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Blood Management

A Patient-Centered Approach

Strategies for Treatment of Coagulopathy

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Overview of the Complex Coagulopathy Associated With Hemorrhage

Survival from traumatic hemorrhagic shock (THS) in military and civilian arenas is as elusive as a "cure for cancer." THS is a primary cause of more than 5 million trauma-related deaths worldwide and a leading cause of death of young people. THS is a high-mortality condition that presents with hypovolemic anemia often accompanied by coagulopathy that results in uncontrollable bleeding, systemic inflammation and infection in open wounds and damaged blood vessels.[1]

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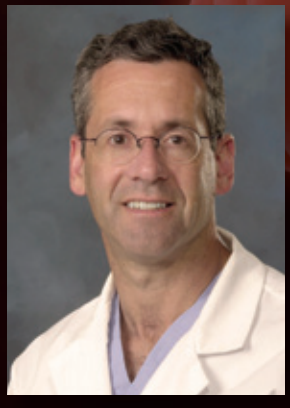
Current Models for Resuscitation Associated With Coagulopathy and Hemorrhage

Blood transfusion is currently the most effective therapy for THS but often not immediately available at out-of-hospital settings where most traumatic injuries occur (remote sites of accidents or battlefields). Current available prehospital therapy for THS is infusion of isotonic crystalloid solutions (less commonly, colloids). However, large volumes of crystalloids used to maintain or restore BP in THS patients generally cause fluid overload resulting in dilution of hemostatic and other beneficial mediators. In addition, crystalloids are devoid of oxygen essential to maintain vital organ functions and coagulation factors that enable clot production. The conservative approach to hemorrhagic trauma management has been to transport the patient as rapidly as possible to the nearest trauma facility to improve outcome by controlling bleeding and aggressively resuscitating the victim, focusing on the airway, breathing and circulation. There is some evidence that early low-volume resuscitation may improve outcome.[2] In exsanguinating trauma without significant brain injury, hypotensive resuscitation is favored by some.[3]

Upon arrival at major trauma institutions, blood component resuscitation is frequently driven by massive transfusion protocols trending toward 1:1:1 RBC:FFP:platelet ratios.[4]



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Associated with Hemorrhage

Despite the primarily retrospective military and civilian data[5] and lack of robust PRCTs,[6] the trauma surgical community, in spite of some controversy, remains enthusiastic about such ratios given possible beneficial impact on mortality perhaps related to the rapidity of component administration and the reduction in crystalloid use. Prospective studies are urgently needed to guide clinicians in assessing both benefits and potential unintended consequences of ratio-guided massive transfusion. The PROPPR study (Pragmatic Randomized Optimal Platelet and Plasma Ratios, http://cetir-tmc.org/research/proppr) will investigate different ratios of blood products given to trauma patients who are predicted to require massive transfusions.

Current Increased Use of Antifibrinolytics in Hemorrhage in Trauma, Obstetrics

Use of antifibinolytics, commonly used in cardiac bypass and valve surgery, have been incorporated into the treatment of trauma-associated coagulopathy and are being studied in obstetric hemorrhagic as well. While routine use is not common, administration of antifibrinolytics (tranexemic acid) within three hours of the injury may be of benefit. Use of a thrombelastograph or similar device to assess coagulation profiles before and after treatment can be very helpful in determining the real-time efficacy of the treatment.[7]

Acute Traumatic Coagulopathy

Acute traumatic coagulopathy (ATC) is an acute endogenous coagulopathy that develops rapidly after injury and is associated with increased mortality.[8-12] In the setting of major traumatic injuries, Mitra and colleagues examined the association between acute coagulopathy and early mortality. ATC was significantly associated with early death, independent of transfusion status and severity of injury.[13] Brohi and colleagues reported that one in four patients who sustained severe traumatic injury were coagulopathic on admission to the hospital.[14] A recent review of animal models of trauma-induced coagulopathy reported that both severe tissue injury and hemorrhagic shock were initiators for the development of ATC following traumatic injury. The authors noted that subsequent events such as hypothermia, acidosis and hemodilution contributed to the development of trauma-induced coagulopathy (TIC).[15] In a review of mechanisms related to trauma and coagulopathy, Hess and colleagues reported on the multifactorial nature of coagulopathy and listed six key initiators: tissue trauma, shock, inflammation, acidemia, hypothermia and hemodilution. They also noted that early coagulopathy was related to tissue injury and shock with exacerbations related to treatment with intravenous fluid therapy and subsequent hemodilution; uncontrolled bleeding further worsened the coagulopathy with ensuing hypothermia and academia.[16] Others have reported early development of coagulopathy in severely injured patients and exacerbation of coagulopathy from hypothermia, acidosis and aggressive early resuscitation with acellular fluids contributing to hemodilution.[9-11] Cohen and colleagues noted ATC related to tissue injury and hypoperfusion mediated by activation of protein C pathways. The authors reported an association of higher plasma protein C levels and poor outcomes after traumatic injury.[17] Hypoperfusion is thought to lead to endothelium releasing factors, which activates both protein C (inhibiting thrombin formation) and tissue plasminogen activator (resulting in hyperfibrinolysis).[18]

A number of investigators have suggested using point-of-care testing to assist with earlier recognition and guidance of therapy in ATC.[8-10] Investigators have highlighted the challenges in differentiating microvascular hemorrhage due to coagulopathy from surgical bleeding in injured patients. They suggested using individualized goal-directed therapy based on viscoelastic coagulation tests to assist with differentiation and to guide therapy as opposed to relying on the infusion of protocol-driven fixed ratio resuscitation (fresh frozen plasma: red blood cells: platelets). Furthermore, the rapidity of diagnostic tests may allow hemostatic therapy to be tailored to the individual patient and therefore reduce the risk for under- or over-transfusion.[19]

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Challenges in Measuring Coagulopathy Associated With Hemorrhage

Coagulopathy due to hemorrhagic shock is complex and multifactorial. Mechanisms include tissue injury, shock, hemodilution, hypothermia, inflammation and acidosis. Thus, measuring and quantifying coagulopathy associated with hemorrhage is difficult. Plasma-based tests such as activated partial thromboplastin time (aPTT) and prothrombin time (PT) were developed half a century ago to monitor hemophilia and anticoagulation therapy. These tests reflect only the small amount of thrombin formed during initiation of coagulation and have never been validated for prediction of hemorrhage in a clinical setting, nor to guide transfusion therapy during severe bleeding.[20]

There is a lack of quality evidence to identify an INR (or PT/aPTT), fibrinogen level or platelet count to trigger blood component transfusion in patients with critical bleeding requiring massive transfusion.[21] This is due to the dynamic and complex interactions of thrombin, fibrinogen, tissue factor, platelets, other clotting factors and endothelium in the bleeding patient, which is modified by shock, resuscitation, hypothermia and acidosis.[22]

Further research is needed to determine when FFP, platelets, cryoprecipitate or fibrinogen concentrate are effective and result in improved outcome and to clarify the role of point-of-care testing in enhancing care.

Management of Obstetric Hemorrhage

Hemorrhage in the obstetric setting, including postpartum hemorrhage, can rapidly become life-threatening and require massive transfusion. A standardized team response to massive obstetric hemorrhage can lead to optimal outcomes and may reduce associated morbidity and mortality. Such a response is facilitated by using guidelines and checklists such as those developed by the California Maternal Quality Care Collaborative,[23] which involves four ascending levels of response for obstetrical hemorrhage:

Stage 0) all births – evaluate for risk factors and actively manage the third stage of labor (e.g., oxytocin, fundal massage);

Stage 1) OB hemorrhage – activate the "hemorrhage protocol," assemble appropriate personnel and prepare for transfusion;

Stage 2) continued OB hemorrhage – assess coagulation status, consider surgical or interventional radiology interventions, transfuse blood products;

Stage 3) critical OB hemorrhage with cumulative blood loss > 1,500 ml – aggressively transfuse based on vital signs and blood loss using a massive transfusion protocol and perform conservative or definitive procedures to stop the bleeding (uterine artery ligation, hysterectomy, selective embolization). Expert opinion currently favors maintenance of a higher fibrinogen level in MT for obstetric patients. Blood salvage is now advocated, although there are many logistical problems with this technique and it is not widely employed.

Whether or not Factor VIIa or tranexamic acid should be given to women with significant postpartum hemorrhage is unclear. The World Maternal Antifibrinolytic Trial (WOMAN Trial) aims to determine the effect of early administration of tranexamic acid on mortality, hysterectomy and other morbidities in a randomized, double-blind, placebo-controlled trial among 15,000 patients.[24] However, no standard practice can be recommended at this point in time.

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Transfusion Guidelines and the Individual Patient:

The Difference Between Clinical Setting and Randomized Studies – European View

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With the improvement in blood safety, in particular radical reduction of envelope viral risk, we now face increasing concerns regarding transfusion-associated negative outcomes, including morbidity and mortality. In contrast, in a French survey of anesthesia-related mortality, the estimated number of anesthetic procedures performed in France was 7,756,121/year with a total of 419 deaths totally or partly related to anesthesia.[1] Several usual causes of death were identified, but the consequences of hemorrhage and anemia played a disturbing role. It was estimated from this survey that about 100 perioperative deaths might occur in France every year as the result of inadequate blood management. Surprisingly, a great number of deaths were associated with delayed or absent red blood cell transfusion, whereas few complications occurred after a transfusion in this population. About two-thirds of the deaths occurred more than 24 hours after surgery. According to the root-cause analysis, anemia was suspected to have led to myocardial ischemia and cardiovascular death, which remains a major cause of death after non-cardiac surgery.[2,3,4]

"Current transfusion guidelines recommend red blood cell transfusion for anemia with associated symptoms. Unresolved is whether the presence of clinical symptoms of anemia is a late and possibly irreversible sign. The answer is controversial for many reasons."

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Current transfusion guidelines[5] recommend red blood cell transfusion for anemia with associated symptoms. Unresolved is whether the presence of clinical symptoms of anemia is a late and possibly irreversible sign. The answer is controversial for many reasons. Although not related to anemia, in the POISE study,[6] 5 percent of patients undergoing non-cardiac surgery had a perioperative myocardial infarction (MI). Most MI (74.1 percent) occurred within 48 hours of surgery. Moreover, 65.3 percent of patients did not experience ischemic symptoms. The 30-day mortality was 11.6 percent (48 of 415 patients) among patients who had a perioperative MI and 2.2 percent (178 of 7936 patients) among those who did not (P 0.001). It is important to notice that mortality rates were elevated and similar between those with (9.7 percent; adjusted OR = 4.76 [95 percent CI, 2.68 to 8.43]) and without (12.5 percent; adjusted OR = 4.00 [CI, 2.65 to 6.06]) ischemic symptoms.

Mortality rates related to red cell transfusion have been the subject of contradictory results in both observational and randomized controlled trials. In one of the first randomized studys, with 840 ICU patients, Hebert et al. compared restrictive threshold to maintain Hb between 7-9g/dl and a liberal transfusion threshold to maintain Hb in the 10-12g/dl.[7] The mortality rate was lower in the restrictive group (17 percent) as compared to the liberal group (23 percent). However, these results may not apply to postoperative patients who require active rehabilitation. Two randomized, controlled studies have compared two transfusion strategies in hip fracture surgery and have given opposite results. The study by Foss et al. included 120 patients and has shown a significant increase in mortality rate in the restrictive group (8-10g/dl) versus liberal (10g/dl), but no difference in active rehabilitation, fatigue walking and dizziness.[8] The two groups were not completely comparable, however. The recently published FOCUS study[9] included 2,000 elderly patients with known coronary heart disease. No difference was detected with regard to mortality, morbidity and physical activity between the restrictive (only transfused if Hb = 8g/dl and presence of symptoms) and the liberal group (transfusion to maintain Hb = 10g/dl). In this study, the average Hb level of the restrictive group remains close to

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9g/dL throughout the study period, and the mean Hb of the liberal group was higher than 10g/dl. Second, although not significant, there is a trend toward a small proportion of MI in the restrictive group. It should be noted that all patients in the restrictive group who had symptoms were transfused. This latest trial suggests the conservative approach, although not completely generalizable, is safe.

All records, particularly a large Norwegian registry[2] of more than 67,000 hip and knee interventions, show that MI is the leading cause of mortality. Postoperative predictors are kidney failure and bleeding. Bleeding, if acute and unchecked, can result in severe anemia that could lead to ischemia, resulting in MI. In clinical practice, checking for tachycardia and electrocardiographic signs of myocardial ischemia are not done routinely as in randomized trials. In addition, in clinical practice, time elapsed from blood sample collection to hemoglobin level results and subsequent transfusion may be quite long.

In the case of significant bleeding, patients may spend significant time under the recommended Hb threshold. Expedited diagnosis of the cause and prompt treatment cannot be overemphasized, including transfusion support when appropriate.

What Should the Clinician Do at the Bedside?

When contemplating a transfusion, one should note that allogeneic blood is associated with potential adverse events. Indeed, transfusion is independently associated with increased mortality, acute pulmonary edema (TRALI and TACO), hospital-acquired infection, increased length of stay and considerable cost. As a result of all this, strategies have been developed to reduce the need for red cell transfusion. Such measures include the implementation of "restrictive" transfusion thresholds, preoperative blood mass optimization, perioperative blood salvage and pharmaceutical interventions to reduce bleeding. Current transfusion guidelines are helpful, but they are not applicable to all situations. One must remember that each patient transfusion requirements are different and so is their clinical condition. An effort to detect, diagnose and promptly treat anemia would result in restrictive transfusion or complete avoidance of transfusion while protecting the patient from anemia complications. The emergence of non-invasive point-of-care devices for the detection of hemoglobin (spot or continuous) levels may be of great value in reducing the turnaround time of tests results. In France, our approach to anemia in the recovery room and anemia at postoperative day five are not managed in the same way. Bedside evaluation may result in differing transfusion triggers in the recovery room versus the ward. To better define these thresholds would require future large-scale studies.

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Perioperative Coagulation Management: Out With the Old (Plasma) and In With the New (Prothrombin Complex Concentrates)?

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Despite efforts to educate care providers and limit the number of inappropriate and/or ineffective plasma transfusions, the annual usage of plasma products grew from 3.3 million units in 1998 to 4.5 million units in 2009.[1] The majority of these plasma transfusions are administered in the perioperative period, particularly in the setting of cardiac surgery.[2] Importantly, historic estimates suggest 25-30 percent of plasma units are transfused without evidence-based indications.[3] In addition, concerns related to the liberal use of plasma products, including life-threatening complications such as transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO), have been increasingly appreciated.[4] In addition to the need for ongoing transfusion education, these data have resulted in increased interest in safe and effective alternatives to plasma transfusion. This article will highlight our current understanding of plasma transfusion and potential plasma alternatives in the perioperative setting.

Current State of Plasma Products

Although fresh frozen plasma (FFP) is the most frequently utilized plasma component, alternative plasma products are available; plasma frozen within 24 hours of collection (FP24)

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as well as thawed plasma. The latter may be transfused for up to five days after thawing, provided it remains under refrigeration (*Plasma Components: An Update from COBM, 2011*). In addition to these plasma products, biological industries collect a batch of human plasma (2,000-4,000 liters) and manufacture purified plasma-derived biotherapeutics such as albumin, α1-antitrypsin, antithrombin, immunoglobulin, factor (F)VIII, fibrinogen, and von Willebrand factor.[5] The industry standards of these products evolved since the epidemic of acquired immunodeficiency syndrome (AIDS) in the 1980s.The manufacturing processes involve viral inactivation (solvent-detergent or heat treatment) and viral removal steps (e.g., nano-filtration) that are not available for FFP/FP24. These products come in lyophilized powders that can be quickly reconstituted and intravenously administered without blood type matching. In the U.S., plasma-derived factor concentrates are indicated for the replacement of hereditary factor deficiencies.

Plasma Transfusion: Indications, Efficacy and Risks

Despite limited indications (Table 1, page 22), plasma transfusion is rampant in the perioperative setting. Evidence-based indications for plasma administration in this setting include the replacement of multiple coagulation factor deficits in patients with active microvascular bleeding, and more recently, a fixed-ratio administration with RBC transfusion after massive hemorrhage. The role of plasma in this latter scenario remains controversial and is the subject of ongoing clinical trials (e.g., Pragmatic, Randomized Optimal Platelets and Plasma Ratios; NCT01545232). Notably, plasma transfusion to normalize mild to moderate abnormalities in PT/INR without clinical bleeding is not supported by current guidelines[6] nor clinical data.[2,7] For additional details, readers are referred to a recent report on the evidence-based indications for perioperative plasma transfusion.[8]

Historically, major concerns relating to blood component therapies have focused on allergic/anaphylactic reactions and the vertical transmission of infectious disease. However, improvements in blood banking practices have led to dramatic reductions in infectious complications (Busch MP, *JAMA*. 2003). More recently, transfusion-related pulmonary complications such as TRALI and TACO have become growing concerns with transfusion therapies.[4] These findings are particularly notable given the poor recognition and documented under-reporting of these syndromes.[9] Fortunately, the incidence of TRALI has fallen substantially due to specific plasma risk-reduction measures (e.g., exclusion of multiparous females from the plasma donor pool, anti-HLA and anti-HNA antibody testing in at-risk donors).[10]

Are Prothrombin Complex Concentrates (PCCs) Alternatives to Plasma?

In light of the concerns noted above, interest in alternatives to plasma transfusion has begun to gain steam. Much of this interest has focused on the use of recombinant-activated FVII,[11] but enthusiasm related to fewer bleeding complications and/or need for RBCs has been tempered by increased risks of thromboembolism.[12] In the meantime, PCCs have gained attention as a potential alternative to plasma transfusion in Europe. PCCs are sterile, lyophilized concentrates of vitamin-K dependent FII, FVII, FIX and FX. Variable quantities of protein C and protein S are present in some products. PCCs that contain low concentrations of FVII [Profilnine SD (Grifols, Barcelona, Spain), Bebulin VH (Baxter, Vienna, Austria)] are called 3-factor PCCs, while those containing therapeutic levels of FVII are termed 4-factor PCCs [Beriplex P/N (CSL Behring, Marburg, Germany), Octaplex (Octapharma, Vienna, Austria)]. FEIBA is a partially activated form of PCC indicated for hemophilia A patients with inhibitors.

Currently, 3-factor PCC products and FEIBA are available in the U.S. The sole FDA-approved indication for 3-factor PCC administration is the prevention or control of bleeding in patients with hemophilia B. The American College of Chest Physicians presently recommends PCCs (off-label in the U.S.) as an alternative to plasma transfusion for the treatment of serious or life-threatening bleeding associated with VKA.[13] The recommendation was largely based on rapid and complete reversal of VKA using 4-factor PCCs.[14] Additional benefits of PCC include lower infusion volumes, no requirement for blood typing, and improved safety due to pathogen-reduction procedures. Although definitive data are lacking, the risk for TRALI is presumed to be remote,[15] and the low-volume nature of these products reduces the risk of TACO. While interest in the use of PCCs in additional clinical contexts (e.g., cardiac surgery, massive bleeding) has grown, evidence supporting these practices remains insufficient.

Are PCCs Associated With Thromboembolic Complications?

The primary concern with PCC administration is a thromboembolic complication. For the available 3- and 4-factor PCCs, risk for thromboembolic complications is generally considered low.[15,16] However, recent reports in patients experiencing acute stroke have raised concerns about thromboembolic complications after PCC administration.[17] Importantly, in studies that have suggested an increased risk for thromboembolism with PCCs, it remains unclear if such complications are due to underlying thromboembolic risks or whether they are directly related to PCCs.

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Role of Point-of-Care Testing

Taken together, plasma transfusion is not a benign procedure and its indication must be carefully assessed. PCC may be an efficacious alternative to plasma in replacing vitamin K-dependent factors, but PCC does not provide therapeutic levels of other plasma factors, including fibrinogen. With hereditary coagulation disorders, a specific factor for replacement is usually known. In contrast, deficient factors requiring supplementation in the perioperative setting are typically less clear, and failure to choose the right target will result in the lack of effect, wasted resources and possible complications.

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Historically, it has been difficult to assess multi-factorial hemostatic defects using laboratory-based coagulation tests. Modern versions of viscoelastic coagulation tests, thrombelastography (TEG, Haemonetics, Niles, IL) and rotational thromboelastometry (ROTEM, TEM Systems, Durham, NC), have gained popularity because they can be used at the bedside (point of care [POC]) for rapid assessment of the overall state of procoagulant factors, platelets, fibrin polymerization and fibrinolysis.[18] Testing for fibrin-specific clot is also available as a functional fibrinogen (FF) assay on the TEG as well as with FIBTEM on the ROTEM.[19] Monitoring fibrin-specific clot during both non-cardiac and cardiac surgery led to the recognition of early and frequent loss of plasma fibrinogen.[18,20] Subsequently, several randomized trials of fibrinogen replacement have demonstrated its blood-sparing effects.[21,22] As cryprecipitates are not available in most of Europe, plasma-derived fibrinogen concentrate has become a preferred approach for fibrinogen replacement. Weber and Gorlinger, et al. recently conducted a randomized comparison of conventional laboratory analyses versus POC tests (ROTEM plus whole blood aggregometry) in 100 patients after complex cardiopulmonary bypass cases.[23] Each group was initially treated with the fibrinogen concentrate (25-50 mg/kg) according to the threshold of laboratory fibrinogen levels (<150-200 mg/dl) or FIBTEM (<10 mm) value. In the conventional group, plasma (15 ml/kg, ~4 units) could be used empirically if more than 4 units of erythrocytes were already transfused. PCC or plasma was given for prolonged INR or PTT in the conventional group and for delayed clot formation on ROTEM. Platelet transfusion was given for platelet count below 80,000/µl in the conventional group, but the decision was based on platelet function on the ROTEM or platelet aggregometry in the POC group. This study was terminated early because the interim analysis after 100th patient indicated the lower transfusion rate for erythrocytes (98 percent versus 84 percent, P=0.031) along with plasma (80 percent versus 40 percent, P<0.001) in the POC group. Further, the use of factor concentrates, including fibrinogen and PCC, was reduced in the POC group. The need for rFVIIa was significantly decreased in the POC group (24 percent versus 2 percent, P=0.002). These data indicate that the overuse of blood component therapies and factor concentrates can be reduced by timely POC testing.

Table 1: Evidence-Based Indications for Plasma Administration[8]

Replacement of inherited single coagulation factor deficiencies for which no virus-safe fractionated product exists.
Replacement of multiple coagulation factor deficiencies with associated severe bleeding and/or disseminated intravascular coagulation (DIC).
As a component of plasma exchange in patients with thrombotic thrombocytopenic purpura.
Reversal of warfarin anticoagulation when severe bleeding is present when prothrombin complex concentrates are not available.
Prevention of dilutional coagulopathy in patients with major trauma and/or massive hemorrhage.

Summary

Although plasma transfusion remains a common practice for acute VKA reversal and perioperative bleeding, there is a paucity of supporting clinical data. In particular, the use of plasma in an effort to normalize mild to moderate coagulation test abnormalities in patients without active bleeding is unlikely to be of benefit. The implementation of well-designed

transfusion algorithms that include POC testing should be considered as measures to standardize the use of plasma and other hemostatic products, including PCCs. Though the use of factor concentrates in acquired coagulopathy are considered off-label, these products potentially reduce the risks of allogeneic transfusion. Ongoing clinical trials will shed additional light on the utility of plasma transfusion as well as the efficacy and safety of PCCs in perioperative settings.

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For a complete list of References, please refer to the back of the online version of the *ASA NEWSLETTER* at **asahq.org** or email **communications@asahq.org**.

BOOK/MULTIMEDIA EDUCATION AWARD

The Anesthesia Foundation announces the Book/Multimedia Education Award to be presented at the ANESTHESIOLOGY™ 2013 annual meeting.

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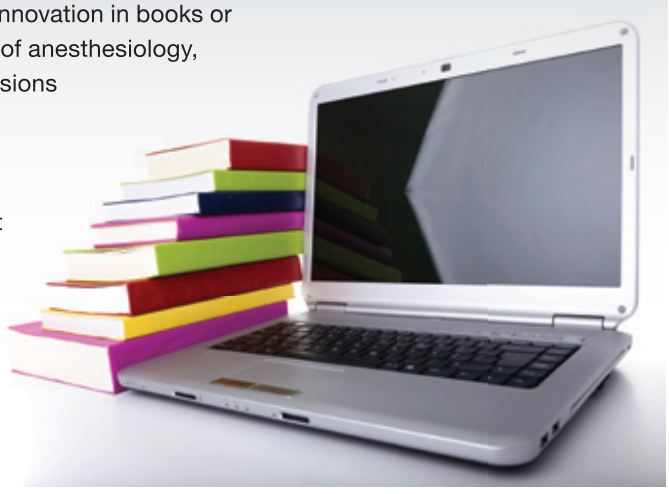
Deadline for receipt of contributions is **December 15, 2012.**

For further information and specific criterion, please contact Kathryn E. McGoldrick, M.D., Professor and Chair of Anesthesiology, New York Medical College, Valhalla, NY 10595; telephone: (914) 493-7693, fax: (914) 493-7927; **www.anesthesiafoundation.org/index.html**.



Learning From Others:

A Case Report From the Anesthesia Incident Reporting System

Anesthesia Quality Institute
ANESTHESIA INCIDENT REPORTING SYSTEM (AIRS)

Detailed review of unusual cases is a cornerstone of anesthesiology education. Each month, the AQI-AIRS Steering Committee will abstract a case and provide a detailed discussion based on a submission to the national Anesthesia Incident Reporting System. Feedback regarding this item can be sent by email to ***r.dutton@asahq.org****. Report incidents to* ***www.aqiairs.org****.*

Case 2012-12: Snatching Defeat From the Jaws of Victory

A 23-year-old woman was admitted after a side-impact motor vehicle collision. Thoracic aortic injury was discovered by multi-detector CT scan, and the patient was brought to the O.R. for open repair. The patient was hemodynamically stable and neurologically intact. Following uneventful induction of general anesthesia, placement of a left-sided double-lumen endotracheal tube (ETT) was attempted. The larnygoscopic view was grade 3, and the first attempt resulted in esophageal intubation. The tube was removed and correctly placed by a more experienced operator. The case proceeded uneventfully. The anesthesia team elected to keep the patient anesthetized during transport to the intensive care unit, in deference to the patient's other injuries, the 6-hour length of surgery, and a transfusion requirement of 7 units of red blood cells and 4 units of plasma.

The double-lumen tube was removed, and replacement was attempted with a 7.0 mm single-lumen ETT. Visualization of the larynx was again difficult, and the ETT was again placed in the esophagus. Assistance and back-up equipment were requested. Successful endotracheal placement was finally achieved after multiple attempts over 15 minutes, punctuated by intermittent – and difficult – mask ventilation. During this period, the patient's oxygen saturation ranged from 66 to 90 percent and blood pressure from 90/50 to 185/102 mmHg. Following confirmation of successful intubation with end-tidal capnography the patient was re-anesthetized and transferred to the ICU. The patient was extubated one day later, and the subsequent course of care was unremarkable. The case was reported to AIRS as a "near miss."

Discussion: Tube change-over at the end of a long surgical procedure is a landmine for the anesthesia team. It can be a no-win situation in which success is routinely expected and difficulty or failure is regarded as a sign of technical incompetence. After all, the patient had a perfectly good airway when the procedure started.

There are many variables that conspire to make reintubation a dangerous procedure. Some of these are unavoidable. Double-lumen tube placement is more difficult than conventional intubation and may require alterations in technique.[1] The original intubation attempt and ongoing irritation from the ETT itself may cause laryngeal edema and distorted airway anatomy. Head-down positioning, I.V. fluids and postsurgical inflammation can cause unexpected tissue edema. And the course of surgery and the state of resuscitation may make the patient less tolerant of physiologic stress. But these are not the variables that usually create a bad outcome. Rather, the most common risks are those that result from correctable human and systems failings, especially the hazardous attitude (an aviation term) of the providers involved.[2]

After a long and intricate surgical procedure there is a strong desire to wrap things up and get out of the O.R. This may be accompanied by a sense of relief that the work is done and a corresponding decrease in vigilance. Tube change-over is often attempted without adequate foresight or preparation, especially if the initial intubation was easy and uneventful. Nursing and support personnel who were attentive to the anesthesia team at the beginning of the case are distracted by other responsibilities. Less care is taken with positioning the patient and the bed to optimize airway visualization. Back-up equipment may have been removed from the room for cleaning or storage. The airway itself may be contaminated with blood or saliva. The depth of anesthesia is often lighter than during induction, and muscle relaxation may have worn off. The patient may be receiving a low fraction of inspired oxygen, reducing the time available

to cope with difficulties. Even the presence of an existing endotracheal tube can contribute to overconfidence, as it creates the laryngoscopic appearance of normal anatomy. Unfortunately this is not an accurate predictor of how the airway will look when the ETT is removed.

Avoiding complications during reintubation requires the same systematic approach that anesthesiologists learn to observe at the beginning of a case, or during a potentially dicey extubation.[3] A checklist can help: an example is shown to the right. First, the need for a change must be discussed. If the patient is unstable or the risk high, it is acceptable to deflate the bronchial tube cuff and pull back the double-lumen tube a short distance. Although ICU care will be more difficult, deferring the procedure might allow for a safer change-over at a later time. Sometimes discretion is the better part of valor.

When the change-over does happen, the guiding principle is to approach it the way that primary intubation would be approached in a patient with a known difficult airway. This includes discussing the plan in advance, then checking equipment, personnel, positioning, anesthesia, muscle relaxation, oxygen and suctioning prior to beginning.

In almost all cases, a tube-exchange catheter should be used to facilitate the change-over, and exchange catheters are available that will work with double-lumen tubes. Use of a hollow catheter will permit insufflation of oxygen or jet ventilation as a temporizing measure if the procedure becomes difficult. Although helpful, the exchange catheter is not a panacea.[4,5] The stylet can be dislodged from the airway during manipulations. Airway tissue edema or collapse can make it difficult to advance the replacement ETT over the stylet, even when the stylet remains in the right place. And the use of a stylet may also contribute to over-confidence in a successful outcome.

Once all personnel are in place – including the surgical team in high risk cases – and the patient is appropriately positioned, suctioned, anesthetized, relaxed and pre-oxygenated, the procedure can begin. The tube exchanger is placed, and the best possible view of the larynx is obtained using a direct or video laryngoscope.[6] The ETT is removed under direct vision, and the new tube placed. Torqueing or even a complete corkscrew of the tube may be needed to pass through an edematous larynx, assuming that the smallest feasible tube is already being used. Correct tube position should be confirmed with end-tidal capnometry or flexible bronchoscopy. With appropriate preparations, tube change-over will go well. If not, the providers should be prepared to follow the steps of the ASA Difficult Airway Algorithm through placement of a supraglottic airway – which can be done with the tube exchange catheter in place and exiting through a bronchoscope adapter at the circuit connection – use of alternative visualization techniques,[7] and cricothyrotomy or tracheostomy.

Conclusion: As the case presentation illustrates, ETT change-over at the end of a long case may be associated with substantial risk for adverse outcome. Embarrassment can be avoided by a systematic approach, while suppressing the urge to underestimate the procedure or take clinical shortcuts.

Checklist for Reintubation:

- Ask "Is this necessary?"
- Locate all needed equipment
- Round up needed personnel
- Confirm adequate anesthesia
- Confirm muscle relaxation
- Confirm optimal positioning
- Review the plan and contingencies
- Preoxygenate the patient
- Suction ETT, mouth and pharynx
- Place tube exchanger
- Obtain best laryngoscopic view (with direct or video laryngoscope)
- Remove old ETT
- Replace new ETT
- Confirm position with capnography and auscultation
- Secure new ETT

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DECEMBER 2012 *ASA NEWSLETTER*

Strategies for Treatment of Coagulopathy Associated With Hemorrhage
Jonathan S. Jahr, M.D.; Colleen G. Koch, M.D., M.S.; Charles E. Smith, M.D.
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Perioperative Coagulation Management: Out With the Old (Plasma) and in With the New (Prothrombin Complex Concentrates)?

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