Hypocalcemia and the Lethal Triad
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CCP-C, SO-ATP

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AGENDA

• Definition
• Case Review
• Hypocalcemia
• Physiology
• Evidence
• Protocols
• Synopsis
• Reference List
• Questions
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**: 8.2-10.5 mg/dL
- **Ionized Serum**: 4.5-5.2 mg/dL
  - 1.3-1.5 mmol/L

*Normal Blood Ca2+ in an healthy adult* 4.64 to 5.28 mg/dL or 1.20‐1.40 mmol/L

**LETHAL DIAMOND – the Role of Ca2+**

- Causes decreased liver metabolism of citrate.
- Citrate not metabolized in the liver binds Ca2+ leading to less available in the blood.
- Low Ca2+ levels associated with lower pH.
- Lower blood pH prolongs clot formation time.
- Ca2+ in the plasma is a necessary co-factor in the clotting cascade.
- Ca2+ drops due to blood loss.
- Transfusion exacerbates further.

**Hypocalcemia**

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**Hypothermia**

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**Acidosis**

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**Coagulopathy**

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**Hypoperfusion**

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**Lethal Diamond**

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- Ca2+ in the plasma is a necessary co-factor in the clotting cascade.
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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.
- D: 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 <1.3mmol/L

<table>
<thead>
<tr>
<th>Acute Signs/Symptoms</th>
<th>Chronic Signs/Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trousseau's Sign</td>
<td>Dementia</td>
</tr>
<tr>
<td>Chvostek's Sign</td>
<td>Dry Skin</td>
</tr>
<tr>
<td>Perioral Paresthesia</td>
<td>Abnormal dentition</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Parkinsonism</td>
</tr>
<tr>
<td>Prolonged QT interval</td>
<td>Extrapyramidal Signs</td>
</tr>
<tr>
<td>Seizures</td>
<td></td>
</tr>
</tbody>
</table>

**Traumatic Hypocalcemia**

DO2 = CaO2 x CO

DO2 = CaO2 x HR x SV

(Spo2 x 1.34 x [HGB]) + (0.0003 x PaO2)
**Traumatic Hypocalcemia**

Do2 = CO x SAO2 x HGB x 1.34

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**Traumatic Hypocalcemia**

<table>
<thead>
<tr>
<th>100mL HR</th>
<th>Class I</th>
<th>Class II</th>
<th>Class III</th>
<th>Class IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Loss(mL)</td>
<td>Up to 750</td>
<td>750-1500</td>
<td>1500-2000</td>
<td>&gt;2000</td>
</tr>
<tr>
<td>Blood Loss(dL)</td>
<td>Up to 7.5</td>
<td>7.5-15</td>
<td>15-20</td>
<td>&gt;20</td>
</tr>
<tr>
<td>Ca++ Loss (mg)</td>
<td>0-75</td>
<td>75-150</td>
<td>150-200</td>
<td>&gt;200</td>
</tr>
</tbody>
</table>

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**Traumatic Hypocalcemia**

![Graph showing the relationship between protein bound Ca++ and free ionized Ca++ with Acidosis and Coagulopathy indicated.](image)

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Hypothermia + Liver = Decreased Citrate Metabolism

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

Physiology - Platelet Plug

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

- PLA2
- Arachidonic Acid
- LOX
- COX
- TXa2
**Physiology-Clotting Cascade**

[Diagram of the physiology-clotting cascade]

**EVIDENCE**

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

Who: UK MERT 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 ~1.12mmo/L
2 units drops iCa++ to <1.0mmo/L
5 units drops iCa++ to <.8mmo/L
Kyle et al., 2017

“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.
When: January 2011
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.
Ho et al., 2016

[Additional text and diagrams related to hypocalcemia and clotting cascade]
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 Protocols**

**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 1 ml of a 10% Calcium Gluconate (100 mg/ml) for each 100 ml citrated blood infused. Infuse over 10-20 min for each 1 to 2 gm of calcium gluconate. Dilute prior to administration (D5w or NS 100-250 ml).

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**JTS CPG**

**DCR May 2018**
- Calcium (consider one 10 ml ampule of 10% calcium chloride, or 30 ml of 10% calcium gluconate) should be given to patients in shock after approximately 4 units of citrated blood products transfused. Ideally, ionized calcium should be monitored.

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**Proposed Protocol-DRC**

**Best**

1. Obtain IV/IO access x2
2. Flush IV/IO w/ 1G TXA.
3. Start infusion of LTOWB/FDP/pRBC/LP through one line w/ fluid warmer attached.
4. Administer 10 ml CaCl or 30 ml CaGlu SIVP.
5. Flush Site.

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**Proposed Protocol-DCR**

**No blood/products**

1. Obtain IV/IO access x2
2. Flush site with 1G TXA.
3. Administer 10 ml CaCl or 30 ml CaGlu SIVP.
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.

Reference List

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Questions?

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