

# Sample Life Science Intelligence Alert: May 2019 - Fluid Resuscitation

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## Journal Articles

### Septic Shock & General Fluid Management

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#### 1. Aggressive crystalloid adversely affects outcomes in a pediatric trauma population.

Eur J Trauma Emerg Surg. 2019 Apr 27. doi: 10.1007/s00068-019-01134-0. [Epub ahead of print]  
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**INTRODUCTION:** Crystalloid resuscitation for trauma patients is deleterious, and minimizing crystalloid use is advocated. The purpose of this study was to evaluate the adverse effects of high-volume resuscitation in pediatric blunt trauma patients.

**METHODS:** This study included a retrospective review of 291 patients with blunt trauma from January 2007 to Apr 2018 at the Children's Hospital, Chongqing Medical University. Patients were dichotomized into low and high groups depending on the average dose of crystalloid fluid administration with a cut-off point during the first 24 or 48 h. Propensity score matching was used based on measurable baseline factors to minimize confounding. The associations between crystalloid administration and clinical outcomes were determined according to the corresponding methods.

**RESULTS:** Patients who received larger doses of crystalloids were more likely than the low-volume group to be associated with severe anemia ( $p = 0.033$ ,  $p = 0.042$ , respectively), RBC transfusion ( $p = 0.016$ ,  $p = 0.009$ , respectively) and longer hospital length of stay ( $p = 0.008$ ,  $p = 0.002$ , respectively). In terms of plasma transfusion and oral solid diet, there were marginally significant differences noted in the dichotomized groups at 24 h ( $p = 0.074$ ), with significant differences at 48 h ( $p = 0.013$ ).

**CONCLUSION:** Significant unfavorable outcomes were noted following excessive crystalloid resuscitation within the first 48 h among pediatric patients with blunt trauma. Our findings support the notion that excessive fluid resuscitation should be avoided.

DOI: 10.1007/s00068-019-01134-0

PMID: 31030222

## **2. Bolus therapy with 3% hypertonic saline or 0.9% saline in emergency department patients with suspected sepsis: A pilot randomised controlled trial.**

J Crit Care. 2019 Mar 28;52:33-39. doi: 10.1016/j.jcrc.2019.03.009. [Epub ahead of print]

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**OBJECTIVE AND DESIGN:** Hypertonic saline administered during fluid resuscitation may mitigate endothelial glycocalyx (EG) shedding and inflammation. The objective of this pilot randomised controlled trial was to measure the effect of hypertonic saline, compared to isotonic saline, on biomarkers of EG shedding and inflammation in emergency department patients with suspected sepsis.

**METHODS:** Patients received either 5 mL/kg of 3% saline (hypertonic group, n = 34) or 10 mL/kg of 0.9% saline (isotonic group, n = 31). Change in serum biomarker concentrations of syndecan-1, hyaluronan, intercellular adhesion molecule-1, vascular cell adhesion molecule-1, interleukin-6, -8, -10, interferon- $\gamma$ , neutrophil gelatinase-associated lipocalin and resistin were compared from baseline (T0) to after fluid (T1), 3 h (T3) and 12-24 h (T24) later, as was serum osmolality, using linear mixed effects models.

**RESULTS:** The hypertonic group had significantly increased mean serum osmolality compared to the isotonic group at T1 (P < .001) and T3 (P = .004). Minor differences were found in some biomarker outcomes, including a decreased fold-change in syndecan-1 at T1 (P = .012) and in interleukin-10 at T24 (P = .006) in the isotonic group, compared to the hypertonic group.

**CONCLUSIONS:** Although a single bolus of hypertonic saline increased serum osmolality, it did not reduce biomarkers of EG shedding or inflammation, compared to patients that received isotonic saline.

**TRIAL REGISTRATION:** ANZCTR.org.au, ACTRN12611001021965, Registered on 23rd September 2011.

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PMID: 30954691

### 3. Cardiovascular determinants of resuscitation from sepsis and septic shock.

Crit Care. 2019 Apr 15;23(1):118. doi: 10.1186/s13054-019-2414-9.

Guarracino F(1), Bertini P(1), Pinsky MR(2).

**FREE full text here:** <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6466803/>

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**BACKGROUND:** We hypothesized that the cardiovascular responses to Surviving Sepsis Guidelines (SSG)-defined resuscitation are predictable based on the cardiovascular state.

**METHODS:** Fifty-five septic patients treated by SSG were studied before and after volume expansion (VE), and if needed norepinephrine (NE) and dobutamine. We measured mean arterial pressure (MAP), cardiac index (CI), and right atrial pressure (Pra) and calculated pulse pressure and stroke volume variation (PPV and SVV), dynamic arterial elastance (E<sub>adyn</sub>), arterial elastance (E<sub>a</sub>) and left ventricular (LV) end-systolic elastance (E<sub>es</sub>), E<sub>es</sub>/E<sub>a</sub> (VAC), LV ejection efficiency (LVEff), mean systemic pressure analogue (P<sub>msa</sub>), venous return pressure gradient (P<sub>vr</sub>), and cardiac performance (E<sub>h</sub>), using standard formulae.

**RESULTS:** All patients were hypotensive (MAP 56.8 ± 3.1 mmHg) and tachycardic (113.1 ± 7.5 beat min<sup>-1</sup>), with increased lactate levels (lactate = 5.0 ± 4.2 mmol L<sup>-1</sup>) with a worsened VAC. CI was variable but > 2 L min<sup>-1</sup> M<sup>-2</sup> in 74%. Twenty-eight-day mortality was 48% and associated with admission lactate, blood urea nitrogen (BUN), and creatinine levels but not cardiovascular state. In all patients, both MAP and CI improved following VE, as well as cardiac contractility (E<sub>es</sub>). Fluid administration improved Pra, P<sub>msa</sub>, and P<sub>vr</sub> in all patients, whereas both HR and E<sub>a</sub> decreased after VE, thus normalizing VAC. CI increases were proportional to baseline PPV and SVV. CI increases proportionally decreased PPV and SVV. VE increased MAP > 65 mmHg in 35/55 patients. MAP responders had higher PPV, SVV, and E<sub>adyn</sub> than non-responders. NE was given to 20/55 patients in septic shock, but increased MAP > 65 mmHg in only 12. NE increased E<sub>a</sub>, E<sub>adyn</sub>, Pra, P<sub>msa</sub>, and VAC while decreasing HR, PPV, SVV, and LVEff. MAP responders had higher pre-NE E<sub>es</sub> and lower VAC. Dobutamine was given to 6/8 patients who remained hypotensive following NE. It increased E<sub>es</sub>, MAP, CI, and LVEff, while decreasing HR, Pra, and VAC. At all times and all steps of the protocol, CI changes were proportional to P<sub>vr</sub> changes independent of treatment.

**CONCLUSIONS:** The cardiovascular response to SSG-based resuscitation is highly heterogeneous but predictable from pre-treatment measures of cardiovascular state.

DOI: 10.1186/s13054-019-2414-9

PMCID: PMC6466803

PMID: 30987647

## Trauma & Hemorrhagic shock

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### **4. Evaluation and management of pediatric patients with penetrating trauma to the torso.**

Pediatr Emerg Med Pract. 2019 May;16(5):1-24. Epub 2019 May 1. Haines E(1), Fairbrother H(2).

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Children with penetrating trauma to the torso require careful evaluation of the chest, abdomen, pelvis, and genital structures for system-specific injuries that may contribute to rapid decompensation and influence the order of emergent resuscitation. Care of the injured child and the effect on clinical outcomes starts in the prehospital setting, with hemorrhage control **and IV fluid resuscitation.**

The evaluation and disposition of the patient in the ED will depend on the mechanism of injury and the severity of trauma. This issue reviews the diagnostic evaluation and management of pediatric patients with penetrating injuries to the torso.

PMID: 31033268

### **5. Plasma for burn shock resuscitation: is it time to go back to the future?**

Transfusion. 2019 Apr;59(S2):1578-1586. doi: 10.1111/trf.15243.

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Patients with burn shock can be challenging to resuscitate. Burn shock produces a variety of physiologic derangements: Patients are hypovolemic from volume loss, have an increased systemic vascular resistance, and may have a depressed cardiac output depending on the extent of the thermal injury. Additionally, the burn wound produces a significant inflammatory cascade of events that contributes to the shock state. Fluid resuscitation is foundational for the initial treatment of burn shock. Typical resuscitation is with intravenous lactated Ringer's in accordance with well-established formulas based on burn wound size. In the past century, as therapies to treat thermal injuries were being developed, plasma was the fluid used for burn resuscitation; in fact, plasma was used in World War II and throughout the 1950s and 1960s. Plasma was abandoned because of infectious risks and complications. Despite huge strides in transfusion medicine and the increased safety of blood products, plasma has never been readopted for burn resuscitation. Over the past 15 years, there has been a paradigm shift in trauma resuscitation: Less crystalloid and more blood products are used; this strategy has demonstrated improved outcomes. Plasma is a physiologic fluid that stabilizes the endothelium. The endotheliopathy of trauma has been described and is mitigated by transfusion strategies with a 1:1 ratio of RBCs to plasma. Thermal

injury also results in endothelial dysfunction: the endotheliopathy of burns. Plasma is likely a better resuscitation fluid for patients with significant burn wounds because of its capability to restore intravascular volume status and treat the endotheliopathy of burns.

DOI: 10.1111/trf.15243  
PMID: 30980739

## **6. Prehospital Blood Product and Crystalloid Resuscitation in the Severely Injured Patient: A Secondary Analysis of the Prehospital Air Medical Plasma Trial.**

Ann Surg. 2019 Apr 13. doi: 10.1097/SLA.0000000000003324. [Epub ahead of print]

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MINI: Hemorrhage is the primary cause of preventable trauma death. Secondary analyses of scene patients from the PAMPer trial demonstrated that prehospital packed red blood cell and plasma had the greatest reduction in 30-day mortality compared with crystalloid-only resuscitation. Patients with hemorrhagic shock should receive prehospital blood products when available, preferably packed red blood cell and plasma. OBJECTIVE: The aim of this study was to determine whether prehospital blood products reduce 30-day mortality in patients at risk for hemorrhagic shock compared with crystalloid only resuscitation.

SUMMARY OF BACKGROUND DATA: Hemorrhage is the primary cause of preventable death after injury. Large volume crystalloid resuscitation can be deleterious. The benefits of prehospital packed red blood cells (PRBCs), plasma, or transfusion of both products among trauma patients is unknown compared with crystalloid.

METHODS: Secondary analysis of the multicenter PAMPer trial was performed on hypotensive injured patients from the scene. The trial randomized 27 helicopter bases to prehospital plasma or standard resuscitation. Standard resuscitation at the sites was equally divided between crystalloid and crystalloid + PRBC. This led to 4 prehospital resuscitation groups: crystalloid only; PRBC; plasma; and PRBC+plasma. Cox regression determined the association between resuscitation groups and risk-adjusted 30-day mortality. The dose effect of resuscitation fluids was also explored.

RESULTS: Four hundred seven patients were included. PRBC+plasma had the greatest benefit [hazard ratio (HR) 0.38; 95% confidence interval (95% CI) 0.26-0.55,  $P < 0.001$ ], followed by plasma (HR 0.57; 95% CI 0.36-0.91,  $P = 0.017$ ) and PRBC (HR 0.68; 95% CI 0.49-0.95,  $P = 0.025$ ) versus crystalloid only. Mortality was lower

per-unit of PRBC (HR 0.69; 95% CI 0.52-0.92, p = 0.009) and plasma (HR 0.68; 95% CI 0.54-0.88, P = 0.003). Crystalloid volume was associated with increased mortality among patients receiving blood products (HR 1.65; 95% CI 1.17-2.32, P = 0.004). CONCLUSION: Patients receiving prehospital PRBC+plasma had the greatest mortality benefit. Crystalloid only had the worst survival. Patients with hemorrhagic shock should receive prehospital blood products when available, preferably PRBC+plasma. Prehospital whole blood may be ideal in this population.

DOI: 10.1097/SLA.00000000000003324  
PMID: 30998533

## Clinical Trials

### **Microcirculatory Guided Goal Directed Fluid Therapy in Septic Shock; a Feasibility Study (MICRORESUS)**

<https://clinicaltrials.gov/ct2/show/NCT03898674>

Prospective single centre study to assess the feasibility of fluid resuscitation guided by macrocirculatory and microcirculation parameters in patients in the early stages of septic shock. The investigators will utilise a novel point of care tool to assess microcirculatory sublingual perfusion in patients with septic shock. This, in combination with conventional haemodynamic monitoring will determine the timing and volume of resuscitative fluid administration. The feasibility of this technique will be determined prior to embarking on a pilot RCT. [King's College, London]

### **Outcomes of Septic Shock Patients Treated With a Metabolic Resuscitation Bundle Consisting of Intravenous Hydrocortisone, Ascorbic Acid and Thiamine**

<https://clinicaltrials.gov/ct2/show/NCT03913468>

This is a retrospective chart review that will measure the impact on outcomes in septic shock patients who were resuscitated with a novel combination of medicines called iHAT (intravenous hydrocortisone - ascorbic acid-thiamine). Septic shock patients treated with this combination of drugs over the past two years will be compared with similar, concurrent septic shock patients who were not treated with this drug given that adoption of this therapy has been variable. [University of Wisconsin]

### **SOFI: A Quality Improvement Project to Standardize Use of Intravenous Fluids in Hospitalized Pediatric Patients (SOFI)**

<https://clinicaltrials.gov/ct2/show/NCT03924674>

This project aims to better describe and standardize the use of IVF in inpatient pediatric settings across the U.S. and evaluate the impact of an intervention bundle on maintenance IVF use. This project aims to improve health care value by reducing the number of routine laboratory draws. [PI at Seattle Children's Hospital, multiple other hospitals and children's hospitals participating]

## Patents

### **EP2849634B1 Method for managing blood loss of a patient**

Gauss Surgical Inc.

<https://ip.com/pat/EP2849634B1>

One variation of the method for managing blood loss of a patient includes: receiving an image of a physical sample; extracting a feature from an area of the image corresponding to the physical sample; estimating a blood volume indicator of the physical sample according to the extracted feature; estimating a patient blood loss based on the blood volume indicator; estimating a euvolemic patient hematocrit based on an estimated patient blood volume and the estimated patient blood loss; receiving a measured patient hematocrit; and generating a volemic status indicator based on a comparison between the measured patient hematocrit and the estimated euvolemic patient hematocrit.

### **US10188837 Cardiopulmonary resuscitation catheter and related systems and methods**

University of Minnesota

<https://ip.com/pat/US10188837>

The disclosed device, systems and methods relate to a novel catheter, system and methods. The various catheter implementations are for use in cardiopulmonary resuscitation and other medical or surgical conditions that require emergency restoration of cerebral and cardiac blood supply. The catheter or catheters have one or more lumens and balloons. Two catheters connected to a control unit can be disposed within the body to occlude and perfuse a region of the circulatory system.

## Funding & Deals

### **Theranova Receives Grant of US\$0.2 M from US Department of Health and Human Services to Develop Device for Improving Sepsis Outcomes**

<http://www.pharmadeals.net/agreements/dealdetails/72482/?displaymode=print&details=detailed&page=9&sortBy=lastUpdate&paramSetID=785176>

Theranova has received a grant of US\$0.2 M from the US Department of Health and Human Services for the development of device for improving sepsis outcomes. This funding involves the development of OmniSense catheter which helps to treat patients suffering from septic shock. This device has the potential to directly track changes in cardiac output and detect fluid overload without any additional invasiveness. The previous demonstration with this device showed that it has capacity to provide clinically relevant readings of changes in intra-abdominal pressure. This initial work will lead to the further clinical studies with the goal of improving outcomes for critically ill patients suffering from septic shock and other forms of haemodynamic insult.

### **Predictive Health Company Potrero Medical Closes \$26.6 Million in Oversubscribed Series C Financing**

<https://www.prnewswire.com/news-releases/predictive-health-company-potrero-medical-closes-26-6-million-in-oversubscribed-series-c-financing-300677861.html>

### **Path Ex awarded SBIR Phase II grant**

[https://nsf.gov/awardsearch/showAward?AWD\\_ID=1831150&HistoricalAwards=false](https://nsf.gov/awardsearch/showAward?AWD_ID=1831150&HistoricalAwards=false)

The broader impact/commercial potential of this Small Business Innovation Research (SBIR) Phase II project will be the development of a fluidic platform for selective bacterial and endotoxin removal from blood. This technology can potentially serve as a novel blood cleansing therapeutic for diseases such as sepsis.

## Other from News & Social Media

### **Webinar: Sepsis Data Abstraction: Open Forum**

<https://www.sepsis.org/event/webinar-sepsis-data-abstraction-open-forum/>

*Webinar already happened 25 April 2019. It appears that you could register to view the recording.* Sepsis is a very complex condition that has very specific core measure data abstraction rules making it challenging for abstractors. This webinar will be presented by two teams, each including a sepsis coordinator and an abstractor, to discuss the obstacles to abstract sepsis data along with clinical and abstraction tips.

### **Rapid Infuser Market: Global Industry Analysis and Opportunity Assessment**

<https://www.futuremarketinsights.com/reports/rapid-infuser-market>

June 2019 publication date, we do not have access to full text from this publisher  
410 Medical is listed as a “medium scale manufacturer/provider”

### **Interdisciplinary action needed to tackle sepsis**

<https://www.esicm.org/key-messages-to-come-out-of-the-recent-european-sepsis-alliance-meeting/>

11 April 2019

A number of important, key messages were agreed at last month’s meeting of the European Sepsis Alliance. The meeting took place in Brussels on 18 March and brought together healthcare professionals, policymakers, researchers, and industry representatives, as well as patient and family representatives.

More information and documents linked from the bottom of the article.

### **Hasbro Children's Hospital implements new sepsis protocols**

25 April 2019

<https://turnto10.com/features/health-landing-page/health-check-kids/health-check-kids-hasbro-implements-new-sepsis-protocols>

[With new protocols in place since October](#), they've been able to get to many of those patients early on. "When patients come in, specifically in the emergency department, when patients come in, once the nurse enters their vital signs, it will trigger, based on vital signs, whether or not this patient might meet sepsis criteria," Rozenfeld said. Even a suspected case will trigger immediate treatment, which includes antibiotics and fluids.