COAGULOPATHY IN SURGERY

BY:  
DR F.DOCRAT  
MODERATOR:  
PROF PRETORIUS
DEFINITION of COAGULOPATHY

• Coagulopathy
  – Bloods ability to clot is impaired
  – Prolonged or excessive bleeding

• However for some
  – The term also covers thrombotic states
  – Due to the complexity of the hemostatic pathways
    the two conditions can exist simultaneously
COAGULOPATHY OF TRAUMA

• Haemorrhage accounts for 40% of all trauma deaths
• Control of bleeding is difficult when coagulopathy is established
• Acute coagulopathy is identified on admission
  – 1 of 4 trauma patients
  – 4 fold increase in mortality
LETHAL TRIAD OF TRAUMA

- Hypothermia
  - Decreased myocardial performance

- Coagulopathy
- Lactic acidosis

- Metabolic Acidosis
TISSUE TRAUMA

- Injury severity closely associated with the degree of coagulopathy

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- Crush injury
  - Activation of coagulation
  - Consumption of clotting factors

- Severe TBI
  - Release of brain specific thromboplastin causing consumption of clotting factors
  - Increased bleeding
• Tissue damage initiates coagulation

  – Endothelial damage in area of injury

  • Lead to exposure of subendothelial type III collagen
  • Tissue factor which bind Von Willebrand factor, platelet and activated factor 7
  • Increased fibrinolysis
SHOCK

• Prime driver of early coagulopathy
  – Direct tissue trauma
  – Systemic hypoperfusion

• Prolonged clotting times

<table>
<thead>
<tr>
<th>BASE DEFICIT</th>
<th>&lt;6MMOL/L</th>
<th>&gt;6MMOL/L</th>
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</thead>
<tbody>
<tr>
<td>% PROLONGED CLOTTING TIMES</td>
<td>2%</td>
<td>20%</td>
</tr>
<tr>
<td>Class of haemorrhagic shock</td>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-----------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Blood loss (mL)</td>
<td>Up to 750</td>
<td>750–1500</td>
</tr>
<tr>
<td>Blood loss (% blood volume)</td>
<td>Up to 15</td>
<td>15–30</td>
</tr>
<tr>
<td>Pulse rate (per minute)</td>
<td>&lt; 100</td>
<td>100–120</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Pulse pressure (mm Hg)</td>
<td>Normal or increased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Respiratory rate (per minute)</td>
<td>14–20</td>
<td>20–30</td>
</tr>
<tr>
<td>Urine output (mL/hour)</td>
<td>&gt; 30</td>
<td>20–30</td>
</tr>
<tr>
<td>Central nervous system/mental status</td>
<td>Slightly anxious</td>
<td>Mildly anxious</td>
</tr>
</tbody>
</table>
HEMODILUTION

• Direct loss of coagulation factors through haemorrhage
  – Quickly reduce body’s small stores
    • Fibrinogen (10g)
    • Platelets (15ml)
• Losses are then replaced with fluids
  – That do not contain clotting factors
  – Causing dilutional coagulopathy
HYPOTHERMIA

• Coagulation occurs because of enzyme reactions which are temperature dependent
• Rohrer et al found that aPTT

<table>
<thead>
<tr>
<th>37 Degrees</th>
<th>34 degrees</th>
<th>31 degree</th>
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<tbody>
<tr>
<td>36 seconds</td>
<td>39</td>
<td>46</td>
</tr>
</tbody>
</table>

• Decreases activation of platelets
• Stimulates fibrinolysis which provokes more diffuse bleeding.
• Hypothermia is common in an injured patient
  – Environmental exposure
  – Decreased heat production by underperfused muscle
  – Increase heat loss from exposed body cavities during surgery
  – Administration of cold IV fluids
    • Packed red cells reduce temp by 0.25 C
    • 1L of room temperature fluid reduces by 0.5C
INFLAMMATION

• Trauma is an inducer of inflammation
• Activation of inflammation lead to derangements of coagulation
• Monocytes
  – Express tissue factor
  – Adhere to platelets at the site of injury
• Alteration in coagulation pathways
  – Endothelial activation of thrombomodulin-protein C pathway
  – Competitive binding of C4b protein to protein S
ACIDEMIA

• Produced by
  – Low flow states
  – Excess ionic chloride administration during resuscitation

• Activity of coagulation factor complexes on cell surfaces are markedly reduced in acidic environment
  – Activity of FXa/Va complex reduced by
    • 50% at pH 7.2
    • 70% at pH 7.0

• Acidemia
  – Leads to increased degradation of fibrinogen
  – Impairs function of plasma proteases
  – Can be corrected by administration of buffer solutions
    • This does not correct coagulopathy
UNDERLYING DISEASE

• Trauma not restricted to healthy people
• Underlying coagulation defects
  – Von Willebrand disease
• Patients on oral anticoagulants
• Liver disease
  – Thrombopoietin and hemostatic proteins are synthesised in liver
  – Decreased hepatic function results in prolongation of coagulation
  – Reduced amounts of vit K dependent coagulation factors II, VII, IX and X
  – Inhibit platelet aggregation.
• Renal disease
  – Uremic bleeding due to impaired platelet function
DISSEMINATED INTRAVASCULAR COAGULOPATHY
CAUSES OF DIC

- Sepsis
- Trauma
- Cancer
- Obstetric complications
- Vascular disorders
- Reaction to toxins
- Immunologic disorders
1. Risk assessment
   Does the patient have an underlying disorder known to be associated with DIC?
   If yes: proceed; If no: do not use this algorithm
2. Order the global coagulation test
   Platelet count, PT, fibrinogen, soluble fibrin monomers, or FDP
3. Global coagulation test scores
   Platelet count ($>100=0; <100=1; <50=2$)
   Elevated fibrin-related markers (no increase: 0; moderate increase: 2; strong increase: 3)
   Prolonged prothrombin time ($<3 s=0; >3$ but $<6 s=1; >6 s=2$)
   Fibrinogen level ($>1.0 \text{ g/L}=0; <1.0 \text{ g/L}=1$)
4. Calculate score
   If $\geq 5$: compatible with overt DIC; repeat scoring daily
   If $<5$: suggestive (not affirmative) for non-overt DIC; repeat in the next 1–2 days
COAGULOPATHY OF SEPSIS

• Ranges from mild lab alterations to severe DIC
• Coagulation abnormalities causes by
  – Consumption of platelets and coagulation factors
  – Thrombin generation via TF/FVIIa route
  – Depression of antithrombin and protein C anticoagulant systems
  – Impaired fibrin degradation
Homeostasis Is Lost In Sepsis

- Proinflammatory mediators
- Endothelial injury
- Tissue factor expression
- Thrombin production

↑ Coagulation  ↑ Inflammation

↓ Fibrinolysis

- Increased PAI-1
- Increased TAFI
- Reduced Protein C (Activated Protein C inhibits PAI-1)

Source: Adv Neonatal Care © 2004 W. B. Saunders
HIV COAGULOPATHY

- HIV prothrombotic condition
  - Protein S and C deficiency
- HIV patients are prone to sepsis
  - Hypercoaguable
  - Progress to DIC
- HIV related thrombocytopenia
  - Bone marrow failure
  - Immunological disorder
Figure 1: Multi-factorial etiology of HIV-related venous thromboembolism. AT, antithrombin; sTM, soluble thrombomodulin; TFPI, tissue factor pathway inhibitor; v-WF, von Willebrand Factor; PAI-1, plasminogen activator inhibitor-1; tPA, tissue plasminogen activator. Stronger risk factors for VTE are listed in bold.
LABORATORY TEST

- Platelet count
- Hematocrit
- INR
- Prothrombin time
- Activated partial thromboplastin time
- Fibrinogen
- Test for more complex situations
  - Thromboelastography
  - Platelet function analysis
  - Rotec
<table>
<thead>
<tr>
<th>Condition</th>
<th>Prothrombin Time</th>
<th>Activated Partial-Thromboplastin Time</th>
<th>Fibrinogen Level</th>
<th>D-Dimer Level</th>
<th>Bleeding Time</th>
<th>Platelet Count</th>
<th>Findings on Blood Smear</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin K deficiency or use of vitamin K antagonist</td>
<td>Prolonged</td>
<td>Normal or mildly prolonged</td>
<td>Normal</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
</tr>
<tr>
<td>Aspirin or thienopyridines</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Prolonged</td>
<td>Unaffected</td>
<td>Unaffected</td>
</tr>
<tr>
<td>Liver failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Early stage</td>
<td>Prolonged</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
</tr>
<tr>
<td>End stage</td>
<td>Prolonged</td>
<td>Prolonged</td>
<td>Low</td>
<td>Increased</td>
<td>Prolonged</td>
<td>Decreased</td>
<td></td>
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<tr>
<td>Uremia</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Prolonged</td>
<td>Unaffected</td>
<td></td>
</tr>
<tr>
<td>Disseminated intravascular coagulation</td>
<td>Prolonged</td>
<td>Prolonged</td>
<td>Low</td>
<td>Increased</td>
<td>Prolonged</td>
<td>Decreased</td>
<td>Fragmented red cells</td>
</tr>
<tr>
<td>Thrombotic thrombocytopenic purpura</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Unaffected</td>
<td>Prolonged</td>
<td>Very low</td>
<td>Fragmented red cells</td>
</tr>
<tr>
<td>Hyperfibrinolysis</td>
<td>Prolonged</td>
<td>Prolonged</td>
<td>Low</td>
<td>Very high</td>
<td>Possibly prolonged</td>
<td>Unaffected</td>
<td></td>
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</table>
TEG

- Unique lab test that examines whole blood thrombus formation and lysis
- Measures 5 parameters
  - **R time:**
    - time from start to clot formation
    - correlated with coagulation factor activity
  - **K time:**
    - time from tracing going from 2mm to 20mm
    - correlated with speed of clot formation
  - **Alpha angle:**
    - slope of tracing between r and K time
    - correlated with fibrin formation
  - **MA:**
    - greatest amplitude of TEG tracing
    - a marker of platelet function
  - **Whole blood lysis:**
    - amplitude of tracing 60min after MA
Figure 4. Thromboeslastograph (TEG) tracing. The reaction time (R) represents the time to onset of clot formation. K time is a measure of the speed to reach a certain level of clot strength. The angle represents the rate of clot formation. The maximum amplitude (MA) measures the clot strength. Reprinted with permission from Kiraly, J Trauma 2006;61:57–64.
KEEP CALM AND LEARN HOW TO STOP THE BLEEDING
TREATMENT

• Recombinant factor VIIa
• Trauma exsanguination protocol
• Damage control resuscitation
• TEG to guide transfusion
• Tranexamic acid
  – Antifibrinolytic
  – Inhibits activation of plasminogen to plasmin
RECOMBINANT FACTOR VIIa

• Binds directly to surface of activated platelets
• Enhances
  – Thrombin generation
  – Fibrin clot formation
  – Producing a stable clot
• Boffard et al

<table>
<thead>
<tr>
<th></th>
<th>BLUNT</th>
<th>PENETRATING</th>
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<tbody>
<tr>
<td>NUMBER</td>
<td>143</td>
<td>134</td>
</tr>
<tr>
<td>PLACEBO</td>
<td>74</td>
<td>64</td>
</tr>
<tr>
<td>rVIIa</td>
<td>69</td>
<td>70</td>
</tr>
<tr>
<td>REDUCTION rbc UNIT</td>
<td>2.6UNIT</td>
<td>1UNIT</td>
</tr>
<tr>
<td>REDUCTION MASSIVE TRANSFUSION</td>
<td>REDUCED BY 33%</td>
<td>REDUCED BY 19%</td>
</tr>
</tbody>
</table>
TRAUMA EXSANGUINATION PROTOCOL

• Cotton et al implemented the TEP
  – 10U of PRBC
  – 4U of FFP
  – 2U of platelets

• 74% reduction in the odds of mortality
THE “BLOODY VICIOUS CYCLE”

• Injurity severity score > 25
• pH<7.10 + systolic BP<70
• Core temperature <34C

Cosgriff et al

WHEN ALL 4 PRESENT: INCIDENCE OF COAGULOPATHY = 98%
DAMAGE CONTROL

• Damage control surgery
  – Early control of the cause of bleeding
  – Temporary non definitive means

• Damage control resuscitation
  – Limiting fluid resuscitation
  – Concept of permissive hypotension
  – Goal of achieving palpable radius pulse
Management of the major coagulopathy with onset during laparotomy.

H H Stone, P R Strom, and R J Mullins


One of the most frustrating situations ever encountered by the operating surgeon is an open wound in a patient whose blood will not clot and cannot be made to clot. By far the most extreme example is a bleeding diathesis complicating laparotomy. This event is an all-too-common occurrence in the patient who has sustained a major intraabdominal injury or who has a disease process or operation which has been attended by a massive hemorrhage. The coagulopathy can seldom be reversed satisfactorily. Thus, the usual outcome is continued bleeding and thereby death through exsanguination.
• Stage 1- Patient selection
  • Metabolic acidosis
  • Hypothermia coagulopathy

• Stage 2- Hemorrhage control
  • Bleeding vessels-ligate, shunt, repair
  • Bleeding areas-pressure

• Stage 3- Resuscitation in ICU
  • Maximisation of hemodynamics
  • Core rewarming
  • Ventilation support
  • Identification of other injuries
  • PITFALL!!!!ABDOMINAL COMPARTMENT SYNDROME

• Stage 4- Return to theatre
CELL SAVER

- Recovery of blood lost during surgery
- Reinfusing it into the patient
- Advantages
  - Reduced use of blood bank
  - No risk of ABO incompatibility
  - No increased risk of infectious complication
  - No transfusion reactions
- The Association of Anaesthetist of Great Britain and Ireland issued guidelines for the use of intraoperative CS
  - Estimated loss of bloods 1000 ml/>20% blood volume
  - Low initial HB
  - Patients with unusual antibodies or blood types
  - Patients who decline transfusion of allogenic blood
Serious Hazards of Transfusion

- Incorrect blood/component transfused (66.2%)
- Transfusion-transmitted injury (2.1%)
- Graft-vs-host disease (0.6%)
- Acute transfusion reaction (11.5%)
- Delayed transfusion reaction (10.4%)
- Acute lung injury (6.8%)
- Posttransfusion purpura (2%)

N = 2191

Solomon et al conducted a study in Pietermaritzburg

Fig. 2. Blood units available after processing – per case.
Fig. 3. Cases resulting in transfusion – by discipline (O&G = obstetrics and gynaecology).
I see a trauma center in your future.
HYPERCOAGULABLE STATE

- Within 24-36 hours post trauma
  - Surgical stress response
  - Thromboplastin release

<table>
<thead>
<tr>
<th>Hospitalized patients</th>
<th>DVT risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical patients</td>
<td>10–20</td>
</tr>
<tr>
<td>General surgery</td>
<td>15–40</td>
</tr>
<tr>
<td>Stroke</td>
<td>20–50</td>
</tr>
<tr>
<td>Hip or knee arthroplasty, hip fracture surgery</td>
<td>40–60</td>
</tr>
<tr>
<td>Major trauma</td>
<td>40–80</td>
</tr>
<tr>
<td>Critical care patients</td>
<td>10–80</td>
</tr>
</tbody>
</table>

DVT: deep venous thrombosis.
ICU

<table>
<thead>
<tr>
<th>FACTORS BEFORE ICU ADMISSION</th>
<th>FACTORS ACQUIRED IN ICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent surgery</td>
<td>Central venous lines</td>
</tr>
<tr>
<td>Trauma, burns</td>
<td>sepsis</td>
</tr>
<tr>
<td>sepsis</td>
<td>Sedation and paralysis</td>
</tr>
<tr>
<td>Immobilization, spinal cord injury</td>
<td>Mechanical ventilation</td>
</tr>
<tr>
<td>malignancy</td>
<td></td>
</tr>
<tr>
<td>Increasing age</td>
<td></td>
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<tr>
<td>immobization</td>
<td></td>
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<tr>
<td>Previous dvt or pe</td>
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<tr>
<td>pregnancy</td>
<td></td>
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<tr>
<td>NONPHARMACOLOGIC</td>
<td>PHARMACOLOGIC</td>
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<tr>
<td>----------------------------------------</td>
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<tr>
<td>Intermittent pneumatic compression</td>
<td>Unfractionated heparin</td>
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<tr>
<td>Elastic Stockings</td>
<td>Low molecular weight heparin</td>
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<tr>
<td>IVC filter</td>
<td>Oral anticoagulants</td>
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REFERENCES


