

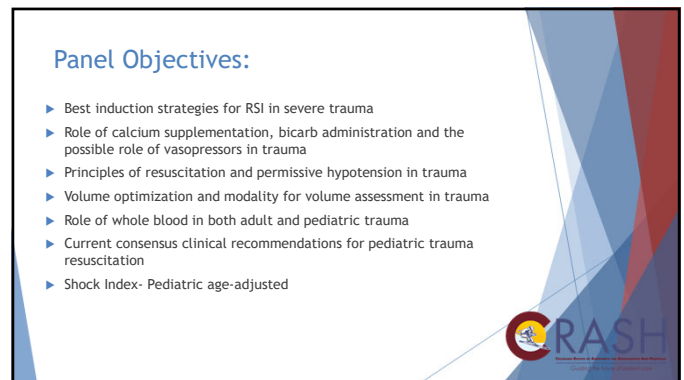
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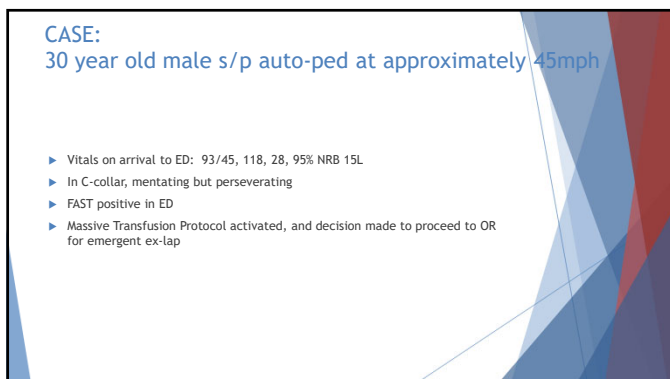
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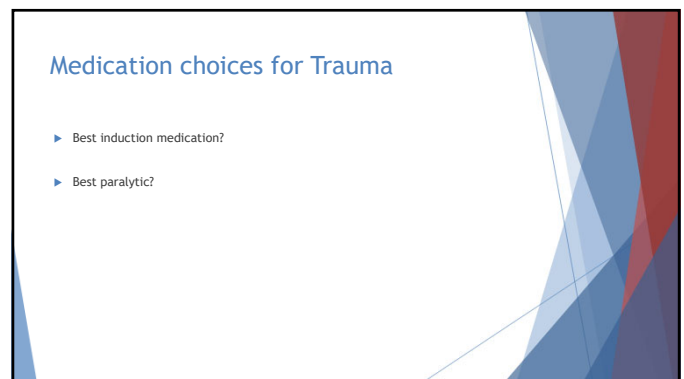
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### What is your induction medication of choice in severe trauma?



- Etomidate
- Propofol
- Ketamine
- Ketofol
- Sux and a smile
- Something else

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### Etomidate vs Ketamine

ETOMIDATE	KETAMINE
<ul style="list-style-type: none"> <li>▶ Rapid onset</li> <li>▶ Provides cardiovascular stability</li> <li>▶ Used as RSI in Adult Trauma—significant lower cortisol levels at 4-6hrs &amp; decreased response to ACTH stim test</li> </ul>	<ul style="list-style-type: none"> <li>▶ Excellent intubating conditions, minimal change to BP</li> <li>▶ ?Negative inotropy—maybe negative chronotropic effect</li> <li>▶ May increase intraocular pressure</li> <li>▶ ?Historic concerns about elevated ICP</li> </ul>

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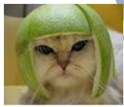
### Ketamine and TBI



- ▶ Historic concerns about use in TBI were **NOT** evidence based
- ▶ Ketamine actually **improves cerebral perfusion** by maintaining MAP, and decreases mortality in TBI
- ▶ Pediatric TBI studies—ketamine consistently decreased ICP and blunted any increases during stimulation without decreasing BP

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### Ketamine -Neuroprotective?



- ▶ Ketamine may even be **neuroprotective** & decrease secondary injury
- ▶ Related to NMDA antagonism; Decrease cortical spreading depolarization, less secondary injury

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### So...Etomidate or Ketamine?

- ▶ Ann Emerg Med 2017:
  - ▶ 968 patients (536 Etomidate, 442 Ketamine for RSI in Trauma)—Institutional switch for RSI in trauma:
  - ▶ No difference in mortality
- ▶ Anesthesia & Analgesia 2018:
  - ▶ Ketamine as RSI in trauma vs other induction agents
    - ▶ Extremely few studies comparing induction agents in trauma
  - ▶ No difference in mortality, LOS, blood transfusion
- ▶ J of Trauma Acute Care 2021:
  - ▶ No difference in 28d Mortality
  - ▶ No difference in blood transfusion

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### What about Ketofol?

KEEP PACE 2019 JTACS:

- ▶ Ketamine + Propofol (0.5mg/kg each) vs Etomidate (0.15mg/kg) for emergent intubation
  - ▶ No difference in MAP change from baseline after induction at 5min, 10min or 15min
  - ▶ No difference in new vasoactive drugs
  - ▶ No difference in difficult intubation
- ▶ Of those with adrenal testing, etomidate group had more evidence of adrenal suppression (81% vs 38%)

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### Conclusions on induction meds:

- ▶ No single best induction agent
- ▶ Remember to reduce dose in setting of hypovolemia!
  - ▶ Induction medication and Opioids
  - ▶ Do NOT reduce NMB dose

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### What is your paralytic medication of choice in major trauma?

Succinylcholine 1 mg/kg  
Succinylcholine 1.5 mg/kg  
Rocuronium 0.6 mg/kg  
Rocuronium 1.2 mg/kg  
Other

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### Paralytic of choice??

#### ROCURONIUM

- ▶ Rapid if RSI dose (55-90sec)
- ▶ No contraindications
- ▶ Prolonged paralysis
  - ▶ Difficult airway
  - ▶ Neuro checks

#### SUCCINYLCHOLINE

- ▶ Rapid onset (30-45sec)
- ▶ Short duration
- ▶ Contraindications
  - ▶ MH risk
  - ▶ Hyperkalemic risk



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### ROC vs SUX

Emergency Medicine study at Level1 Trauma Center 2018

- ▶ Retrospective
- ▶ Assessing peri-intubation factors associated with physician choice of paralytic agent for RSI in the ED

#### Results:

- ▶ Rocuronium was more likely to be chosen:
  - ▶ Abnormal Vitals prior to intubation
  - ▶ Early ED Mortality
- ▶ Rocuronium was associated with:
  - ▶ hypoxemia prior to intubation
  - ▶ increased use of Video Laryngoscopy

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### Paralytic of choice? Roc vs Sux

- ▶ Cochrane Database Review (RCTs and CCT) showed better intubating conditions with **Succinylcholine** for RSI
- ▶ BUT--this did include some studies using 0.6mg/kg Roc
- ▶ Subgroup analysis of 1.2mg/kg Roc--no statistical difference in intubating conditions

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### Conclusions on Paralytic:

- ▶ If 1.2mg/kg Rocuronium is used, either is probably fine
- ▶ Availability of Sugammadex has increased the use of Rocuronium for RSI
  - ▶ Immediate reversal (16mg/kg) is actually faster than resolution of Succinylcholine
- ▶ I generally prefer Succinylcholine, dosed **1mg/kg (TBW)**
- ▶ Again, do NOT reduce the dose of NMB in hypovolemia!

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## Back to the case....

- ▶ Successful induction & intubation
- ▶ Massive Transfusion ensues
- ▶ Surgery begins

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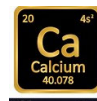
## Labs come back...

- ▶ ABG: 7.18/38/190/-12
- ▶ Na 137, K 4.3, iCa 0.8, Lact 7, Glu 205
- ▶ H/H 8.4, 27, Plt 128,000
- ▶ TEG pending...

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## Let's talk Factor IV....

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- ▶ Calcium is a divalent cation, 45% is biologically active and in ionized state, 55% protein bound (albumin, citrate)
- ▶ Key to bone formation, neural transmission, endocrine physiology, cardiac contractility, vascular constriction, hemostasis and coagulation

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## Hypocalcemia

- ▶ Electrical dysfunction, QT prolongation and increased dysrhythmias
- ▶ Contributes to suppression of myocardial contractility and can contribute to acute CV decompensation
- ▶ less vascular smooth muscle contraction, loss of vasomotor tone
- ▶ Direct association between hypocalcemia and SBP<90 in trauma patients
- ▶ Often undetected and underestimated

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## What's the problem?

- ▶ Citrate toxicity → hypocalcemia
  - ▶ Citrate metabolized quickly by healthy liver
  - ▶ MTP overwhelms liver with citrate (transfusing faster than 1 unit/5min quickly overwhelms healthy liver)
  - ▶ Even more severe with shock liver or traumatized liver
  - ▶ Hepatic clearance of citrate is worsened by hypothermia

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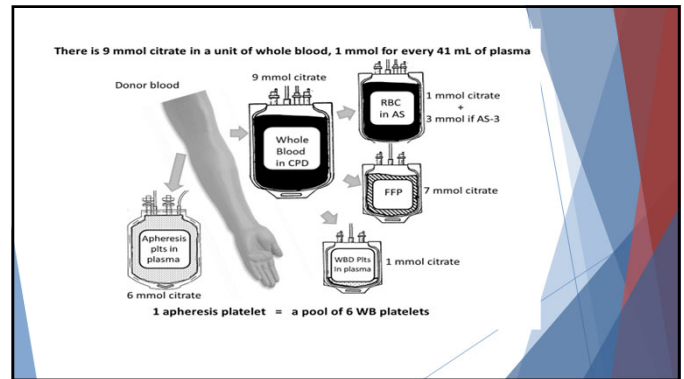
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### Which blood product contains the most citrate?

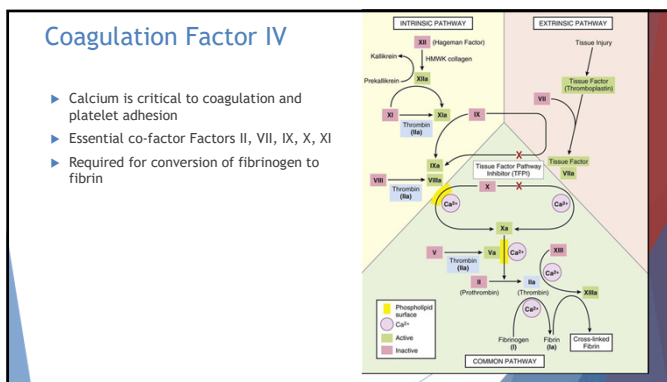
- Whole Blood
- RBC
- FFP
- Platelet
- Cryoprecipitate

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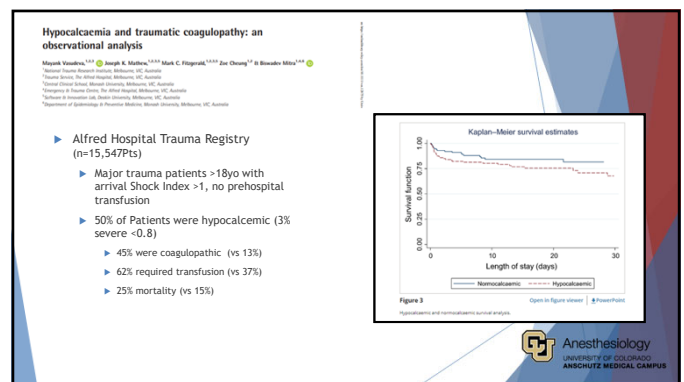
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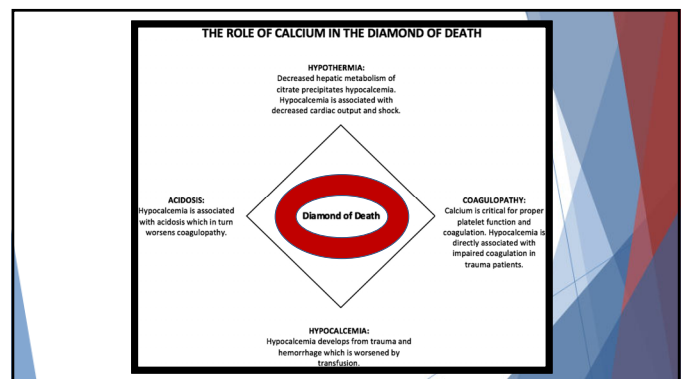


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### Trauma related hypocalcemia

- ▶ Approximately 55% of major trauma patients are hypocalcemic on arrival to ED (even before transfusion) iCa <1.1 mmol/L
- ▶ Admission hypocalcemia (less than 1.1) associated with higher mortality (almost 2x) and increased need for transfusion
- ▶ **Useful independent predictor of MTP in trauma patients**

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## Hypocalcemia in trauma

- ▶ Direct concentration dependent association between severe hypocalcemia and acidosis
- ▶ Ischemic reperfusion can cause hypocalcemia and worsen hypocalcemic coagulopathy

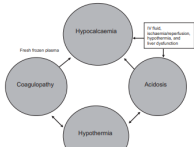


FIGURE 4. Potential contribution of hypocalcemia to the 'vicious cycle' of coagulopathy, hypothermia and acidosis in patients with critical bleeding requiring massive transfusion.

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## Transfusion and hypocalcemia

- ▶ 97% of trauma patients requiring MTP experience hypocalcemia
  - ▶ 71% were severe ( $<0.9\text{mmol/L}$ )
    - ▶ Lower platelets
    - ▶ Received more blood products
    - ▶ Higher mortality



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- ▶ Blood transfusion and hypovolemic shock exacerbate hypocalcemia
- ▶ Current Massive transfusion protocols dictate high ratio early FFP→ independently associated with hypocalcemia
- ▶ Most MTPs recommend replacement only when severe hypocalcemia

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## How do you replete calcium in during trauma resuscitation?

- 1 Amp per 4 units PRBC or 2 FFP
- 1 Amp per cooler
- Wait for ionized calcium level
- Wait for coagulopathy, acidosis
- None of the above

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## How much calcium are we talking?

- ▶ Contractility and hemodynamic are affected at ionized  $\text{Ca}^{++} <0.9$
- ▶ Protocolized early calcium replacement in major trauma?
  - ▶ No well studied published protocols
  - ▶ 1-2 grams IV Calcium Chloride per cooler (3-6grams IV calcium gluconate)
  - ▶ Use POC monitor for guiding replacement in real time
  - ▶ EKG/Tele---very rough guide to calcium
    - ▶ Hypocalcemia prolongs ST segment
- ▶ Moderate **Hypercalcemia 1.3-3mM** is well tolerated
- ▶ Therapeutic target is a high-normal iCa
  - ▶ Massively hemorrhaging patient, better to be hypercalcemia than hypo

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## What about Bicarb?

- Give it heavy handedly in hemodynamically unstable patients
- Give it when  $\text{pH} < 7.2$
- Give it when  $\text{pH} < 7.1$
- Give it only peri-arrest or during CPR
- I never give Bicarb

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## Bicarb in trauma

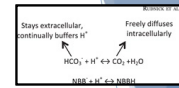
- ▶ Lactic acidosis in trauma is often a marker of hypoperfusion
- ▶ Acidemia can produce detrimental physiologic consequences



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## Detrimental effects of Bicarb:

- ▶ Worsens serum hypocalcemia
- ▶ Decrease vasomotor tone and mean arterial pressure
- ▶ Decrease coronary perfusion pressure
- ▶ Increases carbon dioxide production → decreasing C.O.
- ▶ In setting of cardiac arrest, increased systemic pH but failed to improve intramyocardial pH
- ▶ Myocardia contractility decreases (2/2 hypocalcemia & decreased myocardial oxygen extraction)
- ▶ Rapid administration of bicarbonate infusions have also been associated with lowering of pH
- ▶ Multiple studies in shock (mostly sepsis), show Bicarb failed to improve outcome (ICU LOS, vasopressor requirements, ventilator days, ICU mortality)



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## Conclusions on Bicarb

- ▶ Sodium bicarbonate administration in the setting of lactic acidosis has consistently failed to significantly improve hemodynamic status in humans
- ▶ Effect on intracellular pH depends on ventilation and limitations to CO<sub>2</sub> clearance and the presence of intact intracellular buffering systems
- ▶ If Bicarb is given,
  - ▶ Goal pH >7.2 (no higher)
  - ▶ Ensure adequate ventilation!
  - ▶ calcium replacement is critical to avoiding negative consequences



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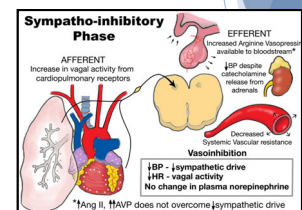
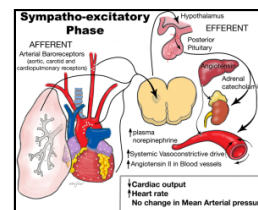
## Is there a role for Pressors in trauma?

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- ▶ Persistent hypotension and hypoperfusion → progressive coagulopathy and organ dysfunction
- ▶ Vasopressor use in severely injured trauma patients is discouraged due to concerns about worsening perfusion resulting in worsening multi-organ dysfunction and increased mortality
- ▶ Vasopressor use was reserved for post resuscitative period (SCI/TBI or Sepsis)

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## Pathophysiology of trauma shock

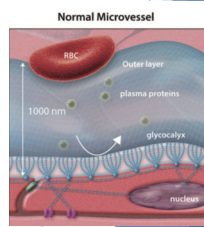


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## Shock induced endotheliopathy

- ▶ Post traumatic endotheliopathy (damage to glycocalyx) → increased vascular permeability, edema and loss of vascular tone
- ▶ Prolonged hypotension/Hypoperfusion →
  - ▶ Vascular relaxation via KATP channels
  - ▶ NO Synthesis
  - ▶ vasopressin deficiency



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## Vasopressors in Trauma

- ▶ Many older studies (retrospective) showed increased mortality with patients who required vasopressors
- ▶ Concerns for increased complications including arrhythmia & anastomotic failure in damage control laparotomy
- ▶ BUT: numerous supportive studies in TBI and SCI for improved neurologic function (MAP >85)



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## Vasopressor Use during Emergency Trauma Surgery

ROBERT M. VAN HAREN, MD, MS, PhD, CHAD M. THORSON, MD, MS, PHILIP J. VALLI, MD, GERARD A. GUERRE, MD, JASON M. JORDAN, MD, ALEXANDRE M. BENOIST, B.S., NICHOLAS NAMIAS, MD, M.B.A., ALAN S. LIVINGSTONE, MD, KENNETH G. PROCTOR, PhD  
From the Donnell-Daugherty Family Department of Surgery, University of Miami Miller School of Medicine, Ruder Trauma Center, Miami, Florida

2018 BJA: Gause et al---showed no increase in mortality in patients who received Norepi

- ▶ vasopressor use is relatively common in the most severely injured patients requiring OR
- ▶ EPI is most often used for cardiac arrest, whereas other vasopressors are used for their vasoconstrictive properties
- ▶ except for EPI, vasopressors during OR are not independently associated with mortality



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## Conclusions on pressors in trauma

- ▶ Vasopressors have a sound mechanism to improve O<sub>2</sub> delivery by
  - ▶ decreasing venous system compliance
  - ▶ augmenting the mean systemic filling pressure,
  - ▶ increasing the stressed blood volume and cardiac output within the circulation
- ▶ Persistent and prolonged shock with severe tissue damage and release of proinflammatory mediators also aggravates vasodilation and necessitates vasopressor administration even after definitive hemorrhage control
- ▶ NOREPI or AVP in traumatic shock resuscitation likely augments the body's physiological response and maintain homeostasis



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## What about fluids in trauma?



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## What are the complications associated with crystalloid administration in the setting of hemorrhagic shock?

- Hypothermia
- Dilutional coagulopathy
- Acidosis
- Higher blood pressure can worsen bleeding
- Increased Mortality
- All of the above

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## History



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## History: Intravenous Saline

- First reported use of intravenous saline for the treatment of disease:
  - Dr. Latta's letter to the Lancet on the success of saline for a patient with cholera

May 23, 1832

*She had apparently reached the last moments of her earthly existence.... once after ounce [of saline] was injected... soon the sharpened features, and sunken eye, and fallen jaw, pale and cold, bearing the manifest impress of death's signet, began to glow with returning animation; the pulse, which had long ceased, returned to the wrist.*



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## History: Intravenous Saline

*The quantity to be injected depends on the effect produced, and the repetition on the demands of the system, which generally vary according to the violence of the diarrhoea; the greater the degree of collapse, the greater will be the quantity needed.*

*The syringe must be quite perfect, so as to avoid the risk of injecting air...*

Your most obedient servant,

Thomas Latta, M.D.

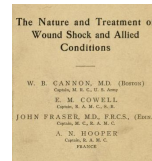
Malignant cholera. Documents communicated by the Central Board of Health, London, relative to the treatment of cholera by the copious injection of aqueous and saline fluids into the veins. Lancet 1832;18:274-80.



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## History: Permissive Hypotension in Trauma

- In August, 1917, the Medical Research Committee (Great Britain) appointed a Special Investigation Committee to undertake the coordination of inquiries into surgical shock and allied conditions [during World War I].



*Injection of a fluid that will increase blood pressure has dangers in itself. Hemorrhage in a case of shock may not have occurred to a marked degree because blood pressure has been too low and the flow too scant to overcome the obstacle offered by a clot. If the pressure is raised [with fluid] blood that is sorely needed may be lost.*

Cannon W, et al. The nature and treatment of wound shock and allied conditions. Chicago: American Medical Association; 1918.



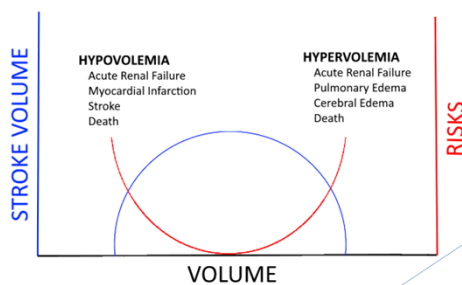
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## Volume and Complications



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## Ideal Volume



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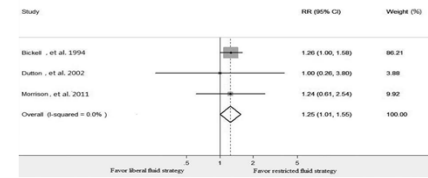
## Harm from crystalloid (Trauma)

- ▶ Increase Mortality (HR 2.5) and Coagulopathy (OR 2.2)
  - ▶ Brown J, et al. Information and the fluid response to injury investigators. Goal-directed resuscitation in the prehospital setting: a propensity-adjusted analysis. *J Trauma Acute Care Surg.* 2013 May;74(5):1207-12.
- ▶ Increase Mortality (OR 1.11)
  - ▶ Hsu E, et al. Prehospital intravenous fluid administration is associated with higher mortality in trauma patients: A National Trauma Data Bank analysis. *Ann Surg.* 2020 Dec.
- ▶ Increased Mortality (19% vs 7%)
  - ▶ Dreyer A, et al. Prehospital volume resuscitation—Did evidence defeat the crystalloid dogma? An analysis of the TraumaRegister DG04 2002–2015. *Scand J Trauma Resusc Emerg Med.* 2019 Apr;24:42.
- ▶ Increased Mortality (OR 1.11)
  - ▶ Hsu E, et al. Prehospital intravenous fluid administration is associated with higher mortality in trauma patients: A National Trauma Data Bank analysis. *Ann Surg.* 2017 Feb;265(2):371-7.
- ▶ Increased Mortality (OR 1.1)
  - ▶ Joseph B, et al. Improving mortality in trauma laparotomy through the evolution of damage control resuscitation: Analysis of 1,020 consecutive trauma laparotomies. *J Trauma Acute Care Surg.* 2017 Feb;82(2):328-333.
- ▶ Increased Risk of ARDS (OR 3.4), Multiple Organ Failure (OR 2.9), and Surgical Site Infection (OR 2.8)
  - ▶ Kocakali G, et al. Information and fluid response to injury investigators. Aggressive early crystalloid resuscitation adversely affects outcomes in adult blunt trauma patients: an analysis of the Gao Grand database. *J Trauma Acute Care Surg.* 2013 May;74(5):1215-21; discussion 1221-2.
- ▶ Increased Risk of Abdominal Compartment Syndrome (9.9 L vs. 2.7 L,  $p < 0.001$ )
  - ▶ Audebert R, et al. Secondary abdominal compartment syndrome after severe extremity injury: are early, aggressive fluid resuscitation strategies to blame? *J Trauma.* 2008 Feb;64(2):385-9.
- ▶ Increase Mortality (HR 1.1) and Coagulopathy (PTT 56 vs 39.1, INR 2.2 vs 1.4)
  - ▶ Norbert C, et al. Hypertensive resuscitation strategy reduces transfusion requirements and worse coagulopathy in trauma patients with hemorrhagic shock: preliminary results of a randomized controlled trial. *J Trauma.* 2013 Mar;75(3):515-20.

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## Restrictive vs Liberal Fluid Resuscitation in Trauma Patients

### ▶ Meta-analysis of RCT trials

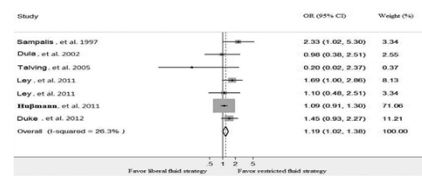


Wang C, et al. Liberal versus restricted fluid resuscitation strategies in trauma patients: a systematic review and meta-analysis of randomized controlled trials and observational studies. *Crit Care Med.* 2014 Apr;42(4):954-61.

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## Restrictive vs Liberal Fluid Resuscitation in Trauma Patients

### ▶ Meta-analysis of observational trials



Wang C, et al. Liberal versus restricted fluid resuscitation strategies in trauma patients: a systematic review and meta-analysis of randomized controlled trials and observational studies. *Crit Care Med.* 2014 Apr;42(4):954-61.

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## Permissive Hypotension in Trauma

- ▶ Permissive hypotension is **permitting** the blood pressure to be low by **deliberately giving less crystalloid** in active bleeding trauma patients
- ▶ The intervention is restrictive volume resuscitation not deliberate hypotension
- ▶ This is analogous to permissive hypercapnia for ARDS whereby the intervention is low tidal volumes and permitting hypercapnia

Disease State	Intervention	Permissive	Goal
Hemorrhagic Shock	Restrictive Fluid Resuscitation	Hypotension	Limit harm due to crystalloids
ARDS	Low Tidal Volume	Hypercapnia	Limit harm due to VILI

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## Permissive Hypotension

- ▶ Crystalloids cause harm in hemorrhagic shock
  - ▶ Hypothermia
  - ▶ Dilutional coagulopathy
  - ▶ Acidosis (Normal Saline)
  - ▶ Higher BP can worsen bleeding
- ▶ Recall "Trauma Triad of Death"
  - ▶ Hypothermia
  - ▶ Coagulopathy
  - ▶ Acidosis

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## Permissive Hypotension

- ▶ European Trauma Guidelines 5<sup>th</sup> Ed, 2019
  - ▶ We recommend permissive hypotension with a target systolic blood pressure of 80-90 mmHg (mean arterial pressure 50-60 mmHg) until major bleeding has been stopped in the initial phase following trauma without brain injury. (Grade 1C)
  - ▶ In patients with severe TBI (GCS  $\leq 8$ ), we recommend that a mean arterial pressure  $\geq 80$  mmHg be maintained. (Grade 1C)
    - ▶ Note, patients with spinal cord injury should also have higher BP goals (MAP  $> 85$ )
- ▶ Advanced Trauma Life Support 10<sup>th</sup> Ed, 2018
  - ▶ Does not endorse specific blood pressure goals
  - ▶ "Administering excessive crystalloid solution can be harmful"
  - ▶ "Early administration of pRBCs, plasma, and platelets in a balanced ratio to minimize excessive crystalloid administration may improve patient survival"
  - ▶ "Delaying aggressive fluid resuscitation until definitive control of hemorrhage is achieved may prevent additional bleeding"

Spahn D, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition. *Crit Care.* 2019 Mar 27;23(1):98.

Advanced Trauma Life Support Student Course Manual: tenth edition. Chicago (IL): American College of Surgeons; 2018.

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### Which is true regarding vasopressors and venous return?

Vasopressin administration can increase venous return  
 Phenylephrine administration does not affect venous return  
 Alpha-1 receptor agonists can increase the ratio of stressed to unstressed volume thereby increasing venous return  
 The unstressed volume is the primary driver of venous return  
 What are stressed and unstressed volumes? I don't know.

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## Blood Volume Homeostasis

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### Volume: What regulates it?

- ▶ Kidneys
  - ▶ SLOWEST
  - ▶ Governed by RAAS and ADH
- ▶ Interstitial space
  - ▶ SLOWER
  - ▶ Governed by Starling forces
    - ▶ Can take 1-2 hours to restore intravascular volume during hemorrhage
- ▶ Venous system
  - ▶ FAST
  - ▶ Governed by stress vs unstressed volume
    - ▶ Immediate source of intravascular volume during hemorrhage

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### Venous Function

- ▶ Veins contain 70% of blood volume
- ▶ Serve as a reservoir for blood
- ▶ 30 times more compliant than arteries
  - ▶  $C = \Delta V / \Delta P$
- ▶ Veins contain a high population of alpha-1 receptors
- ▶ Clinically, this pertains mostly to the splanchnic vasculature (highly compliant vessels) and to a lesser degree the cutaneous vasculature (compliant, but less than splanchnic veins)

Gelman S, et al. Venous Function and Central Venous Pressure: A Physiologic Story. Anesthesiology 2008; 108:735-748

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### Dualities: Artery vs Vein

- ▶ Arteries function as large resistors and small capacitors
- ▶ Veins function as large capacitors and small resistors

Source: Southern Illinois University (<http://www.siumed.edu>)

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### Stress vs. Unstressed Volume

**A**

**B**

elastance =  $\Delta P / \Delta V$  = slope  
 compliance (C) =  $1/\text{slope}$   
 $= V_s - V_0 / \Delta P$   
 $= V_t - V_0 / \Delta P$   
 $C = V_s / P$

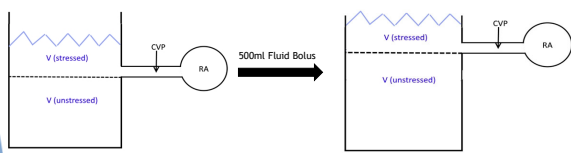
Park D, et al. The role of venous return in critical illness and shock-part I: physiology. Crit Care Med. 2013 Jan;41(1):235-52.

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### Example: Fluid Bolus

- ▶ Healthy patient with high vascular compliance
  - ▶ Volume bolus expands unstressed volume
  - ▶ Stressed volume stays the same and CVP is unchanged

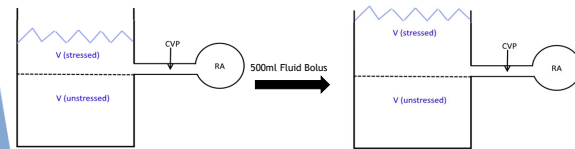


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### Example: Fluid Bolus

- ▶ CHF patient with low vascular compliance (arteriosclerosis)
  - ▶ Arteriosclerosis and high catecholamine state decrease vascular compliance
  - ▶ Volume bolus expands stressed volume
  - ▶ Unstressed volume stays the same and CVP increases

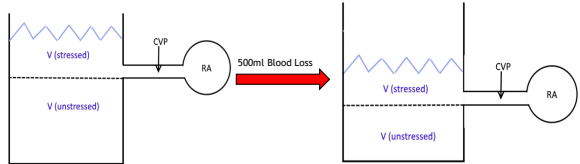


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### Example: Hemorrhage

- ▶ Healthy patient
  - ▶ Catecholamines increase causing venoconstriction (decrease venous compliance)
  - ▶ Volume moves from unstressed to stress volume to maintain CVP

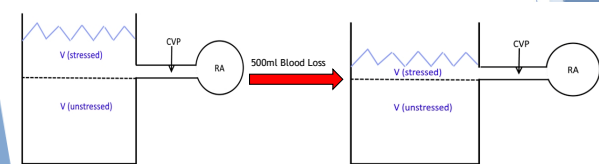


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### Example: Hemorrhage

- ▶ CHF patient with low vascular compliance (arteriosclerosis)
  - ▶ Venosconstriction in response to catecholamines is blunted
  - ▶ Stress volume decreases and CVP decreases



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### Stress vs Unstress Volume Clinical Implications

- ▶ Explains why CVP is not an accurate modality to assess volume status
- ▶ Explains why young, healthy patients may lose a significant amount of blood with little change in vitals
  - ▶ Studies show that maternal vitals signs may initially be normal in PPH despite losing up to 1000 mL of blood<sup>1</sup>
- ▶ Explains how vasopressors may be a useful temporary adjunct to maintain preload in a variety of clinical scenarios: spinal anesthesia, neurogenic or septic shock
- ▶ Explains why more sophisticated measures to assess volume status should be utilized instead of relying on vitals alone to guide volume resuscitation

<sup>1</sup> Pacagnella R, et al. A systematic review of the relationship between blood loss and clinical signs. *PLoS One*. 2013;8(3)

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### Which of the following is true regarding volume assessment modalities?

Qualitative arterial line variability is a poor modality to assess volume status

Qualitative pleth variability is not accurate due to automatic gain adjustment of the waveform to maximize the appearance of the signal

After adequate volume resuscitation for hemorrhagic shock, the base deficit will completely normalize within minutes

All patients with a large base deficit need to be volume resuscitated

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## Volume Status Assessment Modalities

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## Modalities to Assess Volume Status

- ▶ Static Modalities
  - ▶ Shock Index, Base Deficit, Capillary Refill Time, etc.
- ▶ Dynamic Modalities
  - ▶ Arterial Line Variability,  $\Delta CO$  with Fluid Bolus, Pleth Variability Index, etc.

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## Shock Index

- ▶ Shock Index =  $\frac{HR}{sBP}$
- ▶ SI  $\geq 1.0$  is highly predictive of massive transfusion (MT) in trauma patients
  - ▶ SI  $\geq 1.0$  RR of 9.67 (95% CI 6.09-15.36) for MT (>10 units in 24 hours)
  - ▶ SI also highly predictive of post partum hemorrhage (SI > 1.4, sensitivity 100%, specificity 70%)
- ▶ Heart rate is not predictive of MT in the geriatric (>65 years) trauma patient population.
  - ▶ MT and non-MT groups (HR of 92.6 vs 87.4,  $P > 0.05$ ).
  - ▶ SI in this demographic is still predictive of MT (SI 1.3 in MT vs 0.67 in non-MT,  $P < 0.001$ )

Claassen A, et al. Review article: shock index for prediction of critical bleeding post-trauma: a systematic review. *Emerg Med Australas*. 2014;26(3):223-8.  
Ayadi A, et al. Vital Sign Prediction of Adverse Maternal Outcomes in Women with Hypovolemic Shock: The Role of Shock Index. *PLoS One*. 2016 Feb 22;11(2)  
Ficker SC, et al. Vital Signs Strongly Predict Massive Transfusion Need in Geriatric Trauma Patients. *Am Surg*. 2005 Jul;67(7):652-6.

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## Base Deficit

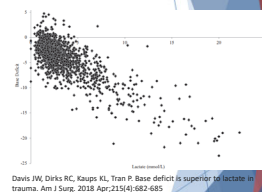
- ▶ Base Deficit (BD) or Base Excess (BE) measures the metabolic component of the acid/base disturbance
- ▶ BD is calculated in the following manner:
  - ▶ 1) Calculate what the pH would be if the  $CO_2$  was 40 mm Hg
  - ▶ 2) Calculate the amount of  $HCO_3^-$  (mmol/L) that would then be required to normalize this pH to 7.4
- ▶ Formal Definition
  - ▶ Base excess is the amount of strong acid (in millimoles per liter) that needs to be added in vitro to 1 liter of fully oxygenated whole blood to return the sample to standard conditions (pH of 7.40,  $P_{CO_2}$  of 40 mm Hg, and temperature of 37 C)

Berndt K. Diagnostic Use of Base Excess in Acid-Base Disorders. *N Engl J Med*. 2018 Apr 12;378(15):1419-1428.

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## Base Deficit

- ▶ BD is not an accurate modality to assess volume status
- ▶ BD is highly correlated to lactate levels
  - ▶ Lactate kinetics are sluggish
  - ▶ Lactate  $T_{1/2}$  is 20 minutes assuming normal liver function
- ▶ BD may not reflect hypovolemic shock in the following situations
  - ▶ Administration of normal saline or  $HCO_3^-$
  - ▶ Renal Failure
  - ▶ DKA
  - ▶ Prolonged  $CO_2$  retention (e.g., COPD)
  - ▶ Toxins (methanol, ASA, ethylene glycol)
  - ▶ Cardiogenic, Septic, or Neurogenic Shock



Davis JW, Dirks RC, Kaups KL, Tran P. Base deficit is superior to lactate in trauma. *Am J Surg*. 2018 Apr;215(4):682-685

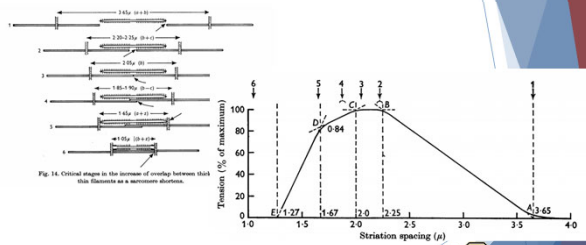
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## Dynamic Modalities

- ▶ Dynamic tests
  - ▶ Physiological basis, optimize frank-starting curve
- ▶ Gold standard
  - ▶  $\Delta CO > 10\%$  with 250ml fluid challenge or passive leg raise
    - ▶ Other indices such as  $\Delta SV$ ,  $\Delta SVI$ ,  $\Delta CI > 10\%$  may also be used
    - ▶ Requires use of PAC, Esophageal Doppler, Pulse Contour Analysis (FloTrac, PICCO, LiDCO), Echocardiography, or Bioreactance
- ▶ Other tests
  - ▶ Arterial Line Variability
  - ▶ Esophageal Doppler
  - ▶ Pulse Contour Analysis
  - ▶ Pleth Variability Index

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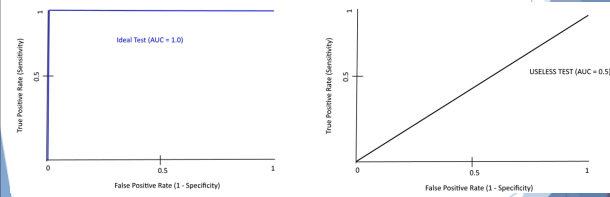
## Volume Optimization Goals



Gordon A. et al. The variation in isometric tension with sarcomere length in vertebrate muscle fibres. *J Physiol.* 1966 Aug; 194(1): 170-192.

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## Receiver Operating Curve (Review)



80

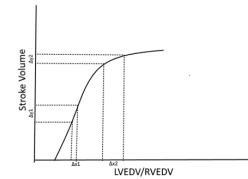
## Arterial Line Variability

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## Arterial Line Variability

- ▶  $\Delta SV$  is a function of  $\Delta$ preload/afterload
- ▶ Positive pressure ventilation
  - ▶ Decreases RV preload
  - ▶ Increases RV afterload
  - ▶ Decreases SV
- ▶ Requires
  - ▶ TV > 8ml/kg
  - ▶ No dysrhythmias
  - ▶ No spontaneous breathing



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## Arterial Line Variability: Calculation

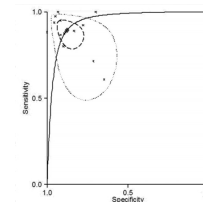
- ▶ Systolic Pressure Variation
  - ▶  $SPV = \left( \frac{SBP_{max} - SBP_{min}}{SBP_{mean}} \right) \cdot 100\%$
- ▶ Pulse Pressure Variation
  - ▶  $PPV = \left( \frac{PP_{max} - PP_{min}}{PP_{mean}} \right) \cdot 100\%$
- ▶ Interpretation
  - ▶ Volume responsive: SPV or PPV > 12%
  - ▶ Indeterminate: SPV or PPV 8-12%
  - ▶ Not Volume Responsive: SPV or PPV < 8%

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## Arterial Line Variability: Evidence

- ▶ Meta-analysis of 29 studies
  - ▶ 9 MICU
  - ▶ 16 Cardiac ICU
  - ▶ 4 Intra-operative
- ▶ SPV
  - ▶ ROC: 0.86
- ▶ PPV
  - ▶ ROC: 0.94



Marik P. et al. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: A systematic review of the literature. *Crit Care Med.* 2009 Sep;37(9):2642-7.

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## Arterial Line Variability: Eyeball Technique

### The Ability of Anesthesia Providers to Visually Estimate Systolic Pressure Variability Using the "Eyeball" Technique

Robert H. Thiele, MD, Douglas A. Colquhoun, MB ChB, MSc, Franziska E. Blum, MD, and Marcel E. Durieux, MD, PhD

- **Methods**
  - 50 Anesthesia Providers (30 residents and 20 attendings)
  - Asked to give volume or not based on visually observed arterial line variability
- **Results**
  - 3% elected to treat when (SPV < 8%)
  - 60% elected to treat when (SPV 8 - 12%)
  - 37% elected to treat when (SPV > 12%)

Thiele R, et al. The ability of anesthesia providers to visually estimate systolic pressure variability using the "eyeball" technique. Anesth Analg. 2012 Jul;115(1):176-81.

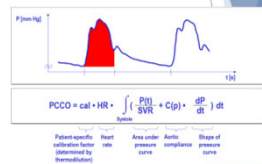
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## Pulse Contour Analysis

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## Pulse Contour Analysis

- Analysis of arterial waveform to calculate stroke volume
  - $\text{Pulse Pressure} \propto \text{Stroke Volume}$
  - $\text{Pulse Pressure} \propto \frac{1}{\text{Compliance}}$
- **Calibrated**
  - PICCO, LIDCO
  - Uses thermodilution to calculate compliance for calibration
- **Uncalibrated**
  - FloTrac
  - Uses patient demographic data to calculate compliance



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## Pulse Contour Analysis: Evidence

- **2nd Generation FloTrac Software**
  - Volume Responsive:  $\Delta \text{CO} > 15\%$  with 500ml fluid
  - ROC: 0.92 with  $\Delta \text{SV} > 15\%$  with PLR<sup>1</sup>
- **3rd Generation FloTrac Software**
  - Volume Responsive:  $\Delta \text{CO} > 15\%$  with 250ml fluid
  - ROC: 0.85 with  $\Delta \text{CO} > 9\%$  with PLR<sup>1</sup>

Wong et al. Journal of Intensive Care (2016) 31(1)

Journal of Intensive Care

RESEARCH

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Journal

Fluid responsiveness prediction using Vigileo FloTrac measured cardiac output changes during passive leg raise test

Arnon Kogut, Martin Bland, and Thomas Fardouin

<sup>1</sup>Briels M, et al. Changes in stroke volume induced by passive leg raising in spontaneously breathing patients: comparison between echocardiography and Vigileo/FloTrac device. Crit Care. 2009;13(8):R195.

<sup>2</sup>Ridge A, et al. Fluid responsiveness prediction using Vigileo FloTrac measured cardiac output changes during passive leg raise test. J Intensive Care. 2016 Oct 6:4-63.

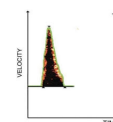
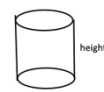
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## Esophageal Doppler Monitor

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## Esophageal Doppler

- Esophageal probe measuring blood velocity in the descending aorta
- Aortic area can be approximated by demographics (age, height, weight)
- **Stroke Volume = Aortic Area X VTI**
  - $\text{VTI (height)} = \text{distance column of blood moved during systole}$
  - $\text{VTI} = \int_{\text{systole start}}^{\text{systole end}} \text{Velocity} \cdot dt$



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## Esophageal Doppler: Evidence

- ▶ Stroke Volume Variation (i.e.  $\Delta \text{respSV}$ )
  - ▶  $\text{SVV} = \left( \frac{\text{SV}_{\text{max}} - \text{SV}_{\text{min}}}{\text{SV}_{\text{mean}}} \right) \times 100\%$
  - ▶  $\text{SVV} > 14\%$  predictor of fluid responsive
- ▶ FTc - Systolic ejection time corrected for heart rate
- ▶ SVV ROC: 0.91
- ▶ FTc ROC: 0.49

Gulnot P, et al. Ability of stroke volume variation measured by esophageal Doppler monitoring to predict fluid responsiveness during surgery. *Br J Anaesth*. 2013 Jan;110(1):28-33.

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## Esophageal Doppler: Pitfalls

- ▶ Descending aorta receives approximately 70% of total blood flow
  - ▶ EDM does 70:30 correction to calculate total CO
  - ▶ Shock states divert blood away from mesenteric circulation
  - ▶ Lowering percentage of blood flow in the descending aorta
- ▶ Velocity Calculation
  - ▶ EDM assumes 45 or 60° correction of doppler signal
- ▶ Blood flow is laminar and not uniform
- ▶ EDM assumes aortic area using patient demographics

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## Pleth Variability Index

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## Pleth Variability Index

- ▶ Perfusion Index (PI) is calculated as the pulsatile infrared signal (AC) indexed against the non-pulsatile infrared signal (DC). The AC and DC signals reflect the absorption of infrared light.

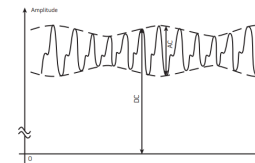
$$PI = \frac{AC}{DC} \times 100\%$$

- ▶ The Pleth Variability Index (PVI)

$$PVI = \frac{PI_{\text{max}} - PI_{\text{min}}}{PI_{\text{max}}} \times 100\%$$

- ▶ Requires

- ▶ TV > 8ml/kg
- ▶ No dysrhythmias
- ▶ No spontaneous breathing



Pleth Variability Index: A Dynamic Measurement to Help Assess Physiology and Fluid Responsiveness. *Resumo Technical Bulletin*. 2013.

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## Pleth Variability Index: Evidence

- ▶ Advantages
  - ▶ Non-invasive
  - ▶ Large meta-analysis of 25 studies both in the operating room and the intensive care unit showed a ROC of 0.82<sup>1</sup>
- ▶ Disadvantages
  - ▶ Proprietary technology from Masimo
  - ▶ Qualitative analysis of the waveform is not accurate due to automatic gain adjustment to maximize the appearance of the signal
  - ▶ Unclear cut-off value
    - ▶ Studies utilize a range of cut-off values from 7-20%
  - ▶ PVI is inaccurate in the setting of large volume resuscitation
    - ▶ A study in patients undergoing orthotopic liver transplant found a ROC of 0.55<sup>2</sup>

<sup>1</sup>Tsai T, et al. Reliability of pleth variability index in predicting preload responsiveness of mechanically ventilated patients under various conditions: a systematic review and meta-analysis. *BMC Anesthesiol*. 2015 May 6;15(1):57.

<sup>2</sup>Konur H, et al. Evaluation of pleth variability index as a predictor of fluid responsiveness during orthotopic liver transplantation. *Kardiol J Pol*. 2019; Jul;32(7):373-80.

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## Update in Pediatric Trauma

Walter A. Kohn, MD  
Associate Professor  
University of Colorado School of Medicine  
Director of Pediatric Anesthesia  
Denver Health Medical Center

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### How many of you would consider using whole blood in pediatric blunt or penetrating trauma?

Never, it is not safe

I would consider but my institution does not use it

Yes, we use whole blood for pediatric trauma

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### Objectives

- ▶ What is LTOWB
- ▶ Whole blood in adult civilian trauma
- ▶ Upcoming adult studies
- ▶ Pediatric trauma resuscitation review
- ▶ WB in pediatric trauma
- ▶ Safety of WB in pediatric patients
- ▶ Consensus clinical recommendations
- ▶ Calcium in pediatric trauma
- ▶ Shock index, pediatric age-adjusted

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### Whole Blood (LTOWB)

- ▶ Cold stored 4°C in refrigerator
- ▶ Platelets typically stored at room temperature
- ▶ Low titer (low anti-A and anti-B)
- ▶ Platelet replete
- ▶ Contains RBC, platelets, plasma
- ▶ Rh factor less important in acute trauma

Gallagher et al 2020

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### Whole Blood in Adult Trauma

ORIGINAL ARTICLE

Large volume transfusion with whole blood is safe compared with component therapy

Jared Robert Gallagher, MD, MPH, Alexandra Dixon, MD, MPH, April Cockcroft, DO, Maverick Grey, BA, Elizabeth Dewey, MS, Andrew Goodman, BS, and Martin Schreiber, MD, Portland, Oregon

Gallagher et al 2020

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### LTOWB

- ▶ LTOWB as part of MTP safe
- ▶ No change in mortality or transfusion reactions
- ▶ Can approximate the ideal 1:1:1 ratio than component therapy alone
- ▶ Easier, fewer bags to transfuse initially
- ▶ Can give at least 4-6 units to adults without evidence of hemolysis
- ▶ No difference in mortality at 24 hours or 30 days
- ▶ No difference in transfusion reactions in WB group
- ▶ Underpowered study to look at massive transfusion with WB transfusion alone

Gallagher et al 2020

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### Whole Blood, Fixed Ratio, or Goal-Directed Blood Component Therapy for the Initial Resuscitation of Severely Hemorrhaging Trauma Patients: A Narrative Review

Mark Walsh <sup>1,2</sup>, Gerard E. Moore <sup>1,2</sup>, Hunter B. Moore <sup>1</sup>, Scott Thomas <sup>1</sup>, Hui C. Kwan <sup>1</sup>, Jacob Speychenck <sup>1</sup>, Matthew Marner <sup>1</sup>, Connor M. Blatch <sup>1,2</sup>, John Stillman <sup>1,2</sup>, Anthony V. Thomas <sup>1</sup>, Anne G. Gifford <sup>1,2</sup>, John Arena <sup>1</sup>, Daniel Fulkerson <sup>1</sup>, Stefani Vande Loo <sup>1</sup>, Lucas Nijkhech <sup>1,2</sup> and Quincy K. Tran <sup>1,2</sup>

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## Safety of LTOWB in Pediatric Patients

- ▶ 2021 University of Pittsburgh
  - ▶ 47 patients transfused for hemorrhagic shock due to trauma
  - ▶ LTOWB advantages compared to BCT: faster resolution of shock, reduced transfusion requirements following initial resuscitation
  - ▶ Primary outcome laboratory evidence of hemolysis or report of transfusion reaction
- ▶ 2021 Conclusion: up to 40 ml/kg LTOWB serologically safe
- ▶ 2016 criteria for administering LTOWB initially age  $\geq 3$  yrs and weight  $\geq 15$  kg
- ▶ 2019 revised to age > 1 yr

Morgan et al. 2021

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## REVIEW ARTICLE

## Resuscitative practices and the use of low-titer group O whole blood in pediatric trauma

Katrina M. Morgan, MD, Christine M. Leeper, MD, MS, Mark H. Yazer, MD, Philip C. Spinella, MD, and Barbara A. Gaines, MD, *Pittsburgh, Pennsylvania*

[illegible]

**KEY WORDS:** Pediatric trauma, whole blood, balanced resuscitation.

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Authors	Population	Study Type	Results
Shaw et al. (1997)	<ul style="list-style-type: none"> <li>• "High crime" (Urban areas with serious crime)</li> </ul>	<ul style="list-style-type: none"> <li>• RT comparing new vs. existing schools</li> </ul>	<ul style="list-style-type: none"> <li>• Significant benefits for programs starting and ending in high crime areas</li> </ul>
Engler et al. (1998)	<ul style="list-style-type: none"> <li>• "High crime" (Severely exposed children 1 yr or older)</li> </ul>	<ul style="list-style-type: none"> <li>• Retrospective study comparing WB and CT</li> </ul>	<ul style="list-style-type: none"> <li>• No treatment effects</li> <li>• Significant benefits for programs starting and ending in high crime areas</li> </ul>
Engler et al. (1998)	<ul style="list-style-type: none"> <li>• "High crime" (Severely exposed children 1 yr or older)</li> </ul>	<ul style="list-style-type: none"> <li>• Retrospective study comparing children who received WB or CT with children who received WB or CT</li> </ul>	<ul style="list-style-type: none"> <li>• Significant benefits for programs starting and ending in high crime areas</li> </ul>
Engler et al. (1998)	<ul style="list-style-type: none"> <li>• "High crime" (Severely exposed children 1 yr or older)</li> </ul>	<ul style="list-style-type: none"> <li>• Retrospective study comparing WB and CT</li> </ul>	<ul style="list-style-type: none"> <li>• Significant benefits for programs starting and ending in high crime areas</li> </ul>
Arnold et al. (2002)	<ul style="list-style-type: none"> <li>• "High crime" (Urban areas with serious crime)</li> </ul>	<ul style="list-style-type: none"> <li>• Retrospective study comparing WB and CT</li> </ul>	<ul style="list-style-type: none"> <li>• No treatment effects</li> <li>• Significant benefits for programs starting and ending in high crime areas</li> </ul>
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Wagner et al. (2002)	<ul style="list-style-type: none"> <li>• "High crime" (Urban areas with serious crime)</li> </ul>	<ul style="list-style-type: none"> <li>• Retrospective study comparing WB and CT</li> </ul>	<ul style="list-style-type: none"> <li>• No treatment effects</li> <li>• Significant benefits for programs starting and ending in high crime areas</li> </ul>
Engler et al. (1997)	<ul style="list-style-type: none"> <li>• "High crime" (Urban areas with serious crime)</li> </ul>	<ul style="list-style-type: none"> <li>• Retrospective study comparing WB and CT</li> </ul>	<ul style="list-style-type: none"> <li>• No treatment effects</li> <li>• Significant benefits for programs starting and ending in high crime areas</li> </ul>

CT, computed tomography; DOD, Department of Defense trauma registry; ETV, intensive care unit; INR, international normalized ratio; ISS, Injury Severity Score; TBI, traumatic brain injury; RBC, red blood cell; TQIP, Trauma Quality Improvement Program database; WB, whole blood.

Morgan et al 2003

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- ▶ Addresses potential concerns for hemolysis and RhD sensitization
- ▶ Need for future studies in use of WB for pediatric trauma, multicenter trials, and prehospital administration WB
- ▶ Unclear which subset of pediatric patients will benefit most

Morgan et al. 2002

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### CONSENSUS STATEMENT

Pediatric traumatic hemorrhagic shock consensus  
conference recommendations

Robert T. Russell, MD, MPH, Joseph R. Sparaz, MD, MPH, Michael A. Beckwith, MD, Peter J. Abraham, MD, Melania M. Bembica, MD, PhD, MPH, Matthew A. Borgman, MD, Randall S. Bard, MD, PhD, Barbara A. Gaines, MD, Mubeen Jafri, MD, Cassandra D. Josephson, MD, Christine Leeper, MD, Julie C. Leonard, MD, MPH, Jennifer A. Muszynski, MD, MPH, Kathleen K. Nicot, MD, Daniel K. Nishijima, MD, MAS, Paul A. Stricker, MD, Adam M. Vogel, MD, Trinda E. Wong, MD, MS,

**ABSTRACT:** Hemorrhage shock in pediatric trauma patients remains a challenging and preventable cause of death. There is little high-quality evidence available to guide current practices of hemorrhage shock and hemorrhage resuscitation in the hospital. We sought to generate clinical recommendations, expert consensus, and good practice statements to aid providers in care for these difficult patients. The Pediatric Trauma Hemorrhage Shock Consensus Conference provides included evidence reviewed relevant to six subgroups and 14 consensus meeting topics. A panel of experts from 10 pediatric hospitals and 10 adult hospitals met to discuss the following topics (1) blood product and fluid resuscitation for hemorrhagic resuscitation, (2) utilization of prehospital blood products, (3) use of tranexamic acid, (4) platelets, (5) cryoprecipitate, (6) plasma, (7) fibrinogen, (8) whole blood, (9) damage control resuscitation, and (10) transfusion. The following recommendations were developed: 1) 10 expert consensus statements, 2) 14 expert consensus statements, and 3) good practice statements. The statement, the panel's voting outcome, and the rationale for the statement intend to guide the reader in the use of the recommendations. The statement, the panel's voting outcome, and the rationale for the statement experiencing hemorrhage shock. With a broad interdisciplinary representation, the Pediatric Trauma Hemorrhage Shock Consensus Conference systematically evaluated the literature and developed clinical recommendations, expert consensus, and good practice statements concerning topics in hemorrhage shock. *J Trauma Acute Care Surg* 2015;78:525-534. © 2015 Wolters Kluwer Health | All rights reserved.

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- ▶ Panel of 16 consensus multidisciplinary committee members
- ▶ 21 recommendations:
  - ▶ 2 Clinical recommendations
  - ▶ 14 expert consensus statements
  - ▶ 5 good practice statements
- ▶ Evaluated literature on 6 topics:
  - ▶ Blood products and fluid resuscitation
  - ▶ Utilization of prehospital blood products
  - ▶ Use of hemostatic agents
  - ▶ Tourniquet use
  - ▶ Prehospital airway and BP management
  - ▶ CCT or TEG based resuscitation

## Clinical Recommendations

- ▶ In traumatically injured children in hemorrhagic shock:
- ▶ Prioritize the use of blood products over crystalloids
- ▶ Use of LTOWB can be considered for resuscitation
- ▶ If BCT, target high plasma:RBC ratios
- ▶ Target high platelet:RBC weight-based ratios
- ▶ Consider prehospital transfusion by EMS based on product availability and clinical judgement
- ▶ Empiric use of TXA within 3 hrs of injury might be considered

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## Clinical Recommendations

- ▶ Use commercially available tourniquets by individuals with training for exsanguinating extremity hemorrhage
- ▶ Prehospital BP management- suggest against permissive hypotension, instead optimize end organ perfusion and adequate oxygen delivery
- ▶ Initial empiric resuscitation approach using MTPs and balanced product administration
- ▶ Use of TEG or viscoelastic assays recommended for goal directed resuscitation if available to optimize hemostasis and correction of coagulopathy

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 Text BETHANYBENISH100 to 22333 once to join

**There is an unrestrained 3 yo male s/p ejection from a motor vehicle. He presents to the ED by ambulance. You are the anesthesiologist on call. His ionized calcium on arrival is 0.98 mmol/L. What do you do with this number?**

Nothing, only interested in H/H, coags, blood gas

I would treat the calcium but it is just a random lab result

I would treat the hypocalcemia and know that it indicates more about transfusion requirements for this child

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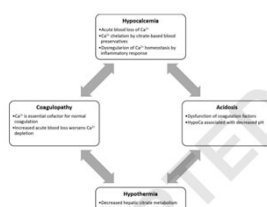
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## Calcium in Pediatric Trauma

- ▶ After first few months of life (>6 months old) calcium metabolism and physiology similar to adults
- ▶ Role of calcium in normal physiologic function:
  - ▶ Effective coagulation
  - ▶ Cardiac contractility
  - ▶ Muscle function
  - ▶ Component of bone mineral matrix
- ▶ Pediatric hearts are more vulnerable to myocardial dysfunction in presence of hypocalcemia (↓ SR)
- ▶ Age and weight adjustments for treatment of hypocalcemia
- ▶ IV access more challenging in children
- ▶ Extravasation of CaCl can lead to tissue necrosis

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## Hypocalcemia



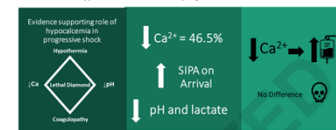
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Figure 1. Linked Diamond Diagram. Adapted from [1] at [2].

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## Hypocalcemia in Pediatric Trauma

Effects of Hypocalcemia in Severely Injured Pediatric Trauma Patients



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