
THE GEORGE WASHINGTON UNIVERSITY



Unconventional Medicine in a Conventional World

Hypocalcemia and the Lethal Triad

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CCP-C, FP-C, TP-C, SO-ATP



AGENDA



- Case Review
- Definition
- Hypocalcemia
- Physiology
- SOF Initiative
- Evidence
- Protocols
- Synopsis
- Reference List
- Questions



Definition



Calcium(Ca^{++}) is a major cation for multiple physiologic functions of the body. *** WHAT DOES Ca^{++} do?***

Ca^{++} is measured in two forms:

- Total Serum: 8.2-10.5mg/dL
- Serum Ionized: 4.5-5.2mg/dL
 - 1.3-1.5mmol/L





Proposal



Hypocalcemia

Acidosis



Coagulopathy

Hypothermia



Case Review



- Location: Cooper University Hospital, Camden NJ
- Approximately 1600 EST A 21 y/o Asian female is brought to the ED via ground transport.
- G: PT is A&Ox1, supine, cool, pale and clammy, with bimanual vaginal pressure from the Resident OBGYN.
- O: PT has a spiral tear from her vagina to her uterus.
- Tx: Methergine, hemabate, mass transfusion, and Pitocin.
- Outcome: Surgical reconstruction of vaginal cavity and uterus, PT positively diagnosed with disseminated intravascular coagulopathy(DIC). Extubated 4 days post op.

- What could have gone better?



Hypocalcemia-Clinical Presentation

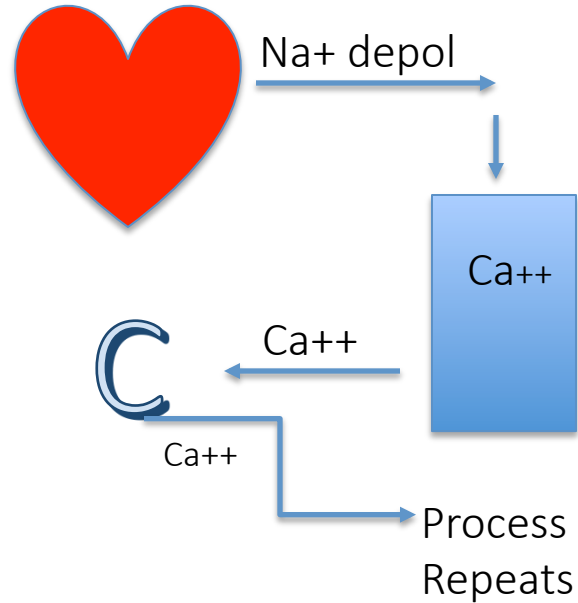


Serum Ionized Calcium <4.5mg/dL

Acute Signs/Symptoms	Chronic Signs/Symptoms
Trousseau's Sign	Dementia
Chvostek's Sign	Dry Skin
Perioral Paresthesia	Abnormal dentition
Fatigue	Parkinsonism
Prolonged QT interval	Extrapyramidal Signs
Seizures	



Traumatic Hypocalcemia



Acidosis

Coagulopathy

Hypothermia

$$DO_2 = CaO_2 \times CO$$



Traumatic Hypocalcemia



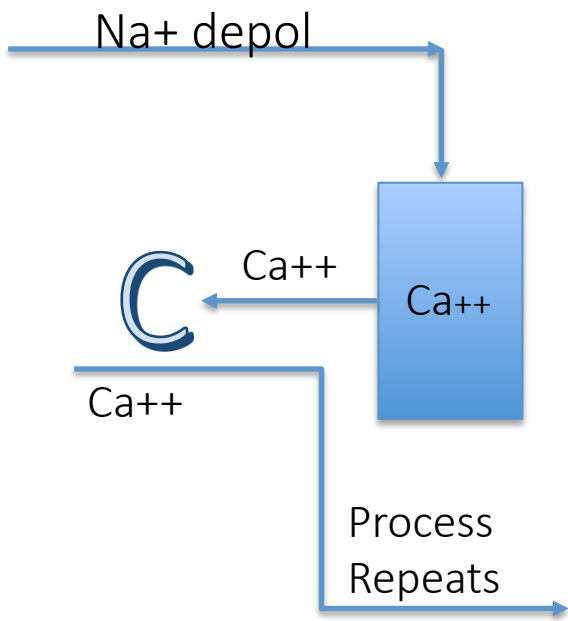
$$DO_2 = CaO_2 \times HR \times SV$$

$$(SpO_2 \times 1.34 \times [HGB]) + (0.0003 \times PaO_2)$$

CO



Traumatic Hypocalcemia



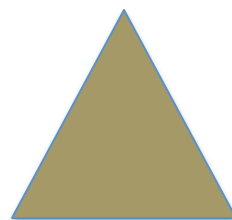
$$Do2 = CO \times SAO2 \times HGB \times 1.34$$



Traumatic Hypocalcemia



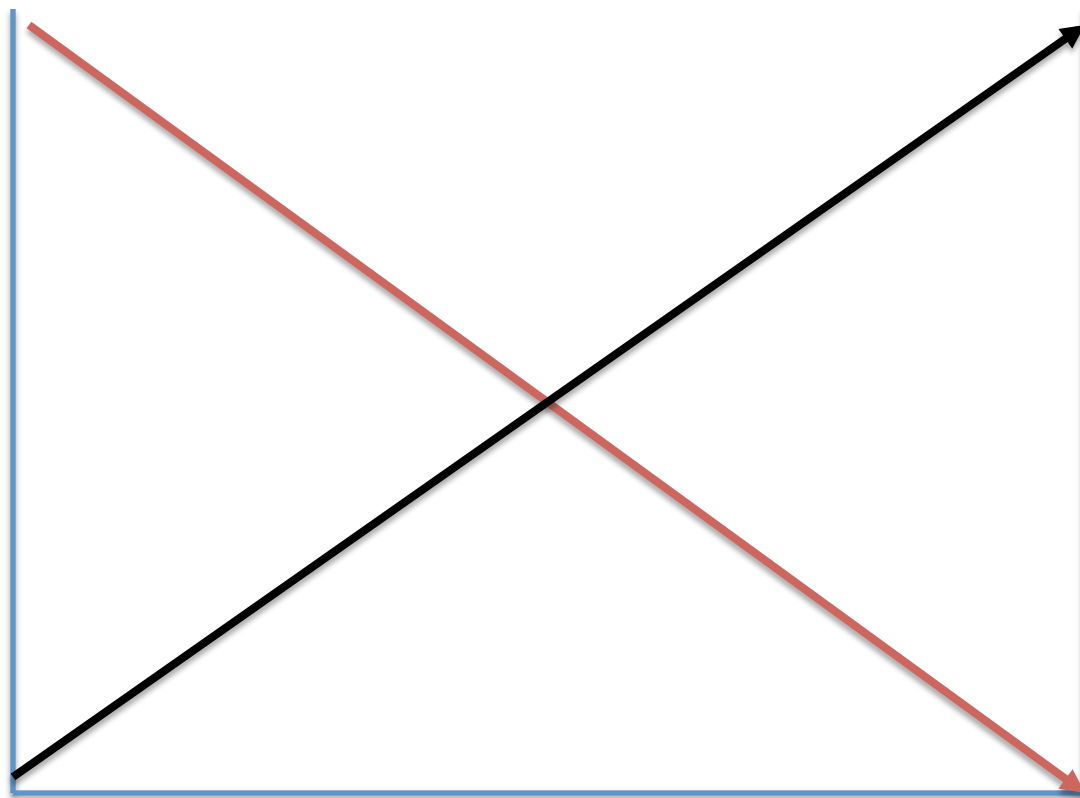
100Kg M	Class I	Class II	Class III	Class IV
Blood Loss(mL)	Up to 750	750-1500	1500-2000	>2000
Blood Loss(dL)	Up to 7.5	7.5-15	15-20	>20
Ca++ Loss (mg)	0-75	75-150	150-200	>200



Coagulopathy



Traumatic Hypocalcemia



Protein

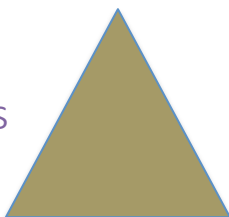
Bound Ca⁺⁺ mg/dL

7 7.1 7.2 7.3 7.4 7.5 7.6 7.7

Free Ionized

Ca⁺⁺ mmo/L

Acidosis



K. Ho 2016

UNCLASSIFIED

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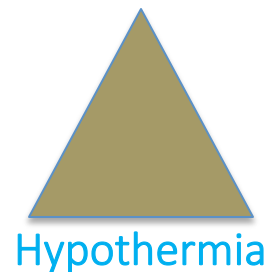


Traumatic Hypocalcemia



- Citrate is metabolized in the liver
- Citrate in blood bags insignificant in a healthy liver
- Hemorrhage leads to hypothermia and decreased iC++

Hypothermia + Liver = Decreased Citrate Metabolism





Traumatic Hypocalcemia



“You can’t
punk
physiology”

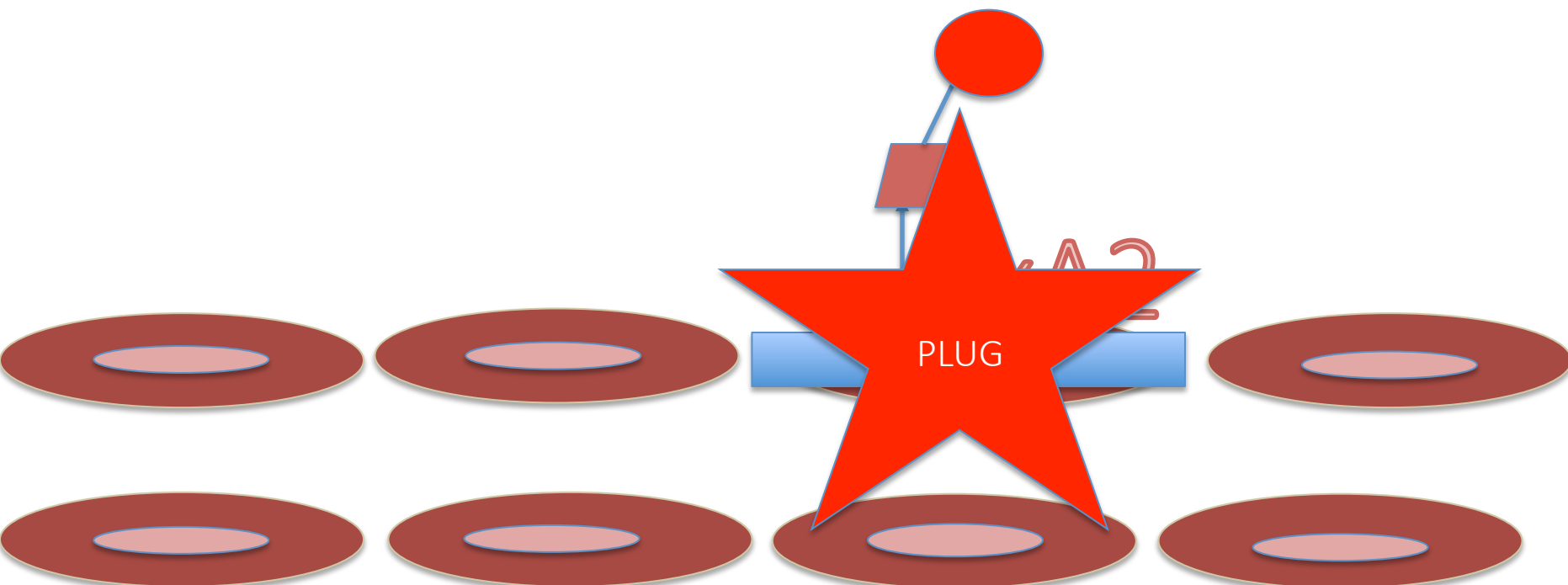
Anonymous



Physiology-Platelette Plug



So what happens when there is an insult to the endothelium?

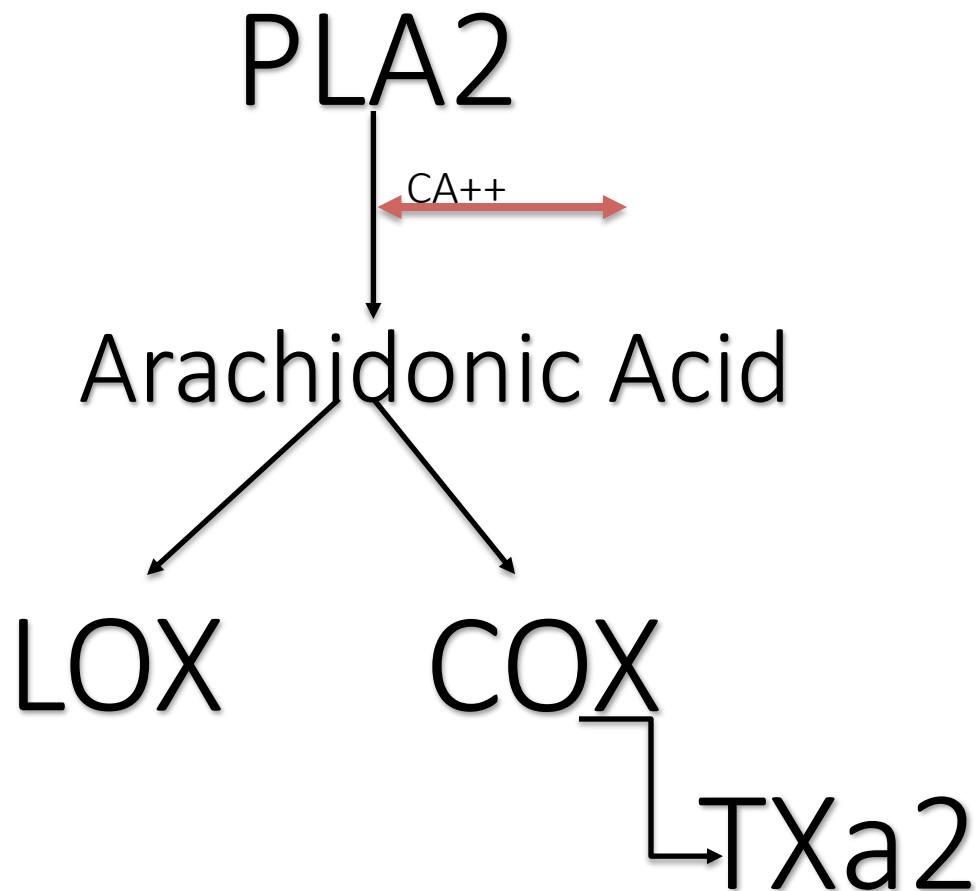




Physiology-Platelette Plug

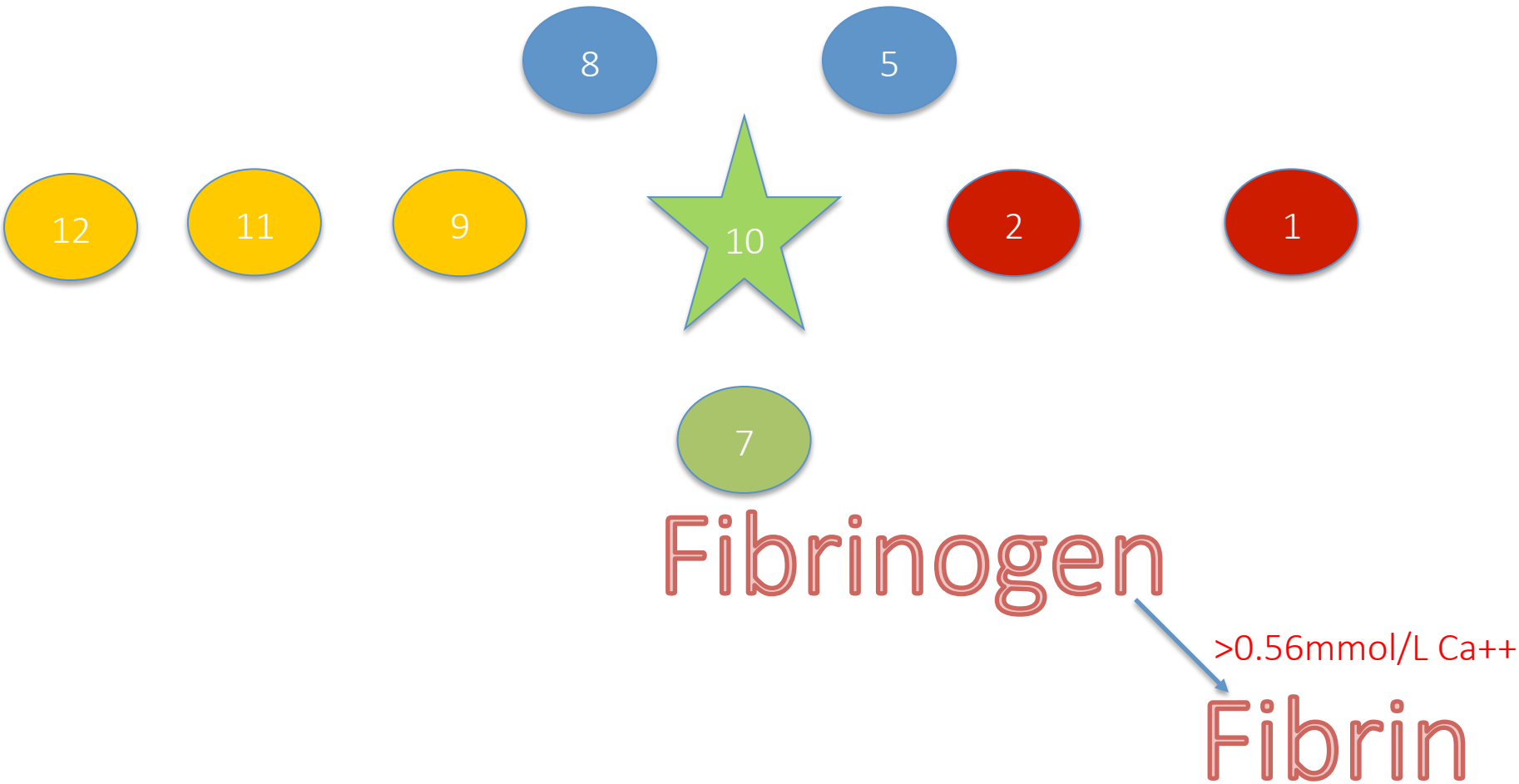


What was the role of calcium in this process?





Physiology-Clotting Cascade





SOF INITIATIVE



“There hasn’t been a new idea since 1776.”

LTC Theodore Redman



SOF INITIATIVE-SOMA 2017



WB Questions?

Hypotensive resuscitation = hemostatic procedure, not optimal treatment

- How long can you go hypotensive with WB (or components)?
- How high can you bring BP without popping clot?

Hemostatic performance limits of stored WB

- CPD to 21d vs. CPDA to 35d vs. components
- WFWB added to stored: optimal ratio (3:1, 4:1, components?)
- Leukoreduction, pathogen reduction, etc. effects?
- New storage solution?
- Better warmers?

LTOWB

- Best titer methodology vs. antibody removal?

Prolonged Field Care

- Can you "stretch" WB with albumin, fibrinogen, PCC?



EVIDENCE



“Ionized calcium levels in major trauma patients who received blood en-route to a military medical treatment facility”

Who: Royal British Military provided a retrospective study.

What: Compare the evidence of hypocalcemia in patients receiving blood transfusions.

When: Jan 2010-Dec 2014

How: 297 SM requiring blood transfusion were divided into a treatment group and non treatment group.

Results: Non-treatment group(166) 70% were hypocalcemic compared to the treatment group 28.3% were hypocalcemic.

Suggestions: 1 unit drops iCa^{++} to ~ 1.12 mmo/L

2 units drops iCa^{++} to < 1.0 mmo/L

5 units drops iCa^{++} to $< .8$ mmo/L

Kyle et al., 2017



EVIDENCE



“Concentration-dependent effect of hypocalcemia on mortality of patients with critical bleeding requiring massive transfusion: a cohort study”

Who: Western Australia University

What: Compare the sensitivity of concentrations to mortality.

How: 352 patients requiring mass blood transfusions from traumatic hemorrhage.

Results: Hypocalcemia was the most critical variable in determining mortality than fibrinogen, or acidosis levels. Determined that there is a **linear** concentration dependent relationship to mortality.



EVIDENCE-A Common Denominator

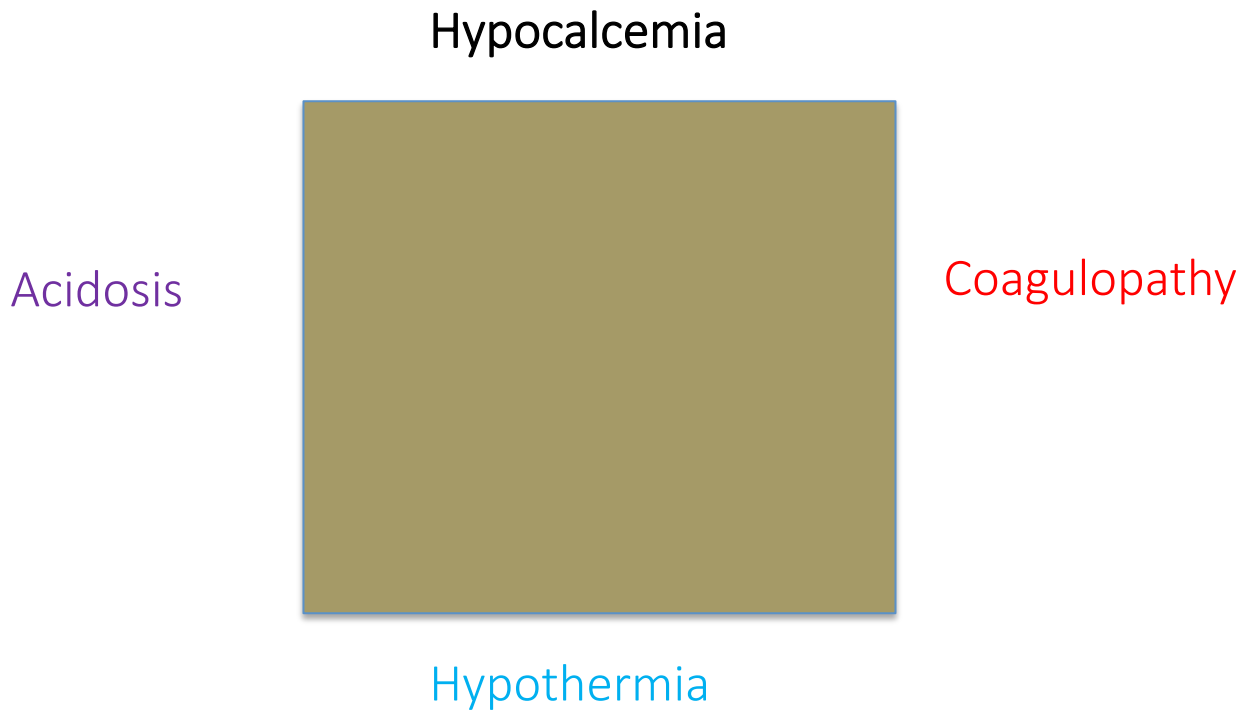


Research

Conclusions



Proposal





Current Protocol-DCR



Transfusion Criteria

- Two or more distal amputations or,
- One proximal amputation, or,
- Non-Compressible hemorrhage with signs of shock (SBP <100mmHg, and/or HR>100bpm).
- Controlled hemorrhage with signs of shock.
- Traumatic arrest within 5 minutes of loss of vital signs.



Current Protocol



TMEPS

Mild Toxicity- Slow or stop transfusion until symptoms subside. Ensure proper mixture and concentration of citrate.

Severe Toxicity- Give 0.45 mEq elemental calcium or approximately 1ml of a 10% Calcium Gluconate(100mg/ml) for each 100mL citrated blood infused. Infuse over 10-20min for each 1 to 2gm of calcium gluconate. Diluted prior to administration (D5w or NS 100-250mL)

C-TECC Guidelines

Administer appropriate IV Fluid bolus (500cc NS/LR) and re-assess casualty. Repeat bolus once after 30 minutes if still in shock.

If Blood products are available, consider resuscitation with plasma(FFP) and packed red blood cells(PRBCs) in a 1:1 ratio.



Proposed Protocol-DCR



Best

1. Obtain IV/IO access x2
2. Start infusion of LTOWB/FDP/pRBC through one line w/ fluid warmer attached.
3. Infuse 1G calcium chloride/gluconate in 100mL bag of NS bolus.
4. After infusion of calcium, flush line, infuse 1G TXA over 1-2min IV push.



Proposed Protocol-DCR



No blood/products

1. Obtain IV/IO access x2
2. Infuse 1G calcium Chloride/Gluconate in 100mL bag of NS bolus w/ fluid warmer.
3. Infuse 1G TXA IV push over 1-2min



Synopsis



- Ionized calcium is a critical electrolyte for multiple physiologic functions throughout the body.
- Hypocalcemia is directly related to the patients outcome.
- Early treatment of hypocalcemia independent from citrate toxicity can decrease mortality rates.
- Identification and treatment should take place in the platinum minutes.
- Further research is needed to be conducted in this field to determine the perfect treatment plan.



Synopsis



School of Medicine & Health Sciences

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Reference List



1. CoTCCC. *Tactical Combat Casualty Care Guidelines 28 August 2017*. 2017
2. Faudree, Kyle, et al. *160th SOAR(A) Medic Handbook 14 August 2013*. 2013
3. Goyal A, Bhimji SS. Hypocalcemia. [Updated 2017 Apr 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2017 Jun-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK430912/>
4. Ho, K. M., & Yip, C. B. (2016). Concentration-dependent effect of hypocalcaemia on in vitro clot strength in patients at risk of bleeding: a retrospective cohort study. *Transfusion Medicine*, 26(1), 57-62. doi:10.1111/tme.12272
5. Hofer AM, Brown EM. Extracellular calcium sensing and signalling. *Nat Rev Mol Cell Biol*. 2003 Jul. 4(7): 530-8.
6. Kyle, T., Greaves, I., Beynon, A., Whittaker, V., Brewer, M., & Smith, J. (2017). Ionised calcium levels in major trauma patients who received blood en route to a military medical treatment facility. *Emergency Medicine Journal*. doi:10.1136/emered-2017-206717



Reference List



7. Lier, H., Krep, H., Schroeder, S., & Stuber, F. (2008). Preconditions of Hemostasis in Trauma: A Review. The Influence of Acidosis, Hypocalcemia, Anemia, and Hypothermia on Functional Hemostasis in Trauma. *The Journal of Trauma: Injury, Infection, and Critical Care*, 65(4), 951-960. doi:10.1097/ta.0b013e318187e15b
8. Marks, A. R. (2003). Calcium and the heart: a question of life and death. *Journal of Clinical Investigation*, 111(5), 597–600. <http://doi.org/10.1172/JCI200318067>
9. Author(s): Marilyn Augustine Mara J. Horwitz. (2017, May 11). Hypocalcemia. Retrieved December 10, 2017, from <http://www.mdedge.com/jfponline/dsm/7332/endocrinology/hypocalcemia>
10. Morrison, J. J., Ross, J. D., Poon, H., Midwinter, M. J., & Jansen, J. O. (2013). Intra-operative correction of acidosis, coagulopathy and hypothermia in combat casualties with severe haemorrhagic shock. *Anaesthesia*, 68(8), 846-850. doi:10.1111/anae.12316



Reference List



11. Murros, J., & Luomanmäki, K. (2009). A Case of Hypocalcemia, Heart Failure and Exceptional Repolarization Disturbances. *Acta Medica Scandinavica*, 208(1-6), 133-136. doi:10.1111/j.0954-6820.1980.tb01166.x
12. Author(s): Marilyn Augustine Mara J. Horwitz. (2017, May 11). Hypocalcemia. Retrieved December 10, 2017, from <http://www.mdedge.com/jfponline/dsm/7332/endocrinology/hypocalcemia>
13. *Tactical Medical Emergency Protocols (TMEPS) JSOM AT-P Handbook 8th ed, 2014*
14. The thrombin–fibrinogen interaction. (2004, September 17). Retrieved November 6, 2017, from <http://www.sciencedirect.com/science/article/pii/S0301462204001784>
15. Zhu, W.-Z., Wang, S.-Q., Chakir, K., Yang, D., Zhang, T., Brown, J. H., ... Xiao, R.-P. (2003). Linkage of β_1 -adrenergic stimulation to apoptotic heart cell death through protein kinase A-independent activation of Ca^{2+} /calmodulin kinase II. *Journal of Clinical Investigation*, 111(5), 617–625. <http://doi.org/10.1172/JCI200316326>



Questions?



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