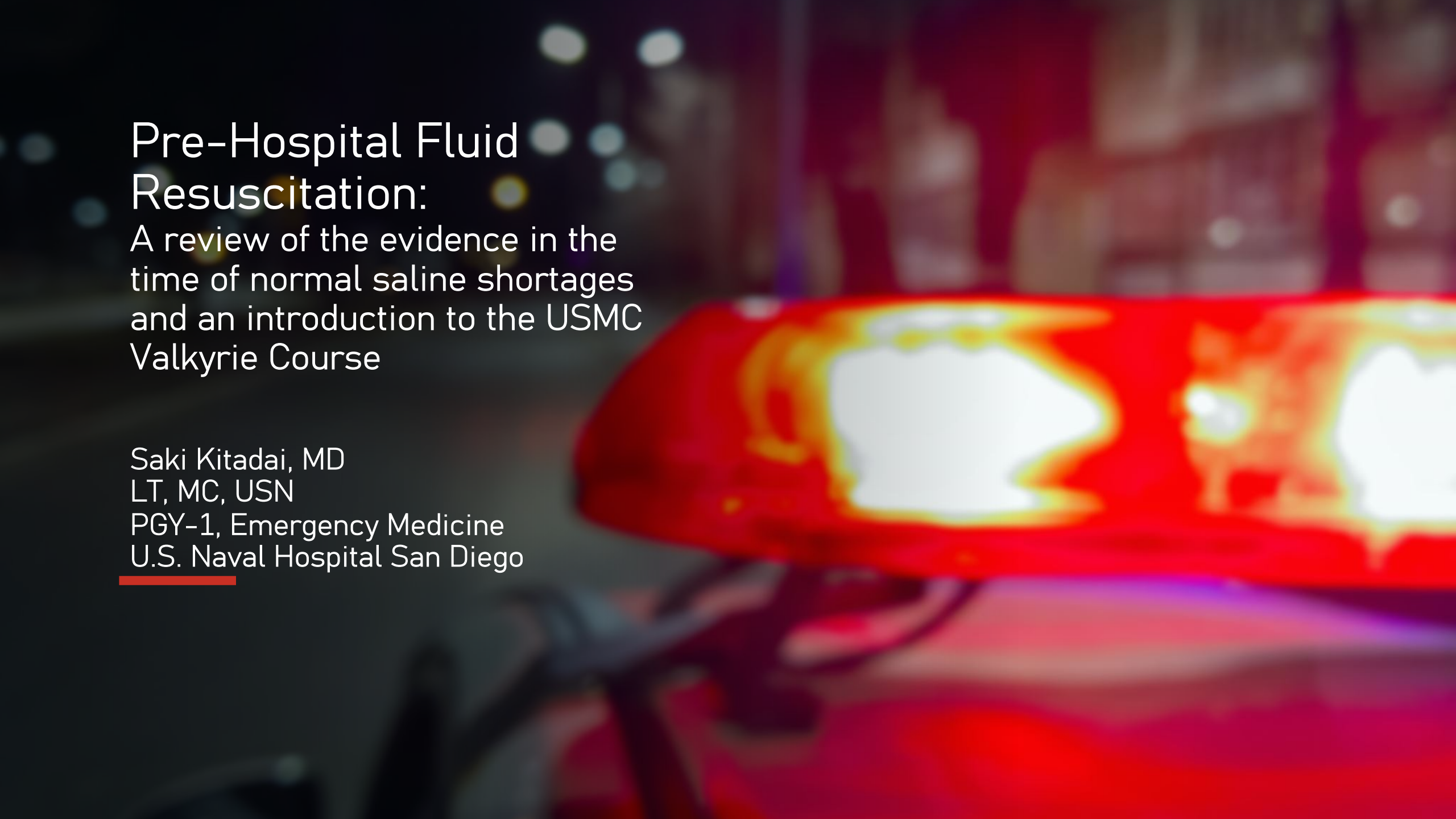

Pre-Hospital Fluid Resuscitation:

A review of the evidence in the time of normal saline shortages and an introduction to the USMC Valkyrie Course

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Disclaimer

The views expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

A COURT FOR KING CHOLERA.

A History of Resuscitative Fluids

- 1830's: Saline infusions during Cholera outbreak

  "place the patient in nearly his ordinary state as to the quantity of blood circulating the vessels"

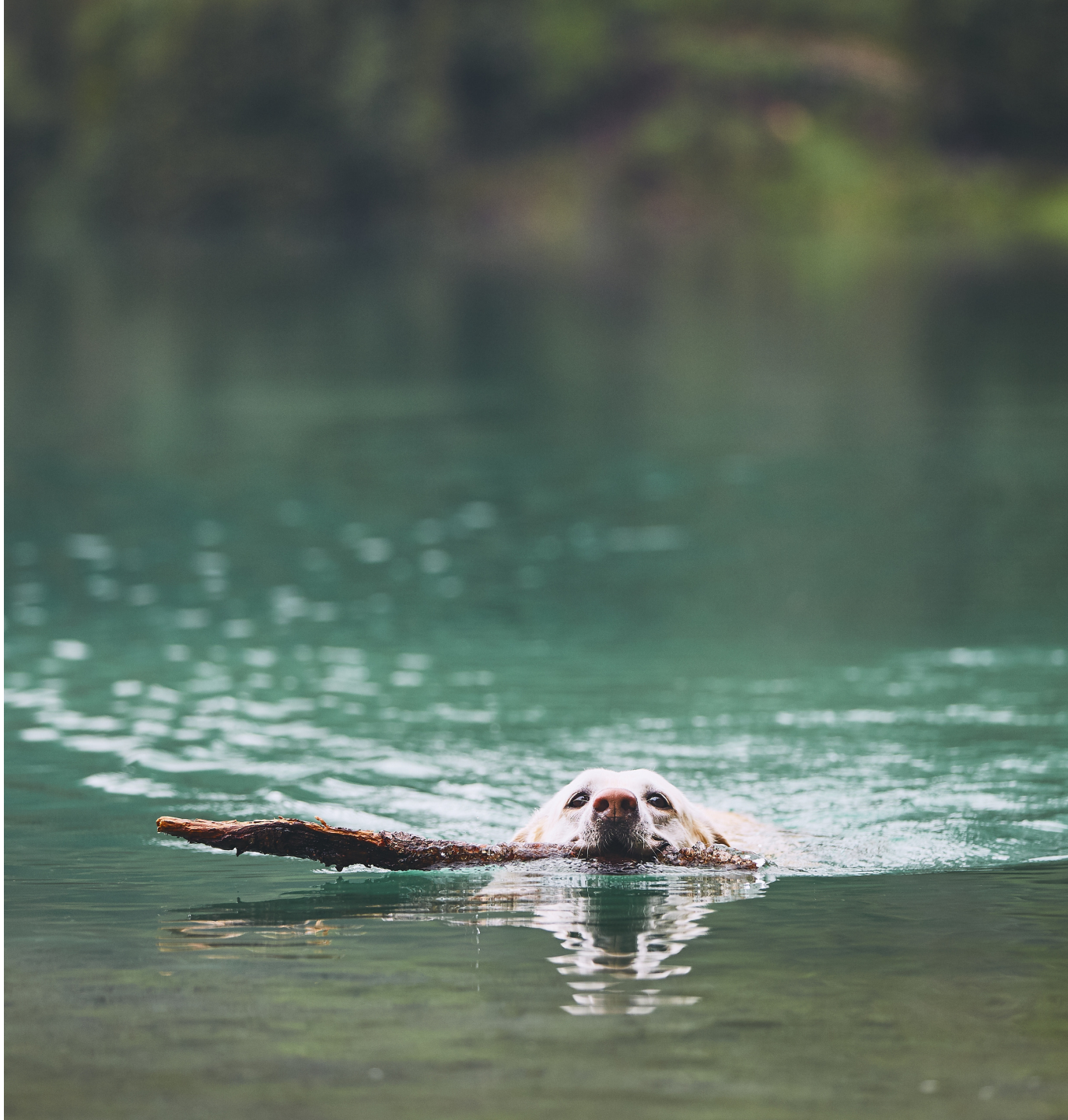
- 1883: Normal Saline mistakenly named in a study by a Dutch scientist Hamburger
- 1885: Sidney Ringer and Lactated Ringers for rehydration of children with gastroenteritis.
- 1941: development of blood fractionation allowed human albumin to be used, large quantities for resuscitation of Pearl Harbor victims in the same year.

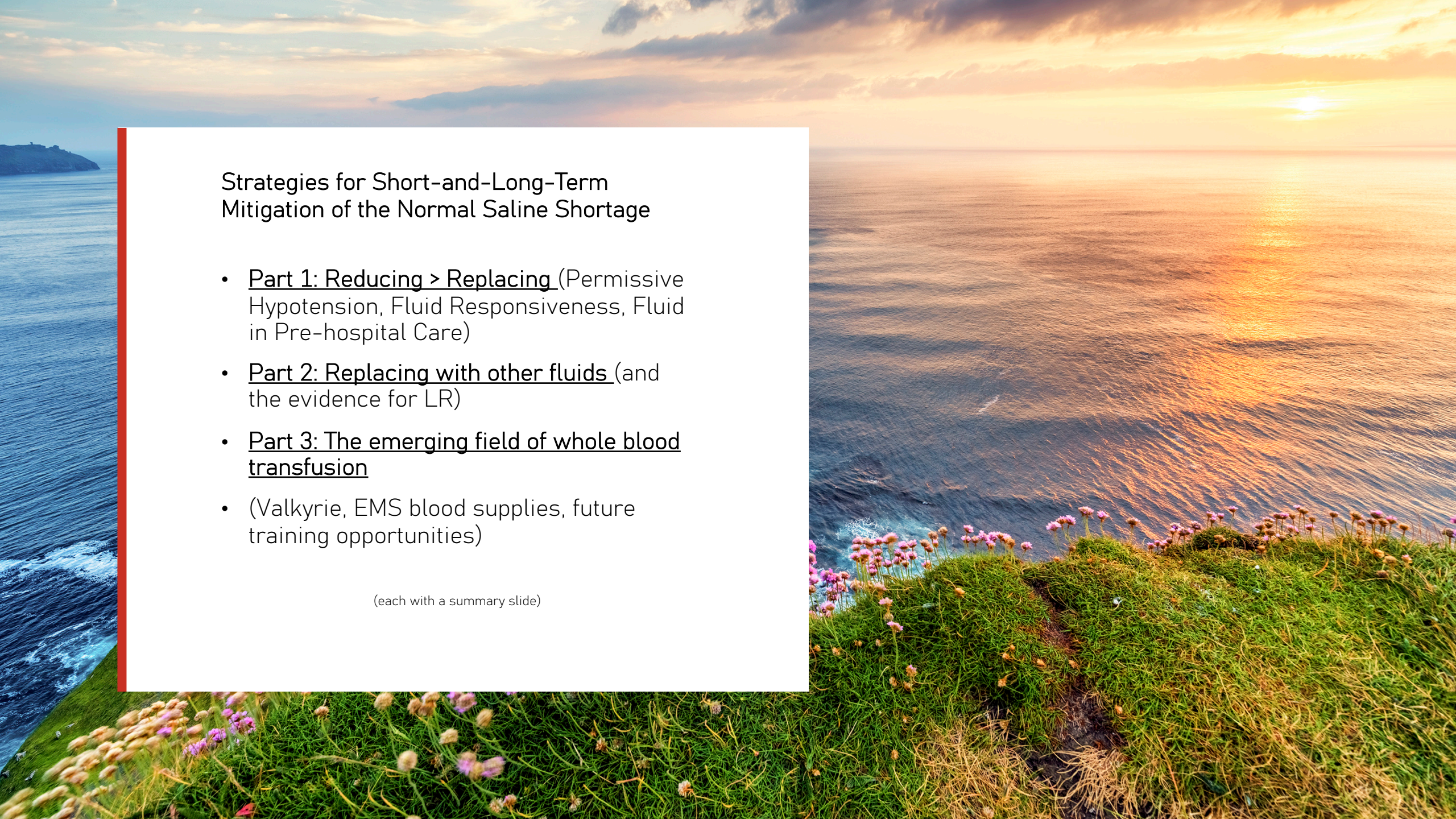
Vs. The History of Blood Transfusions

- = A history of the battlefield
- NS infusions did little to stabilize shock and save lives
- Robertson (Canadian physician) performed first blood transfusion in the field, published several papers documenting success
- Fell out of favor by the Vietnam War
- To Be Continued…

What is the Current NS Shortage?

- ~200 million liters used in US per year
- ASHP reporting shortages in Flush syringe, irrigation & large volume bags
- Reasons cited: manufacturing delay, third party delay, increased demand, and good ole fashioned “no comment”
- Saline vials routed to COVID-19 vax containers
- Defect in saline plungers forcing stopping in sales
- Estimated resupply time
- Negative implications for meds administration and resuscitation





Strategies for Short-and-Long-Term Mitigation of the Normal Saline Shortage

- Part 1: Reducing > Replacing (Permissive Hypotension, Fluid Responsiveness, Fluid in Pre-hospital Care)
- Part 2: Replacing with other fluids (and the evidence for LR)
- Part 3: The emerging field of whole blood transfusion
- (Valkyrie, EMS blood supplies, future training opportunities)

(each with a summary slide)

Part 1: Reduce > Replace

The case for permissive hypotension

- A guideline for hemorrhagic/ hypovolemic shock that recommends systolic blood pressure goals below physiologic "normal":

  60–70 mmHg for penetrating trauma

  80–90 mmHg for blunt trauma without TBI

  100–110 mmHg for blunt trauma with TBI

- What's wrong with large-volume fluid resuscitation?

- Vincent and De Baker [1] divided resuscitative methods into four stages, by therapeutic strategy. Permissive hypotension has generally been used only in the initial rescue and optimization phases of recovery.

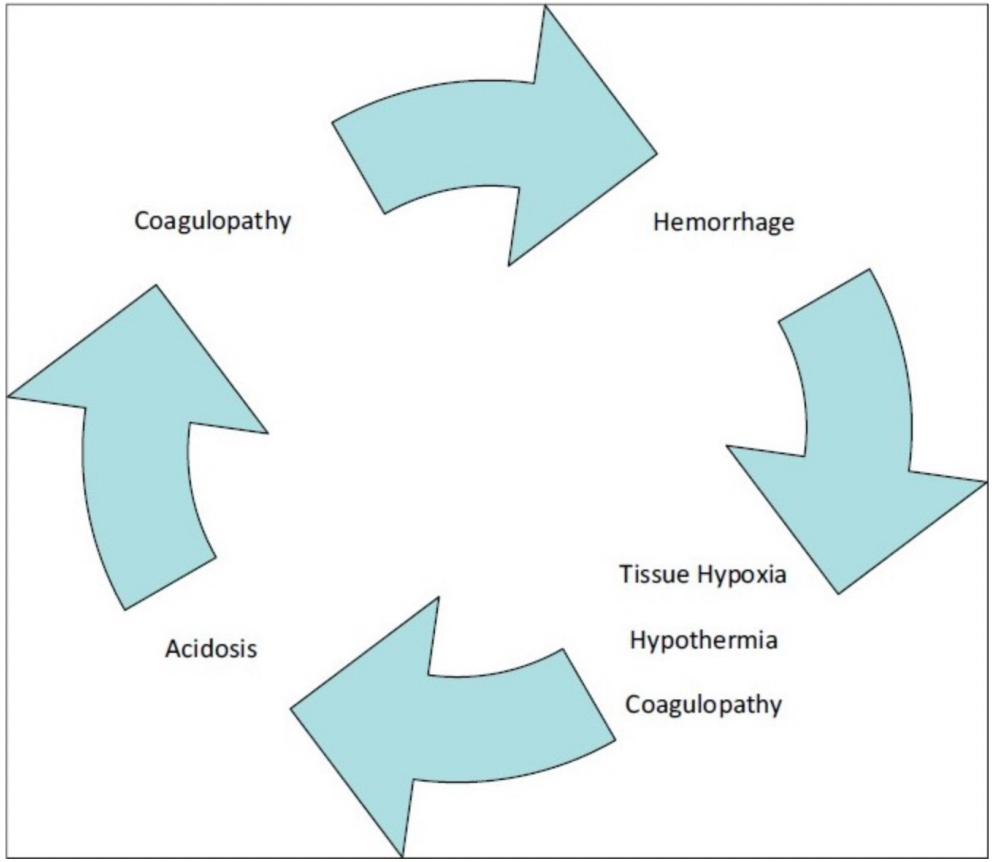
  Rescue or salvage (re-establishing minimum perfusion in life-threatening hypovolemic shock) = pre-hospital

  Optimization

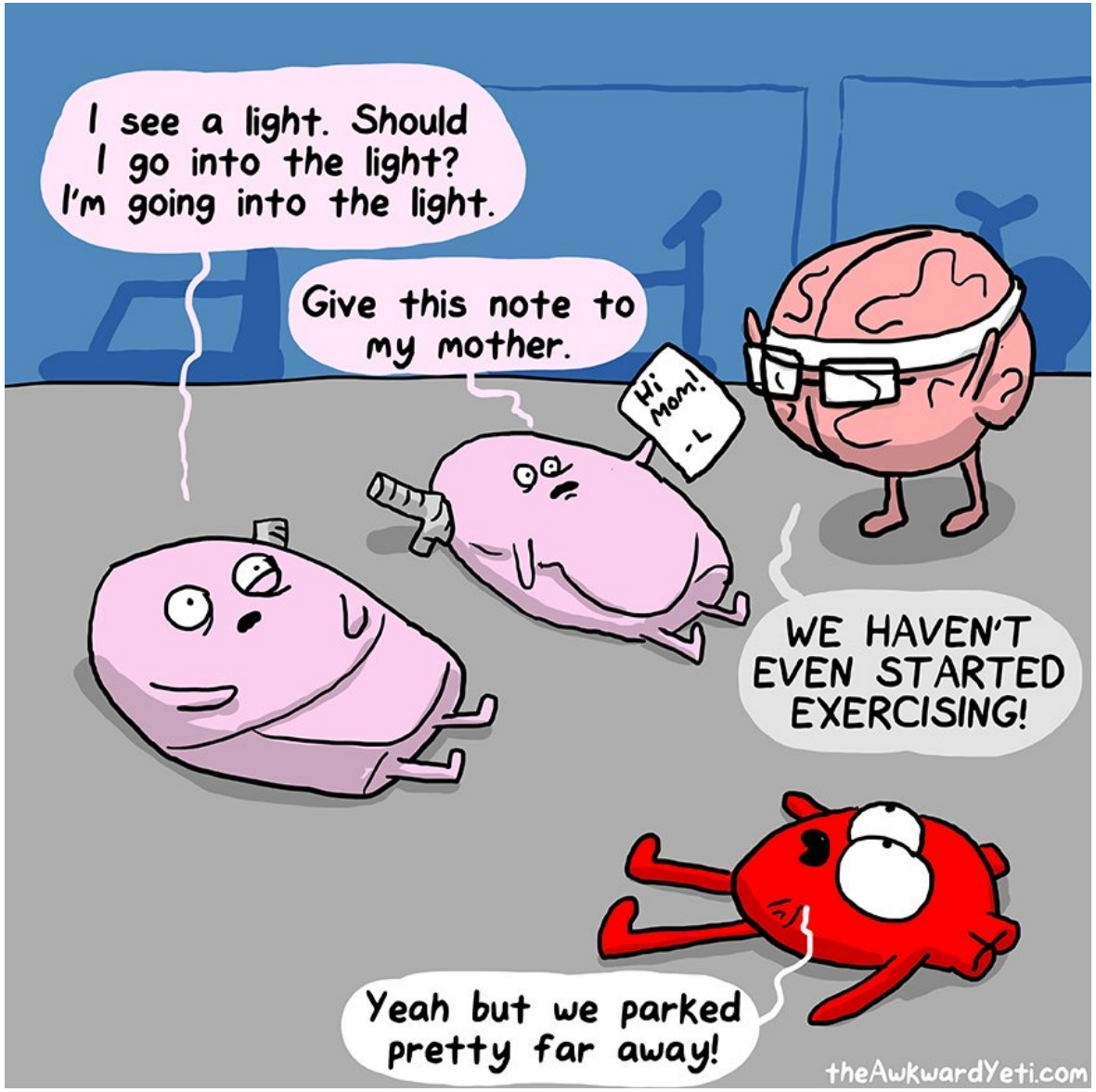
  Stabilization

  Deescalation

Figure 1: The "Vicious Cycle" from Kashuk et al.[4]



International Journal of Critical Illness and Injury Science



Part 1: Reduce > Replace

The case for permissive hypotension (cont.)

How long can hypotensive resuscitation be tolerated?

- Unclear at this time, but large animal studies have shown increased metabolic stress, tissue hypoxia, and mortality associated with sustained SBP and MAP <65mmHg

  Their cut off for "prolonged" duration= 8 hours!

Part 1: Reduce > Replace

What about for sepsis?

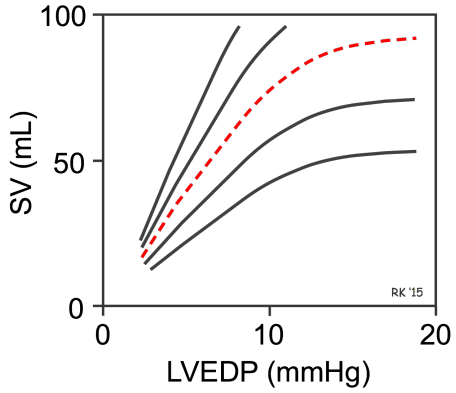
Surviving Sepsis campaign has **weak recommendations** suggesting resuscitation with "*either balanced crystalloids or saline*" that can be given within the *first 3 hours* of resuscitation

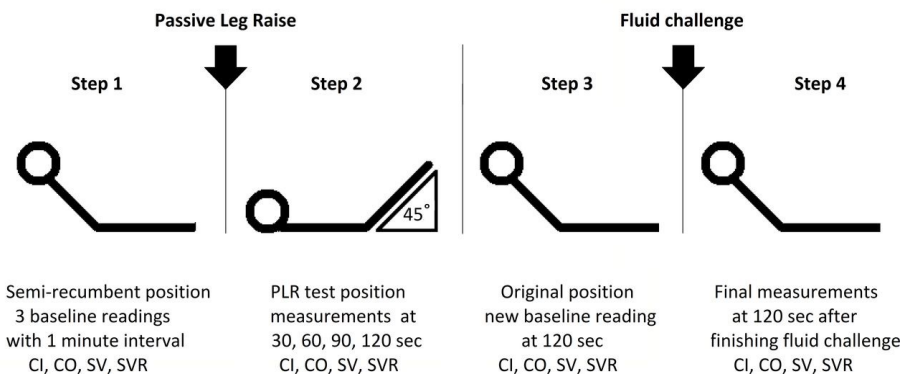
45. There is insufficient evidence to make a recommendation on the use of restrictive versus liberal fluid strategies in the first 24 hr of resuscitation in patients with sepsis and septic shock who still have signs of hypoperfusion and volume depletion after the initial resuscitation.	***No recommendation***	**NEW** "We suggest using either balanced crystalloids or saline for fluid resuscitation of patients with sepsis or septic shock" ***Weak recommendation*** , *low quality of evidence* "We suggest using crystalloids over gelatins when resuscitating patients with sepsis or septic shock." ***Weak recommendation*** , *low quality of evidence*
5. For patients with sepsis induced hypoperfusion or septic shock we suggest that at least 30 mL/kg of IV crystalloid fluid should be given within the first 3 hr of resuscitation.	**Weak**, *low quality of evidence*	**DOWNGRADE** from ***Strong*** , low quality of evidence "We **recommend** that in the initial resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 hr"

Part 1: Reduce > Replace

Fluid responsiveness

- Another method to administer fluids more judiciously in sepsis
- Patients who have decreased systolic or diastolic function will not respond to a fluid challenge, even if they are intravascularly depleted.
- Patients are considered fluid responsive if **stroke volume** increases by at least 10% after a fluid challenge of **500 mL of crystalloid**. Pulse pressure variation, passive leg raising test, and SV variation are other reliable markers.
- *Only patients who are fluid responsive should receive additional fluids.*





The BMJ

Part 1: Reduce > Replace

Delayed Resuscitation

- "Scoop and Run": delayed resuscitation seems a better option when transport time to definitive care is shorter
- Median time to transport for SD County? Fluids given during transport? Indications?
- Evidence against pre-hospital crystalloid resuscitation from other countries

  Cross-national, multi-center-large-scale retrospective cohort study of Asian counties

  Trauma patients receiving prehospital crystalloids had higher in-hospital mortality and poor functional outcomes

  Median transport time was 10 minutes for pts with fluids, 11 mins with no fluids

Summary of Part 1

- Conservative fluid administration (permissive hypotension, fluid responsiveness, delayed resuscitation) can not only help mitigate the IVF shortage but also improve patient outcomes
- Guidelines for pre-hospital fluid resuscitation should be tailored to local EMS transport times and common MOI/MOI

Part 2: Replacing with other fluids

- Where does NS fit into the matrix of IV fluids?

Solute	Plasma	Colloids		Crystalloids			
		Dextran	Gelati	Normal Saline	Ringer's Lactate	Hartmann's Solution	Plasma-Lyte
Na+	135 - 145	154	154	154	130	131	140
K+	4.0 - 5.0	0	0	0	4.5	5	5
Ca2+	2.2 - 2.6	0	0	0	2.7	4	0
Mg2+	1.0 - 2.0	0	0	0	0	0	1.5
Cl-	95 - 110	154	120	154	109	111	98
Acetate	0	0	0	0	0	0	27
Lactate	0.8 - 1.8	0	0	0	28	29	0
Gluconate	0	0	0	0	0	0	23
Bicarbonate	23 - 26	0	0	0	0	0	0
Osmolarity	291	308	274	308	280	279	294
Colloid	35 - 45	100	40	0	0	0	0
Osmolarity (mOsm/L); C		oid (g/L); All othe		olutes (mmol/L)			

REBEL REVIEWS

Part 2: Replacing with other fluids

A case for LR

- Contains K+, Ca2+, lactate
- Less acidic, closer to physiologic composition than NS

Solute	Plasma	Colloids		Crystalloids			
		Dextran	Gelatin	Normal Saline	Ringer's Lactate	Hartmann's Solution	Plasma-Lyte
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Osmolarity (mOsm/L); Colloid (g/L); All other solutes (mmol/L)							

REBEL REVIEWS

Part 2: Replacing with other fluids

NS vs. LR

Safety profile?

- NS: In large volume resuscitation can cause AKI, acidosis, worsened mortality
- LR: Interferes with blood transfusions given calcium content. Can worsen hyperkalemia?

Cross-reactivity?

- LR has several cross-reactivity concerns (Ca can bind to drug and deposit in LU/KD)
- Ketamine, Nicardipine, TXA, Kcentra, Zosyn, Levaquin, Amiodarone, Diltiazem

Cost?

- Surprisingly, the same!
- 1L NS is $5.43 vs 1L LR is $5.43. <-- This information is from the Amerisource Bergen (NMCSD's wholesaler) website.
- "I'm honestly a little shocked by this. I thought LR was more expensive."

Part 2: Replacing with other fluids

Review of Evidence NS vs. LR

- SPLIT Trial

  Double-blind, cluster randomized, double-crossover trial in 4 ICUs in New Zealand from April 2014 through October 2014.

  Results: There was no increased risk of kidney injury with NS compared to LR.

- SALT-ED trial

  Single-center, pragmatic, multiple-crossover trial in single hospital from ED→ ICU (aka ED patients requiring ICU admission)

  Results: Hospital-free days did not differ significantly. HOWEVER, LR found to have significantly lower incidence of adverse KD events within 30 days than saline

- SMART trial

  Pragmatic, cluster-randomized, multiple-crossover trial in 5 ICU

  Results: No difference between 0.9% saline and balance fluid in terms of AKI (LR= Non-inferior)

  In addition, Subgroup analysis suggests that saline increases mortality among patients with sepsis or chronic dialysis.

Summary of Part 2

- Don't sleep on LR! Rapidly emerging as first-line for IV fluids with similar cost, storage, safer for large volume resuscitation
- Consider separate safety profiles and drug interactions: Fluids are Meds
- Colloids (albumin, dextran) continues to be second line in the US
- How NS shortage will affect LR availability remains to be seen

Part 3: Replacing blood with blood

Finishing up the history of blood transfusions

- Walking Blood Banks during the wars in Iraq & Afghanistan
- "Golden Hour" → Now closed to 20-30 mins, with "36 mins to blood in"
- 2004: 31st Combat Support Hospital in Baghdad began using ABO type specific whole blood
- 2014: Rangers developed ROLO (Ranger O Low Titer) program, blood products > colloids or crystalloids in hemorrhagic shock
- 2015: First ROLO personnel deployed in 75th Ranger Regiment

  The Ranger Medics receive training during the Special Operations Combat Medic course

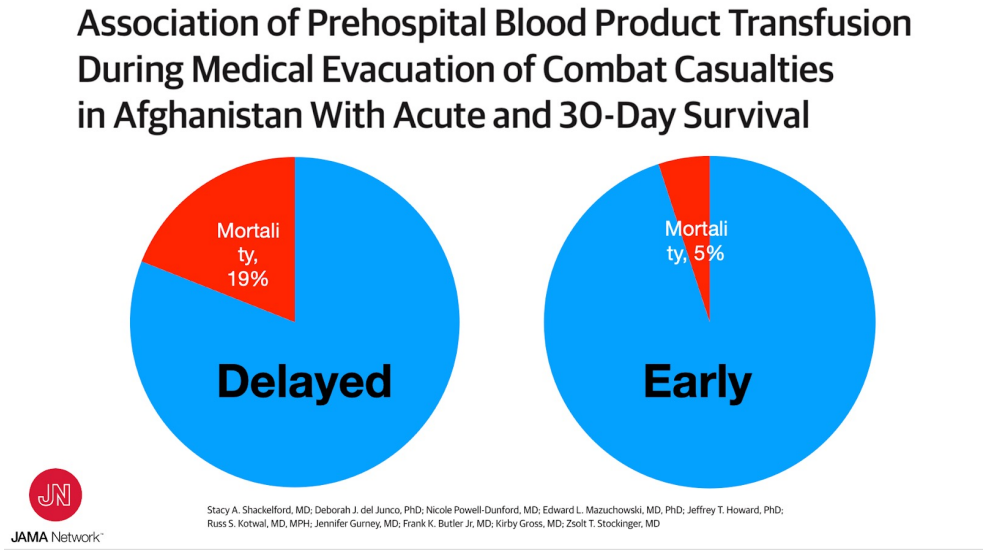
  There is presently no TCCC sanctioned course to train general duty corpsmen or medics in the conduct of FWB transfusion.

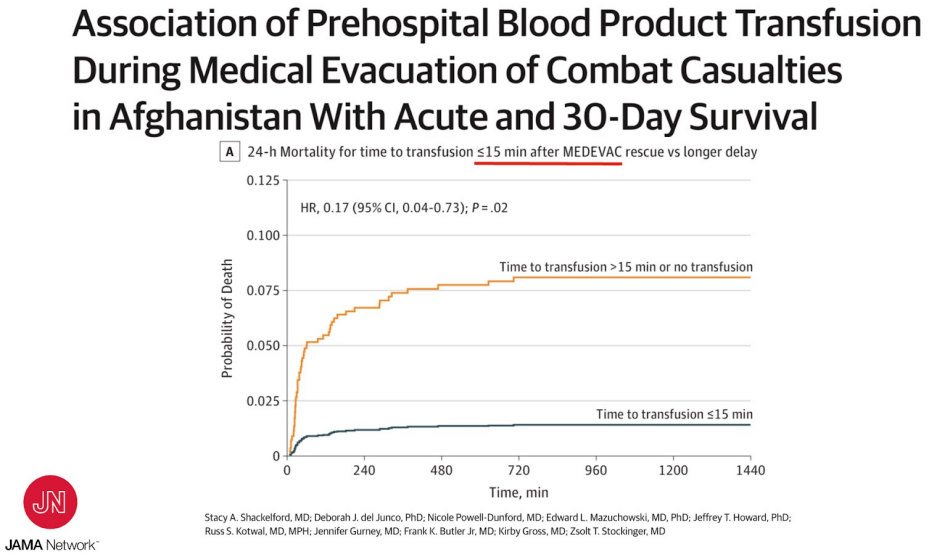
"Blood should be replaced with blood": A whole-blood transfusion strategy for massive trauma

Part 3: Replacing blood with blood

Advancement of WBT on the battlefield

- Within all combat deaths from 2001–2011, the vast majority (~87%) occurring before the casualty arrived at a Role 2 facility.
- Of those, most (75%) were injured so catastrophically, that they were deemed by the Armed Forces Medical Examiner Service to be "not survivable."
- Of the remaining 25%, deemed potentially survivable, 90% of them died from hemorrhage.





Part 3: Replacing blood with blood

USMC Valkyrie Program at Camp Pendleton, CA

- November 2017: 2nd Battalion 5th Marine Regiment 1st Marine Division
- An opportunity for general duty corpsman to be trained in whole blood transfusion

Valkyrie: The training

- 1 instructional day
- Bulk of the training is practical applications with live blood involved
- 3 “dry runs” followed by 2 “wet runs”

  The donor is the patient in the scenario (self-transfusion)
- TCCC (ATLS) is employed with each scenario timed from point of injury
- Applicant also trained on selecting ideal donor from donor cards (pre-screened)
- Use of field kits that can be set up in a variety of locations

Marines.mil

Part 3: Replacing blood with blood

Review > Injury. 2021 Feb;52(2):182-188. doi: 10.1016/j.injury.2020.10.095. Epub 2020 Oct 31.

Effectiveness and safety of whole blood compared to balanced blood components in resuscitation of hemorrhaging trauma patients – A systematic review

Michael Malkin [1], Andrey Nevo [2], Susan I Brundage [3], Martin Schreiber [4]

Affiliations + expand

PMID: 33160609 DOI: 10.1016/j.injury.2020.10.095

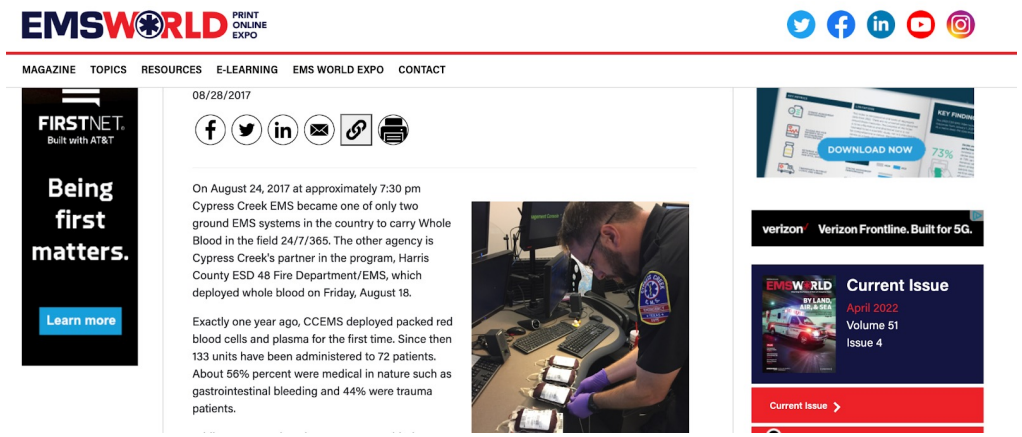
Abstract

Introduction: Hemorrhage is a leading cause of death among trauma patients, and is the most common cause of preventable death after trauma. Since the advent of blood component fractioning, most patients receive blood components rather than whole blood (WB). WB contains all of the individual blood components and has the advantages of simplifying resuscitation logistics, providing physiological ratios of components, reducing preservative volumes and allowing transfusion of younger red blood cells (RBC). Successful experience with fresh whole blood (FWB) by the US military is well documented. In the civilian setting, transfusion of cold-stored low titer type O whole blood (LTOWB) was shown to be safe. Reports of WB are limited by small numbers and low transfusion volumes.

Whole blood in civilian trauma

- First known analysis of large volume WB transfusion in civilian trauma patients was in July 2020: In 42 patients there were 0 transfusion reactions compared to component blood
- Effects on end organ function not well known, and not proven to have better mortality/ Noninferiority study
- As long as blood is low titer, could be cold stored and un-crossmatched with no transfusion reactions.

Part 3: Replacing blood with blood



https://www.jems.com/patient-care/whole-blood-in-ems-may-save-lives/

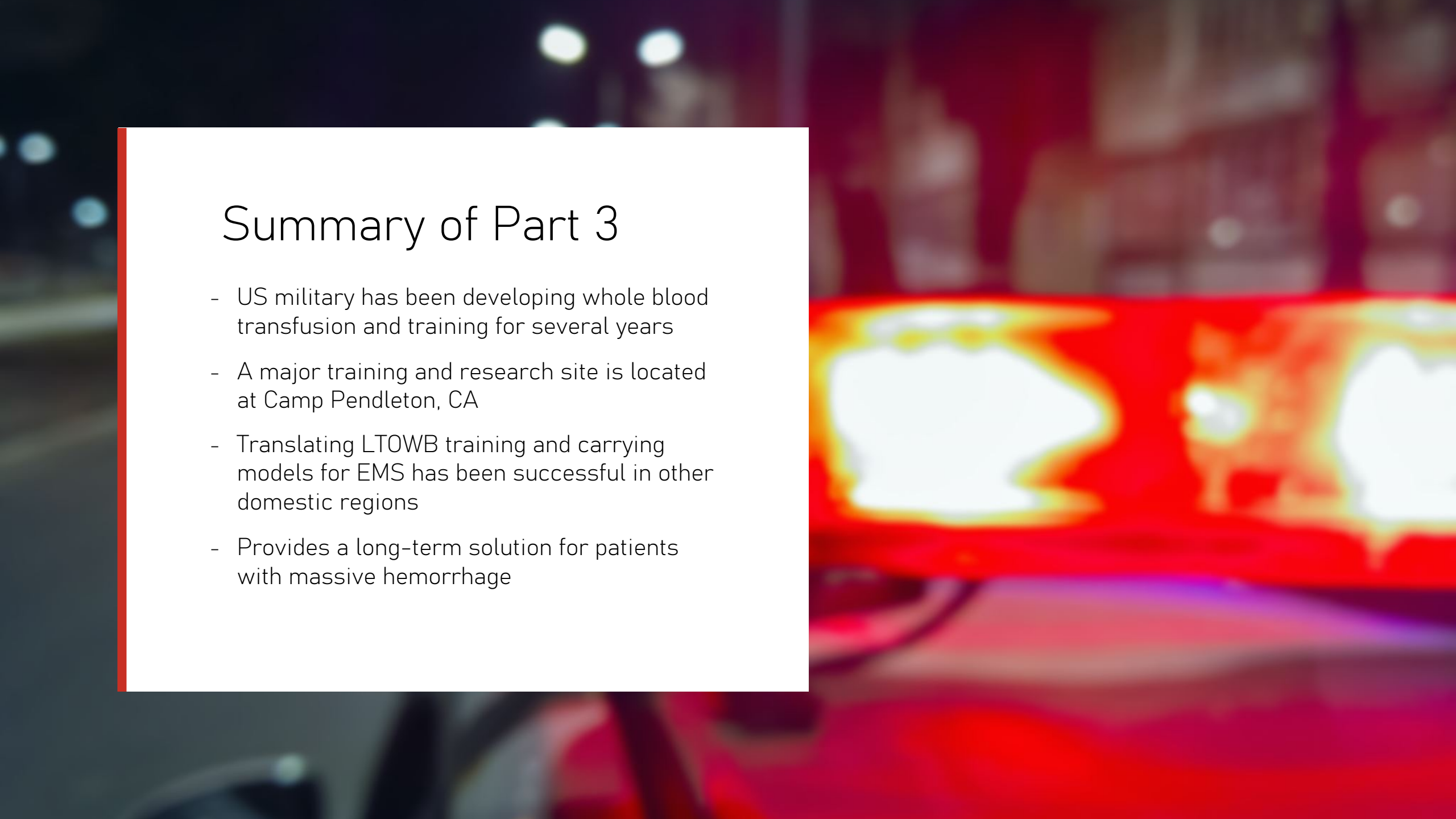
Civilian EMS: Whole blood storage and training

<u>Three options for using LTOWB:</u>

The first option is to draw a unit of FWB from a prescreened low titer donor at the POI.

The second option is collecting whole blood from low titer donors the day before a mission, (stored at 33.8—42.8F, then carrying it on the mission)

The third option is to ship the FDA-licensed cold-stored LTOWB from ASBP Donation Centers to field site← *most feasible for civilian EMS providers.*



Summary of Part 3

- US military has been developing whole blood transfusion and training for several years
- A major training and research site is located at Camp Pendleton, CA
- Translating LTOWB training and carrying models for EMS has been successful in other domestic regions
- Provides a long-term solution for patients with massive hemorrhage

DISCUSSION