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Literature Abstracts and Articles Update

From the Center for Bloodless Medicine and Surgery Children's Hospital Central California

This update is designed as an aid to help healthcare professionals stay informed on the latest blood management healthcare developments. It is a way to see how people in the field of pediatric healthcare are preparing today for the challenges of a new era and beyond.

We hope that from time to time this monthly update will prove useful to you in keeping updated about all that is happening in the world of pediatric bloodless medicine and surgery.

Steve Cade – Coordinator

Blood transfusion policy among European pediatric intensive care physicians.

J Intensive Care Med. 2004 Jan-Feb;19(1):38-43. Nahum E, Ben-Ari J, Schonfeld T. Intensive Care Unit, Schneider Children's Medical Center of Israel, Petah Tiqva, Israel. enahum@cw.bc.ca

The objective of this study was to define current blood transfusion practices among European pediatric intensive care physicians treating critically ill children. A questionnaire of case scenarios was administered to members of the European Society of Pediatric and Neonatal Intensive Care (ESPNIC). Of the 258 members of the ESPNIC, 134 (51.9%) pediatric intensive care physicians completed the questionnaire. The suggested blood transfusion thresholds for case scenario 1 (post-orthopedic surgery child) ranged from <7.0 g/dl to 11 g/dl. A total of 57.3% suggested 7 g/dl, 33.6% suggested 8 g/dl, and 6.9% suggested 9 g/dl as a hemoglobin threshold for transfusion (mean, 7.54 +/- 0.75). For case scenarios 2 to 4, the suggested hemoglobin thresholds were 7 g/dl to 12 g/dl. For case scenario 2 (a child with acute respiratory distress syndrome), 22.4% suggested 8 g/dl, 15.7% suggested 9 g/dl, and 41% suggested 10 g/dl as a hemoglobin threshold for transfusion (mean, 9.40 +/- 1.27 g/dl). For case scenario 3 (a post-cardiac surgery infant), 20.1% suggested 7 g/dl, 24.6% suggested 8 g/dl, 21.6% suggested 9 g/dl, and 23.9% suggested 10 g/dl as a hemoglobin threshold for transfusion (mean, 8.72 +/- 1.24 g/dl). For case scenario 4 (a child with septic shock), 23.1% suggested 8 g/dl, 16.4% suggested 9 g/dl, and 41% suggested 10 g/dl as a hemoglobin threshold for transfusion (mean, 9.45 +/- 1.24 g/dl). The threshold for transfusion was not statistically different (P >.05) between the physicians according to their subspecialty, years of experience, or country of origin. The suggested volume of transfused blood was 10 to 15 ml/kg in 427 responses (82.6%) and 20 ml/kg in 89 responses (17.2%). Most physicians, 78/128 (60.9%), did not consider the age of the transfused blood an important factor in their decision to transfuse. Of the 106 (79.1%) physicians who detailed their considerations for elevating the threshold for transfusion, 82 (77.3%) gave a general nonspecific indication, 47 (44.3%) stated hemodynamic instability and shock, and 40 (37.7%) an ongoing bleeding. The hemoglobin threshold for blood transfusion and transfusion volume varies among European pediatric intensive care physicians, for the same patient.

Oncological management of pediatric cancer patients belonging to Jehovah's Witnesses: a two-institutional experience report.

Onkologie. 2004 Apr;27(2):131-7. Tenenbaum T, Hasan C, Kramm CM, Janssen G, Laws HJ, Wessalowski R, Bode U, Gobel U. Department of Pediatric Oncology, Hematology and Immunology, University Children's Hospital, Heinrich Heine University, Dusseldorf, Germany.

OBJECTIVES: Aim of this study was to analyze the feasibility of oncological treatment in pediatric patients belonging to Jehovah's Witnesses and to describe the changing policy in performing transfusions and supportive care measures at two German pediatric cancer institutions. PATIENTS AND METHODS: Over a period of 16 years 21 treatments according to the current cooperative protocols were performed in 14 children of Jehovah's Witnesses. Various hematological supportive care measures such as supplementation with iron, human erythropoietin, interleukin 11, granulocyte colony-stimulating factor and autologous or allogeneic stem cell rescue had been applied. For comparison matched pairs treated in our hospitals not belonging to Jehovah's Witnesses and 50 pediatric and adult oncological patients belonging to Jehovah's Witnesses reviewed from the international literature were analyzed with respect to transfusions and outcome. RESULTS: So far, 9 of 14 children are surviving 16-195 months (median 26 months). During the primary therapy they received markedly less transfusions than the control cohort (-39,1% red blood cell transfusions and -37,5% platelet transfusions). The review of 50 reported cases showed that oncological therapy can also be successfully performed with a restricted transfusion regimen in children and particularly in adults. CONCLUSION: Pediatric cancer patients belonging to Jehovah's Witnesses can be treated similarly to other patients. A restrictive transfusion policy and the broad application of hematopoietic supportive care measures may reduce transfusions. This treatment policy and a continuous collaboration with the Hospital Liaison Committee for Jehovah's Witnesses appears to create an oncological treatment situation with a high compliance of patients and parents where court orders may not be necessary. Copyright 2004 S. Karger GmbH, Freiburg

Comparison of epsilon aminocaproic acid and tranexamic acid in pediatric cardiac surgery.

J Cardiothorac Vasc Anesth. 2004 Apr;18(2):141-3. Chauhan S, Das SN, Bisoi A, Kale S, Kiran U.

OBJECTIVE: This study compared the efficacy of aminocaproic acid and tranexamic acid in reducing postoperative blood loss, as well as blood and blood product requirements in children with cyanotic congenital heart disease. DESIGN: A prospective randomized study. SETTING: Cardiac center of a tertiary care, referral hospital. PARTICIPANTS: One hundred fifty children in the age group of 2 months to 14.5 years with cyanotic congenital heart disease undergoing corrective surgery on cardiopulmonary bypass (CPB). INTERVENTIONS: Patients were randomized into 3 groups. Group A was given aminocaproic acid in a dose of 100 mg/kg after anesthetic induction, 100 mg/kg on CPB and 100 mg/kg after protamine. Group T was given tranexamic acid, 10 mg/kg, after anesthetic induction, 10 mg/kg on CPB, and 10 mg/kg after protamine. Group C was the control group. Main Result: Control group had the longest sternal closure time, maximum blood loss at 24 hours, and maximum requirements of blood and blood products. Among the 2 groups given antifibrinolytics, there was no significant difference in postoperative blood loss, blood and product requirement, and reexploration rates. CONCLUSION: Aminocaproic acid and tranexamic acid are equally effective in reducing postoperative blood loss, as well as blood and blood product requirements in children with cyanotic heart disease undergoing corrective surgery as compared with the control group.

Autologous transfusion techniques: a systematic review of their efficacy.

Transfus Med. 2004 Apr;14(2):123-44. Carless P, Moxey A, O'Connell D, Henry D. School of Medical Practice and Population Health, Faculty of Health, University of Newcastle, New South Wales 2298, Australia.

Shortages of donor blood and fears of transmitted infections have prompted the use of a range of blood-sparing techniques in the peri-operative period. We conducted a systematic review of three techniques that involve the re-infusion of a patient's blood--pre-operative autologous blood deposit (PAD), acute normovolaemic haemodilution (ANH), and cell salvage (CS). We examined the effects of these interventions on the need for peri-operative allogeneic red blood cell transfusion and on clinical outcomes. Controlled clinical studies were identified by computer searches of comprehensive electronic databases and bibliographic searches of published articles. The literature search retrieved a total of 68 randomized trials (RCTs) and 81 controlled observational studies that included data from over 34 000 individuals. In summary, the RCTs found that autologous transfusion techniques consistently reduced the frequency of allogeneic transfusions, with intervention effect sizes ranging from a relative 63% reduction (95% CI 46-74%) with PAD, to 42% (27-53%) with CS and to 31% (16-44%) with ANH. Non-randomized studies reported larger effect sizes than RCTs. PAD increased overall transfusion rates by 30% (95% CI 12-48%) and reduced pre-operative haemoglobin levels by an average of 1.23 g dL(-1). Intervention effects were substantially reduced when these techniques were performed under transfusion protocols. Interpretation of the studies was hampered by

serious methodological weaknesses, particularly inadequate randomization techniques, unblinded measurements and the subjective nature of the outcome variables. The studies reported few clinical outcome and adverse event data. Previous claims regarding reduced rates of mortality and infection with autologous transfusions were not confirmed.

Transfusion of post-operative shed blood: laboratory characteristics and clinical utility.

Eur Spine J. 2004 May 8 Munoz M, Garcia-Vallejo JJ, Ruiz MD, Romero R, Olalla E, Sebastian C. Department of Biochemistry and Molecular Biology, School of Medicine, University of Malaga, Malaga, Spain.

Increased awareness of the potential hazards of allogenic blood transfusion, such as incompatibility reactions, metabolic and immunologic disorders, or transmission of viral diseases, has led to an emphasis on allogeneic blood alternatives. For orthopaedic surgery, several autologous transfusion modalities have emerged as alternatives to allogeneic blood transfusion, avoiding its immunomodulatory effects. Among them, transfusion or return of post-operative salvaged shed blood has become popular in major orthopaedic procedures. However, although the effectiveness of this blood-saving method is well documented, several authors have questioned its safety and recommended the use of washed blood. Therefore, this review analyses the haematologic characteristics of unwashed filtered shed blood, including metabolic status and survival of red blood cells, the components of the haemostatic system, the content of fat particles, bacterial and tumour cells and the possibility of their removal, the content of inflammatory mediators, and the effects on the patient's immune system. From data reviewed in this paper, it can be concluded that post-operative salvage of blood seems to be an excellent source of functional and viable red cells without many of the transfusion-related risks and with some immuno-stimulatory effects. In addition, from our experience, post-operative re-infusion of unwashed shed blood after major spine procedures has proved to reduce post-operative homologous transfusion requirements and to complement pre-operative autologous blood donation, without any clinically relevant complication.

Use of Recombinant Factor VIIa in Infants with Severe Coagulopathy.

J Perinatol. 2004 May;24(5):310-1. Fontaine MJ, Lazarchick J, Taylor S, Annibale D. 1Department of Pathology, Transfusion Medicine Division (M.J.F.), Hematopathology Division (J.L.) Medical University of South Carolina, Stanford University, Stanford, CA, USA.

The risk of hemorrhage in infants with severe coagulopathies unresponsive to fresh frozen plasma (FFP) infusions may preclude therapeutic invasive interventional procedures. We describe the successful use of recombinant factor VIIa (rFVIIa) in two such infants, the first with cirrhosis requiring paracentesis and the second with necrotizing enterocolitis requiring laparotomy. This report reviews the current concepts on the mechanism of action of the drug rFVIIa and considers its expanded use in infants unresponsive to FFP replacement.Journal of Perinatology (2004) 24, 310-311. doi:10.1038/sj.jp.7211086

Enhanced angiogenesis following allogeneic blood transfusion.

Clin Lab Haematol. 2004 Apr;26(2):129-35. Patel HB, Nasir FA, Nash GF, Scully MF, Kakkar AK. Thrombosis Research Institute, Emmanual Kaye Building, Manresa Road, London, UK. tabarouni@aol.com

Blood transfusions are associated with recurrence of solid cancers. Angiogenesis is essential for cancer growth. Our aim was to determine for the first time in a prospective cohort study the effect of prestorage allogeneic leucodepleted SAGM (saline, adenine, glucose, mannitol) red cell transfusion on angiogenic factor levels and in vitro angiogenesis. Forty pretransfusion adult hospital inpatients were selected consecutively. Serum vascular endothelial growth factor (VEGF) and endostatin were measured in each patient before and after prestorage allogeneic leucodepleted SAGM red cell transfusion. All samples were exposed to an in vitro endothelial cell proliferation assay and 10 sample groups were also exposed to an in vitro whole angiogenesis assay. The median number of units transfused was 2 (minimum-maximum, 2-4). Twenty-nine (73%) patients had a rise in VEGF, with an overall increase of 118 pg/ml (quartiles -5, 306; $P < 0.01$). Twenty-eight (70%) patients had a decrease in endostatin, with an overall reduction of 1.2 ng/ml (quartiles 4.0, 0.0; $P = 0.017$). There was an overall 33% increase in endothelial cell proliferation ($P < 0.01$) and a 9.4% increase in in vitro whole assay angiogenesis ($P < 0.01$). Prestorage allogeneic leucodepleted SAGM red cell transfusions are associated with a favourable angiogenic factor imbalance and an elevation in in vitro angiogenesis.

Reducing red cell transfusion by audit, education and a new guideline in a large teaching hospital.

Transfus Med. 2004 Feb;14(1):25-31. Garrioch M, Sandbach J, Pirie E, Morrison A, Todd A, Green R. Department of Anaesthesia, South Glasgow University Hospitals NHS Trust and University of Glasgow, Glasgow, Scotland, UK. magnus.garrioch@doctors.org.uk

Safety concerns combined with the greatly increased costs and difficulties of maintaining the blood supply are major considerations for transfusion services. Previous local surveys demonstrated that hospital blood use at our hospital could be improved. Excessive cross-matching, unnecessary transfusion and high return rates of unused blood were commonplace. Transfusion practice was audited over a 3-month period. An education package with guidelines for transfusion was delivered to all clinician groups within the hospital, over the following 9 months. The audit was repeated exactly 1 year later at the same time period. During the second audit, inpatient hospital numbers increased by 1.02% (from n = 7262 to n = 7336) but no differences in length of stay, cardiovascular morbidity or mortality were demonstrated. Twenty percent (n = 254, 2002; n = 316, 2001) fewer patients received blood, and the number of red cell packs used reduced by 19% (from n = 1093 to n = 880). Total number of patients transfused reduced from 4.4% to 3.5% which, as an absolute difference, is a reduction of 0.9% (CI 0.3-1.5, P = 0.006). The audit, guideline and education package had a major impact on red cell use within the hospital with no adverse effects. Blood use can be improved by the implementation of a suitable education package and guideline. If it is possible to replicate the results of this education programme nationwide, the effect on blood use, with subsequent savings and enhanced patient safety could be significant.

A prospective double blind randomized study comparing the need for blood transfusion with terlipressin or a placebo during early excision and grafting of burns.

Burns. 2004 May;30(3):236-40. Mzezewa S, Jonsson K, Aberg M, Sjoberg T, Salemark L. Department of Surgery, University of Zimbabwe, Harare, Zimbabwe.

INTRODUCTION: Early excision and skin grafting has become the standard of good burn management, but it is associated with major blood loss. AIM: To determine the haemostatic effect of terlipressin compared with placebo. MATERIAL AND METHODS: Fifty-one patients with burns of 10-20% total body surface area had early excision and split skin grafting of deep burns. The surface area of the burn wound and of the healed graft were measured by planimetry. The patients were randomly allocated to medication, either terlipressin or placebo. Blood loss and number of transfused units of blood were recorded. RESULTS: Twenty-one patients received terlipressin, 13 received terlipressin late (cross-over) and 17 received placebo. Six out of 21 patients exposed to terlipressin were transfused with eleven units of packed red blood cells. Seven out of 13 patients crossed over from placebo to terlipressin (late terlipressin) were transfused with 17 units of blood. Eight out of 17 patients exposed to the placebo were transfused with 22 units of blood ($P < 0.05$). Graft healing was 1055 +/- 609 cm2 out of 1452 +/- 11 cm2 in terlipressin and 914 +/- 633 cm2 out of 1288 +/- 720 cm2 in the placebo group (n.s.). CONCLUSION: Terlipressin reduced the need for blood transfusion by a factor of 2.5 compared to a placebo without impairment of graft healing.

Transfusion Of The Injured Patient: Proceed With Caution.

*Shock. 21(4):291-299, April 2004. Silliman, Christopher C *,+,++,[S]; Moore, Ernest E +; Johnson, Jeffrey L +; Gonzalez, Ricardo J [S]; Biffl, Walter L +*

Abstract: Transfusion of the injured patient with packed red blood cells (PRBCs) is a dynamic process requiring vigilance during the acute resuscitative and recovery phases postinjury. Although adverse events have been reported in 2% to 10% of injured patients, the advent of new detection techniques for viral pathogens has markedly decreased the risk of infectious transmission. However, transfusions are strongly associated with immunosuppression in the host, which may occur days after the initial injury and may lead to bacterial infections. Conversely, early transfusion of stored PRBCs, >6 units in the first 12 h postinjury, contributes to an early state of hyperinflammation that is a strong, independent predictor of multiple organ failure (MOF) in those patients with intermediate injury severity scores. The roles of prestorage leukoreduction are also reviewed with respect to the promotion of both immunosuppression and hyperinflammation. We further summarize studies with hemoglobin substitutes, whose use may obviate many of the untoward events of transfusion and promise to lead to better outcomes for injured patients.

'Last-ditch' use of recombinant factor VIIa in patients with massive haemorrhage is ineffective.

Vox Sang. 2004 Feb;86(2):120-4. Clark AD, Gordon WC, Walker ID, Tait RC. Haematology Department, Glasgow Royal Infirmary, Glasgow, UK. campbell.tait@nothglasgow.scot.nhs.uk

BACKGROUND AND OBJECTIVES: The aim of this retrospective study was to assess the effect of activated recombinant factor VII (rFVIIa) on the natural history of massive transfusion episodes. MATERIALS AND METHODS: During 2002, outcome parameters were assessed in 50 patients transfused with more than 10 units of packed red cells. The effect of the addition of rFVIIa in 10 patients, with intractable bleeding, was then observed. RESULTS: Overall mortality was 20% at 24 h and 34% at 7 days. Severe coagulopathy was confirmed as a serious negative prognostic factor and occurred in 42% of patients overall, but in 70% of rFVIIa-treated patients. Transient cessation or reduction of bleeding was noted in 60% of patients following rFVIIa infusion. However, 24-h and 7-day mortality rates were 40% and 70%, respectively, in this group. CONCLUSIONS: Last-ditch rFVIIa therapy in patients resistant to conventional treatment did not rescue these patients or significantly alter outcomes.

New additions to the intensive care armamentarium.

Drugs Today (Barc). 2004 Feb;40(2):157-70.
Rice TW, Bernard GR. Division of Allergy, Pulmonary and Critical Care Medicine, Vanderbilt University School of Medicine, Center for Lung Research, Nashville, Tennessee 37232-2650, USA. todd.rice@vanderbilt.edu

Many advances have improved the care of critically ill patients, but only a few have been through the use of pharmaceutical agents. Recently, the US Food and Drug Administration (FDA) approved drotrecogin alfa (activated), or recombinant human activated protein C, for the treatment of patients with a high risk of death from severe sepsis. Drotrecogin alfa (activated) has antiinflammatory, antithrombotic and fibrinolytic properties. When given as a continuous intravenous infusion, recombinant human activated protein C decreases absolute mortality of severely septic patients by 6.1%, resulting in a 19.4% relative reduction in mortality. The absolute reduction in mortality increases to 13% if the population treated is restricted to patients with an APACHE II score greater than 24, as suggested by the FDA. The most frequent and serious side effect is bleeding. Severe bleeds increased from 2% in patients given placebo to 3.5% in patients receiving drotrecogin alfa (activated). The risk of bleeding was only increased during the actual infusion time of the drug, and the bleeding risk returned to placebo levels 24 hours after the infusion was discontinued. Patients treated in the intensive care unit frequently develop anemia, usually severe enough to require at least one transfusion of red blood cells. With the recent discovery of the harmful effects of allogeneic red blood cell transfusions and the increasing shortage of available red blood cell products, emphasis has been placed on minimizing transfusions. Patients who receive exogenous recombinant human erythropoietin maintain higher hemoglobin levels, in spite of requiring fewer transfusions during their stay in the intensive care unit. Recombinant human erythropoietin appears to be effective whether it is given as 300 units/kg of body weight subcutaneously every other day or as 40,000 units subcutaneously every week. Differences in hemoglobin values were not apparent until at least one week of therapy, but they continued to diverge after that initial week. Furthermore, the incidence of adverse events was similar to that of patients receiving placebo and there was no difference in mortality, suggesting that avoidance of blood transfusions did not translate into increased survival. Thus, recombinant human erythropoietin appears to be both safe and effective in treating the anemia found in critically ill patients, but it is less clear that such treatment is cost effective, especially in the higher dose regimens. Hypotension in patients with septic shock is often difficult to correct. Despite enormous dosages of catecholamines, many of these patients continue to have inadequate blood pressures. Inadequate levels of vasopressin have been identified in patients with septic shock, as well as in other patients with hypotension secondary to refractory vasodilatation. Vasopressin is a peptide hormone secreted from the posterior pituitary in response to hyperosmolality, hypovolemia or hypotension. Levels of vasopressin initially rise in patients with septic shock, but as hypotension persists, vasopressin levels fall below normal. Administration of exogenous vasopressin in physiologic dosages significantly increases blood pressure in patients with shock associated with sepsis and other vasodilatory states. This rise in blood pressure is often significant enough that endogenous catecholamines can be decreased and frequently discontinued entirely. Early withdrawal of the vasopressin replacement infusion results in recurrent hypotension. Unfortunately, randomized, blinded, placebo-controlled trials showing improvement in long-term outcomes such as mortality and length of stay are still lacking.

Meeting the clinical challenge of care for Jehovah's Witnesses.

Transfus Med Rev. 2004 Apr;18(2):105-16.
Bodnaruk ZM, Wong CJ, Thomas MJ. Hospital Information Services for Jehovah's Witnesses (Canada), Georgetown, ON L7G 4Y4, Canada. zbodnaruk@wtbts.ca

Quality patient care entails more than simply biomedical interventions. Respect for the wishes, values, and preferences of patients are important elements of quality care. Unique aspects of the beliefs of Jehovah's Witnesses may present physicians with ethical and clinical conflicts. Witnesses believe that allogeneic blood

transfusion (ie, whole blood, red blood cells, white cells, platelets, and plasma) and preoperative autologous blood deposit (PAD) are prohibited by several Biblical passages. This article reviews the Witness position on medical care, blood components, and fractions, placing these and related interventions into categories that may help physicians to individualize clinical management plans and meet the challenge of caring for patients who are Jehovah's Witnesses. It includes an overview of cost, safety, efficacy, and medicolegal issues related to patient care using transfusion-alternative strategies.

The use of recombinant coagulation factor VIIa in uncontrolled postoperative bleeding in children undergoing cardiac surgery with cardiopulmonary bypass.

Pediatr Crit Care Med. 2004 May;5(3):246-50. Pychynska-Pokorska M, Moll JJ, Krajewski W, Jarosik P. Department of Anesthesiology and Intensive Care (MP-P, WK) and the Clinic of Cardiosurgery (JJM, PJ), Polish Mother Memorial Hospital Research Institute, Lodz, Poland.

OBJECTIVE: To assess the hemostatic efficacy of recombinant coagulation factor VIIa (rFVIIa) in the management of uncontrolled bleeding in postcardiac surgery with cardiopulmonary bypass in children. DESIGN: An open-label study. SETTING: A postoperative intensive care unit. PATIENTS: Eight consecutive pediatric patients with excessive bleeding after cardiac surgery with cardiopulmonary bypass that met the criteria for reexploration and did not respond to optimal transfusions of platelets and fresh frozen plasma. INTERVENTIONS: rFVIIa 30 microg/kg was given as a bolus injection. A higher dose of 60 microg/kg was used if a patient had preoperative coagulopathy, preoperative multiple-organ failure, or indications that required an emergency operation. The same dose was repeated 15 mins after the previous injection if the bleeding had not decreased. If the bleeding had decreased but still exceeded 10 mL/hr for body weight </=5 kg or exceeded 2 mL.kg(-1).hr(-1) for body weight >5 kg, the same dose was repeated 2 hrs after the previous injection. A maximum of four doses could be given before rFVIIa was considered ineffective and a reexploration was needed. MEASUREMENTS AND MAIN RESULTS: Postoperative blood loss was estimated from the volume of chest tube drainage. rFVIIa successfully controlled bleeding and prevented reexploration in all seven patients who received treatment according to the protocol. One patient who received only one dose of rFVIIa required reexploration because a second dose was not available. No adverse events related to rFVIIa were seen. CONCLUSIONS: rFVIIa may be useful in preventing reexploration in uncontrolled postoperative bleeding in children undergoing cardiac surgery with cardiopulmonary bypass. Randomized, placebo-controlled studies are needed to confirm the safety and efficacy of rFVIIa in this clinical setting.

What is the evidence for using hemostatic agents in surgery?

Eur Spine J. 2004 May 7 Erstad BL.Department of Pharmacy Practice and Science, College of Pharmacy, 85721-0207, Tucson, Arizona, USA.

The pharmacological methods used to achieve systemic hemostasis have generated much discussion due to concerns of serious adverse effects (e.g., thromboembolic complications) and costs of therapy in addition to efficacy considerations. There are a limited number of well-controlled trials involving pharmacological hemostasis for spine surgery. In the largest double-blinded randomized controlled trial to date involving spine surgery, there was a trend toward reduced homologous transfusion in patients receiving aprotinin, but the only statistically significant result ($p<0.001$) was a reduction in autologous red cell donations. The findings of this trial are important, since the investigators used a number of restrictive transfusion strategies (e.g., autologous donation, low hematocrit trigger for transfusion, blood-salvaging procedures with the exception of no cell saver) that were not always employed in earlier trials involving hemostatic agents. Smaller studies involving antifibrinolytic agents other than aprotinin have demonstrated reductions in blood loss and transfusion requirements in patients undergoing spine surgery, although the results were not always statistically significant. A very large randomized trial would be required to address comparative medication- and transfusion-related adverse events; such a trial involving patients undergoing cardiac surgery is currently being performed. Additionally, cost-effectiveness analyses are needed to help define the role of these agents based on the data that is available.

Volume replacement and microhemodynamic changes in polytrauma.

Langenbecks Arch Surg. 2004 Apr 28 Vollmar B, Menger MD. Department of Experimental Surgery, University of Rostock, 18055, Rostock, Germany.

Though fluid administration is one of the most basic concepts in resuscitation, there is ongoing controversy and continuing research on the definition of the ideal fluid for resuscitation of trauma and hemorrhage and for intraoperative volume support. In general, crystalloids and colloids, as well as blood, blood substitutes and

oxygen therapeutics, are available. This report briefly revisits the physiological mechanisms underlying resuscitation with crystalloids and colloids, emphasizing colloid-supplemented resuscitation with hypertonic saline. Finally, potential applications of oxygen therapeutics are briefly considered.

Transfusion of post-operative shed blood: laboratory characteristics and clinical utility.

Eur Spine J. 2004 May 8 Munoz M, Garcia-Vallejo JJ, Ruiz MD, Romero R, Olalla E, Sebastian C. Department of Biochemistry and Molecular Biology, School of Medicine, University of Malaga, Malaga, Spain.

Increased awareness of the potential hazards of allogenic blood transfusion, such as incompatibility reactions, metabolic and immunologic disorders, or transmission of viral diseases, has led to an emphasis on allogeneic blood alternatives. For orthopaedic surgery, several autologous transfusion modalities have emerged as alternatives to allogeneic blood transfusion, avoiding its immunomodulatory effects. Among them, transfusion or return of post-operative salvaged shed blood has become popular in major orthopaedic procedures. However, although the effectiveness of this blood-saving method is well documented, several authors have questioned its safety and recommended the use of washed blood. Therefore, this review analyses the haematologic characteristics of unwashed filtered shed blood, including metabolic status and survival of red blood cells, the components of the haemostatic system, the content of fat particles, bacterial and tumour cells and the possibility of their removal, the content of inflammatory mediators, and the effects on the patient's immune system. From data reviewed in this paper, it can be concluded that post-operative salvage of blood seems to be an excellent source of functional and viable red cells without many of the transfusion-related risks and with some immuno-stimulatory effects. In addition, from our experience, post-operative re-infusion of unwashed shed blood after major spine procedures has proved to reduce post-operative homologous transfusion requirements and to complement pre-operative autologous blood donation, without any clinically relevant complication.

Transfusion Predictors in Liver *Transplant*

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In this study we sought to determine the factors influencing red blood cell (RBC) transfusions and to study the transfusion practice of anesthesiologists during liver transplants. A retrospective study of 206 successive liver transplants was undertaken during a period of 52 mo. Transfused blood products were identified. Twenty variables were analyzed in a univariate fashion. For the multivariate analysis, the cases were divided in 2 subgroups: more than 4 RBC units transfused and 4 or less RBC units transfused. The average number of RBC units transfused during a liver transplant was 2.8 (± 3.5) per patient, 32.0% did not receive any RBC, and 19.4% did not receive any blood products during the transplant. Three variables were related to the number of RBC units transfused: the starting International Normalized Ratio value, the starting platelet count, and the duration of surgery. We found that there was a wide difference in the transfusion practice of the anesthesiologists involved in this series of liver transplants. It was difficult to identify predictive factors for RBC transfusions when the transfusion rate was small and because of the variability in human factors. Plasma transfusion did not decrease the rate of RBC transfusions; sometimes it was the contrary. IMPLICATIONS: This is a retrospective study of 206 liver transplants over 52 mo to identify the predictive factors of red blood cell transfusions and the anesthesiologists' transfusion strategies. We conclude that there is a wide difference in transfusion practices among anesthesiologists.

Perioperative Blood Transfusion Is Predictive of Poststernotomy Surgical Site Infection: Marker for Morbidity or True Immunosuppressant?

Thomas R. Talbot,1 Erika M. C. D'Agata,1,a Vicki Brinsko,2 Byron Lee,4 Theodore Speroff,1,3,5 and William Schaffner1,3 Departments of 1Medicine, 2Infection Control, and 3Preventive Medicine and Centers for 4Clinical Improvement and 5Health Services Research, Vanderbilt University School of Medicine, Nashville, Tennessee

To analyze risk factors for the development of adult poststernotomy surgical site infections (SSIs), we performed a retrospective case-control study at a tertiary care hospital. Case patients with poststernotomy SSI between June 1999 and January 2001 were matched to control subjects without poststernotomy SSI according to date of procedure and age. Data were

collected on known SSI risk factors. Of 711 procedures, we identified 38 cases with SSI and 114 matched controls. Univariate analysis revealed that receipt of transfused blood (odds ratio [OR], 3.19; 95% confidence interval [CI], 1.546.62), diabetes (OR, 2.90; 95% CI, 1.276.59), length of stay before hospitalization (OR, 1.19 per day; 95% CI, 1.021.37 per day), and American Society of Anesthesia score (OR, 2.19; 95% CI, 1.044.64) were significantly associated with SSI. Multivariate analysis revealed that transfusion (OR, 3.21; 95% CI, 1.417.31) and diabetes (OR, 3.65; 95% CI, 1.429.36) were predictors for SSI. The exact role of blood transfusion in the pathogenesis of SSI, whether as a direct immunosuppressant or a surrogate marker for morbidity, remains unresolved.

Fluid choice for resuscitation of the trauma patient: a review of the physiological, pharmacological, and clinical evidence:

Can J Anaesth. 2004 May;51(5):500-13. Boldt J. Department of Anesthesiology and Intensive Care Medicine, Klinikum der Stadt Ludwigshafen, Ludwigshafen, Germany.

PURPOSE: Volume replacement regimens are discussed very emotionally. Interpretation of the literature is difficult due to variations in study design, patient population, target for volume replacement, endpoints, and type of fluids. Meta-analyses may not be very helpful because all kinds of patients and very old studies are included. The principles and options for volume replacement were reviewed exclusively in trauma patients and studies from the literature focusing on this problem were analyzed. SOURCE: Using a MEDLINE search, volume replacement therapy in adult trauma patients published in the English language from 1985 to the end of 2002 were identified and analyzed. Studies on prehospital volume replacement, volume replacement in the emergency area or in the operating room, and volume therapy in trauma intensive care unit patients were included. Principle findings: The age-old crystalloid/colloid controvery has still not been resolved but has been enlarged to a colloid/colloid debate. It is now widely accepted that human albumin could easily be replaced by synthetic colloids for volume replacement in trauma patients. No superiority of a specific volume replacement strategy with regard to outcome was found. However, in several studies outcome was not the major endpoint. Although showing some promising results, the importance of hypertonic solutions for volume replacement in the trauma patient is not yet defined. CONCLUSION: The choice of fluid therapy in trauma patients engenders the most controversy and an examination of the body of literature on this subject results in confusion. It is imperative to continue the search for substances that are effective in avoiding the development of post-trauma multi-organ dysfunction syndrome without detrimental side-effects.

Fibrin sealant produced by the CryoSeal(R) FS System: product chemistry, material properties and possible preparation in the autologous preoperative setting.

Vox Sang. 2004 May;86(4):257-62. Buchta C, Dettke M, Funovics PT, Hocker P, Knobl P, Macher M, Quehenberger P, Treitl C, Worel N. Department of Blood Group Serology and Transfusion Medicine, Vienna Medical University, Vienna, Austria.

Background and Objectives The CryoSeal(R) FS has been introduced as an automated device for the production of fibrin sealant from small volumes of plasma. We tested this device and compared the product with commercially available fibrin sealants and with the requirements of the European Pharmacopoeia. Materials and Methods The CP3 program and disposables required were used to manufacture fibrin sealant. The chemistry and mechanical properties of the product were investigated. Results The cryoprecipitate generated with CryoSeal(R) contains concentrated fibrinogen and critical clotting factors. The efficiency of the production process is poor, but the production procedure itself is simple and not time-consuming. The volume of plasma required allows application in the preoperative autologous setting. Conclusions The CryoSeal(R) FS is an automated device for cryoprecipitation and production of thrombin. It can be implemented easily in the clinical routine, although, owing to product specifications, the efficacy of the CryoSeal(R) fibrin sealant requires further clinical trials.

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