enthusiasm at present for the early use of HS solutions for resuscitation after penetrating trauma as their role in promoting ongoing hemorrhage requires further clarification.

BLOOD COMPONENT THERAPY

Coagulopathy is a frequent complication of hemorrhagic shock. Besides tissue trauma, the main precipitating factors are hemodilution, brain trauma, and shock. Faringer reported that 40% of patients with either penetrating injury and massive hemorrhage or blunt trauma and head injury had coagulation abnormalities on admission to hospital.*(13)*

Patients with blunt injuries but no head trauma had normal coagulation. Coagulation abnormalities can also be caused by hypothermia, which is common in massively resuscitated patients. In the past, it was routine to administer components (FFP and platelets) concurrently with packed red cells during trauma resuscitation. There are authorities who continue to make recommendations for such therapy as prophylaxis against the development of coagulopathy.

With respect to bleeding prophylaxis, there is no evidence that the prophylactic administration of FFP decreases transfusion requirements in patients receiving multiple transfusions. Reed compared the incidence of coagulopathy in patients receiving two units of FFP for every 12 units of modified whole blood with those patients receiving no prophylaxis.*(14)* The incidence of coagulopathy was 18% in both groups. Mannucci, reviewing patients receiving at least five units of blood, compared patients receiving blood only with patients receiving one unit of FFP for every three units of blood and with patients receiving two units of FFP and three units of platelet concentrates for every ten units of blood.*(15)* In 94% of the patients, at least one of the routine tests of coagulation was abnormal but there was no difference among the groups with respect to measured laboratory abnormalities or in the requirements for red cells. Murray studied the coagulation changes and response to therapy during packed red cell replacement of major blood loss in patients presenting for elective major surgery.*(16)* Coagulation tests were obtained after the estimated loss of each 0.3 blood volume and before blood product replacement. Increases of the PT and PTT above control occurred in nine of the 12 patients before one blood volume was replaced but no patient had increased clinical bleeding. In four of the seven who had blood replacement of greater than one blood volume, increased clinical bleeding was observed. All four patients had platelet counts of less than 100 x 109-L-1 and platelets were transfused. In two of the four patients, despite a measured increase in the platelet count, the bleeding did not resolve and fresh frozen plasma was then administered. In both these patients fibrinogen concentrations were below 750 mg-L-1 and PT and PTT were 1.5 times control values before the FFP was administered. However, Murray concluded that, if prolongation of PT and PTT in the absence of clinical bleeding had been used as the indication for the administration of FFP, nine of twelve patients would have received FFP

unnecessarily before one blood volume was lost.*(16)*

Prophylactic administration of FFP to patients receiving massive transfusion (> 1 blood volume) or administration based on abnormal laboratory tests of coagulation, in the absence of clinical evidence of untoward bleeding, is not supported by the evidence accumulated to date.*(17)* The incidence of abnormal tests of coagulation is high even in patients receiving as little as five units of blood.*(15)* However, abnormal PT and PTT values have both a poor sensitivity and poor positive predictive value as indicators for potential bleeding tendencies and although prolonged bleeding time (> ten minutes) is a very sensitive predictor of increased bleeding, it has a poor specificity. *(16,18-20)* Patients who have received 10-15 units of blood are unlikely to develop a bleeding tendency as a result of a deficiency of platelets or coagulation factors.*(21)* However, as transfusion requirements increase above one blood volume, it is likely that an increasing number of patients will require either platelet concentrates or FFP or both.*(16)* Both dilutional thrombocytopenia and platelet function defects have been demonstrated to occur in massively transfused trauma patients. *(18,22-24)* The coagulopathy that develops in the massively transfused patient is multifactorial in origin and is not due to washout of the coagulant principles alone. Harke reported 36 patients who received greater than one blood volume transfusion during surgery for trauma or after sustaining major blood loss in surgery.*(24)* There was no simple correlation between the amount of blood lost and replaced and the incidence of coagulopathy but there was a strong correlation between both the incidence and duration of hypotension and coagulopathy. Patients with no or brief periods of hypotension had no abnormalities of coagulation despite massive transfusion, whereas patients who remained hypotensive for longer than one hour had severe coagulopathy. Patients with an intermediate duration of hypotension tended to suffer less severe degrees of coagulopathy than those patients with more prolonged hypotensive episodes. Mortality was positively correlated with the degree of coagulopathy, being 37.5% in those patients with no coagulopathy and increasing to 85.7% in patients with severe coagulopathy. Harke concluded that patients developed coagulopathy not because of the massive transfusion but because the massive transfusion did not occur quickly enough. Ferrara reported the clinical course of patients who received massive transfusion following

trauma.*(25)* The duration of hypotension was not different in the nonsurvivors than in the survivors, but the nonsurvivors were more acidotic and more hypothermic than the survivors. Nonsurvivors received more transfusions but developed coagulopathy despite adequate blood, plasma and platelet replacement. Ferrara concluded that avoidance or correction of hypothermia may be critical in preventing or correcting coagulopathy in the patient receiving massive transfusion. These results offer insight into the observation that, after equivalent degrees of massive transfusion, some patients demonstrate a coagulopathy and others do not.

Patients who have been massively transfused (> one blood volume) and who demonstrate clinical evidence of abnormal coagulation are more likely to do so as a result of thrombocytopenia or platelet dysfunction than coagulation factor depletion. Initial therapy should consist of platelet concentrate administration and FFP should be reserved for patients demonstrating abnormal bleeding in whom platelet concentrates have failed to reverse the bleeding tendencies. Transfused units of stored blood may contribute to the coagulation factor pool and a 6-8 unit transfusion of platelet concentrates contains a plasma volume equivalent to 1-1.5 units of FFP. If FFP is indicated, large volumes (600-2000 ml, 4-8 units) given rapidly are necessary to result in clinically important increases in serum levels of coagulation factors.*(26)*

Platelets should not be administered in the setting of massive transfusion in the absence of documented thrombocytopenia or clinically abnormal bleeding. The CDC-Platelets encouraged the use of platelet counts as a guide to platelet therapy in the massively transfused patient.*(27)* However, in the operating room, a decision to transfuse platelets may have to be made on clinical grounds (ie. clinical evidence of coagulopathy) before the results of the platelet assay are known. In addition, despite the fact that platelet counts < 100 X 109-L-1 HAVE A POOR PREDICTIVE VALUE FOR ABNORMAL BLEEDING, MOST PATIENTS WHO DEMONSTRATE COAGULOPATHY AFTER MASSIVE TRANSFUSION ARE THROMBOCYTOPENIC AND HAVE PLATELET COUNTS < 100 X 109-L-1.*(16,18,23,28)* However, the platelet count cannot be predicted on the basis of the volume of blood transfused.*(14)* Platelet dysfunction may also occur in

massively transfused patients and Harrigan reported that platelet function abnormalities were more likely to result in abnormal bleeding than thrombocytopenia.*(22)*

Following replacement of one blood volume, 35-40% of the platelets remain.*(27)* As blood replacement continues beyond 1.5 blood volumes, clinically important levels of thrombocytopenia become manifest as coagulopathy.*(16)* In the individual patient, it is the dynamic interplay between platelet number and function that determines the platelet count at which abnormal bleeding will become evident. In those patients in whom the clinical bleeding does not resolve with platelet transfusion, administration of fresh frozen plasma is the next logical step.

PROTOCOLS FOR URGENT AND EMERGENCY TRANSFUSION

To ensure maximum safety, donor blood should undergo complete crossmatching against the recipient's blood before being administered. However, situations arise in critical care settings which mandate blood transfusion and do not allow sufficient time (40-60 min) for the performance of a crossmatch. The use of partially crossmatched (abbreviated or quick spin crossmatch), type specific, uncrossmatched or group O blood has been recommended in these situations.*(29-34)* Because group O red blood cells lack A and B surface antigens, they may be given to most patients with a low risk of haemolysis. However, the serum of group O blood may contain high titers of anti-A or anti-B and may cause haemolysis of the recipient's red cells. For this reason, group O blood should be given as packed cells and not as whole blood. In order to avoid sensitization of Rh negative women of child-bearing age, group O Rh negative cells should be transfused to women under the age of 40 yrs.*(29-31)* Otherwise group O Rh positive cells may be administered. Patients may be switched to type specific blood after the administration of up to ten units of group O blood, provided that packed cells have been used.*(31)* Patient serum may be screened for anti-A or anti-B titers if there are concerns about switching to type specific blood after large volumes of group O have been

administered.*(29)* If the gravity of the situation dictates immediate blood transfusion and type specific or partially crossmatched blood is not available, group O red cells may be given.*(33,34)* If time permits, recipient blood may be typed and type specific, uncrossmatched blood may be given. Three percent of patients have unexpected antibodies on serum screening, the majority of these (85%) having one antibody.*(31)* Gervin reported on the adminstration of 875 units of type specfic uncrossmatched blood to 160 hypovolemic trauma patients and noted no reactions.*(33)* Eight percent of the patients had been transfused in the past but, again, demonstrated no evidence of a transfusion reaction. If additional time is available for serological testing an antibody screen and an abbreviated crossmatch (quickspin) will reveal most abnormal antibodies capable of causing agglutination and haemolysis. Only 0.04% of patients will have abnormal antibodies not detected by these latter two tests and the likelihood of an important transfusion reaction is extremely low.*(31)*

Summary

There is new data that suggests that restrained or delayed resuscitation may improve outcome in patients with penetrating trauma. The data is by no means confirmed and further work is required before this recommendation is widely implemented. Further this approach has been evaluated only in patients with penetrating trauma, a relatively small segment of the population of Canadian trauma victims. The administration of large volumes of balanced salt solutions for initial resuscitation of blunt trauma victims is widely carried out. Although inclusion of colloidal solutions in the early resuscitation of trauma victims may be more effective in restoring hemodynamic stability, it is not supported by a meta-analysis of trauma resuscitation series, demonstrating higher mortality when colloids are used. Administration of hypertonic saline solutions are useful in restoring intravascular volume, especially if the time available for administration is limited (i.e.: prehospital phase of care). Finally, coagulopathy after traumatic injury is the end result of multiple pathological events and not due to dilution alone. There are no data that support routine administration of blood components for prophylaxis of coagulopathy after trauma.

REFERENCES

1. Velanovich V. Crystalloid versus colloid fluid resuscitation: a meta-analysis of mortality. Surgery 1989;105:65-71.
2. Kowalenko T, Stern S, Dronen S, Wang X. Improved outcome with hypotensive resuscitation of uncontrolled hemorrhagic shock in a swine model. J Trauma 1992;33:349-53.
3. Stern S, Dronen S, Birrer P, Wang X. Effect of blood pressure on hemorrhage volume and survival in a near- fatal hemorrhage model incorporating a vascular injury. Ann Emerg Med 1993;22:155-63.
4. Bickell WH, Bruttig SP, Millnamow GA, et al. The detrimental effects of intravenous crystalloid after aortotomy in swine. Surgery 1991;110:529-36.
5. Gross D, Landau EH, Klin B, Krauusz MM. Treatment of uncontrolled hemorrhagic shock with hypertonic saline solution. Surg Gynecol Obs 1990;170:106-12.
6. Martin RR, Bickell WH, Pepe PE, et al. Prospective evaluation of preoperative fluid resuscitation in hypotensive patients with penetrating truncal injury: a preliminary report. J Trauma 1992;33:354-62.
7. Bickell WH, Wall MJ, Pepe PE, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. New Engl J Med 1994;331:1105-9.
8. Zornow MH, Todd MM, Moore SS. The acute cerebral effects of changes in plasma osmolality and oncotic pressure. Anesthesiology 1987;67:936-41.
9. Schell RM, Cole DJ, Schultz RL, Osborne TN. Temporary cerebral ischemia. Effects of pentastarch or albumin on reperfusion injury. Anesthesiology 1992;77:86-92.
10. Goulin GD, Duthie SE, Zornow MH, Scheller MS, Peterson BM. Global cerebral ischemia: effects of pentastarch after reperfusion. Anesth Analg 1994;79:1036-42
11. Whitley JM, Prough DS, Brockschmidt JK, etal. Cerebral hemodynamic effects of fluid resuscitation in the presence of an experimental intracranial mass. surgery 1991;110:514-22.
12. Mattox KL, Maningas PA, Moore EE, et al. Prehospital hypertonic

saline/dextran infusion for post-traumatic hypotension; the USA multicenter trial. Ann Surg 1991;213:482-91.
13. Faringer PD, Mullins RJ, Johnson RL, Trunkey DD. Bllod component supplementation during massive transfusion of AS-1 red cells in trauma patients. J Trauma 1993;34:481-7.
14. Reed RL II, Ciavarella D, Heimbach DM, et al. Prophylactic platelet administration during massive transfusion. A prospective, randomized, double-blind clinical study. Ann Surg 1986;203:40-8.
15. Mannucci PM, Frederici AB, Sirchia G. Hemostasis testing during massive blood replacement. Vox Sang 1982;42:113-23.
16. Murray DJ, Olson J, Strauss R, Tinker JH. Coagulation changes during packed red cell replacement of major blood loss. Anesthesiology 1988;69:839-45.
17. Consensus Conference: Fresh Frozen Plasma. Indications and risks. JAMA 1985;253:551-3.
18. Counts RB, Haisch C, Simon TL, Maxwell NG, Heimbach DM, Carrico CJ. Hemostasis in massively transfused trauma patients. Ann Surg 1979;190:91-9.
19. Rodgers RP, Levin J. A critical reappraisal of the bleeding time. Seminars Thromb Hemostas 1990;16:1-20.
20. Burns ER, Lawrence C. Bleeding time: a guide to its diagnostic and clinical utility. Arch Pathol Lab Med 1989;113:1219-24.
21. Myllyl G. New transfusion practice and haemostasis. Acta Anaesthesiol Scand 1988;32:S76-80.
22. Harrigan C, Lucas CE, Ledgerwood AM, Walz DA, Mammen EF. Serial changes in primary hemostasis after massive transfusion. Surgery 1985;98:836-44.
23. Phillips TF, Soulier G, Wilson RF. Outcome of massive transfusion exceeding two blood volumes in trauma and emergency surgery. J Trauma 1987;27:903-10.
24. Harke H, Rahman S. Haemostatic disorders in massive transfusion. Biblthca Haemat 1980;46:179-88.
25. Ferrara A, MacArthur JD, Wright HK, Modlin IM, McMillen MA. Hypothermia and acidosis worsen coagulopathy in the patient requiring multiple transfusion. Am J Surg 1990;160:515-8.
26. Braunstein AH, Oberman HA. Transfusion of plasma components. Transfusion 1984;24:281-6.
27. Consensus Conference: Platelet Transfusion Therapy. JAMA 1987;257:1777-80.

28. Miller RD, Robbins TO, Tong MJ, Barton SL. Coagulation defects associated with massive blood transfusions. Ann Surg 1971;174:794-801.
29. Bernstein DP. Transfusion therapy in trauma. In: Trauma: anesthesia and intensive care. Capan LM, Miller SM, Turndorf H (Eds). Philadelphia: J.B. Lippincott, 1991:167-205.
30. Lefebre J, McLellan BA, Coovadia AS. Seven years experience with group O unmatched packed cells in a regional trauma unit. Ann Emerg Med 1987;16:1344-9.
31. Schwab CW, Shayne JP, Turner J. Immediate trauma resuscitation with type O uncrossmatched blood: a two- year prospective experience. J Trauma 1986;26:897-902.
32. Oberman HA, Barnes BA, Friedman BA. The risk of abbreviating the major crossmatch in urgent or massive transfusion. Transfusion 1978;18:137-41.
33. Gervin AS, Fischer RP. Resuscitation of trauma patients with type-specific uncrossmatched blood. J Trauma 1984;24:327-31.
34. Blumberg N, Bove JR. Un-cross-matched blood for emergency transfusion. One year's experience in a civilian setting. JAMA 1978;240:2057-9

.

Self-Assessment Questions

a) Hypertonic saline solutions more effectively restore intravacular volume compared with isotonic solutions as they:

1. draw fluid from the intracellular space and distribute it through the extracellular space
2. distribute primarily to the intravascular space
3. decrease the reflection coefficient
4. have a "sealing" effect on the traumatised microcirculation.

b) Aggressive fluid resuscitation after penetrating trauma may increase blood loss by:

1. increasing pulse pressure and promoting blood loss through the

injured vessels
2. disrupting clot that is tamponading injured vessels
3. diluting coagulation factors
4. all of the above.

c) Following massive transfusion:

1. platelet dysfunction is as likely to result in coagulaopathy as is thrombocytopenia
2. coagulation factors are not usually limiting until greater than one blood volume is lost and replaced
3. warming of resuscitation fluids is essential to prevent hypothermia and acidosis
4. all of the above.

Answers

Winterlude 95 Programme
Winterlude Main Page
Association of Ottawa Anesthesiologists