

Standard Lab Test Targets

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Inspired Care. Inspiring Science.

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- No relevant financial conflicts of interest

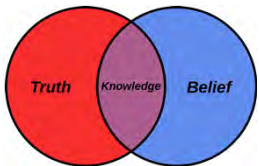
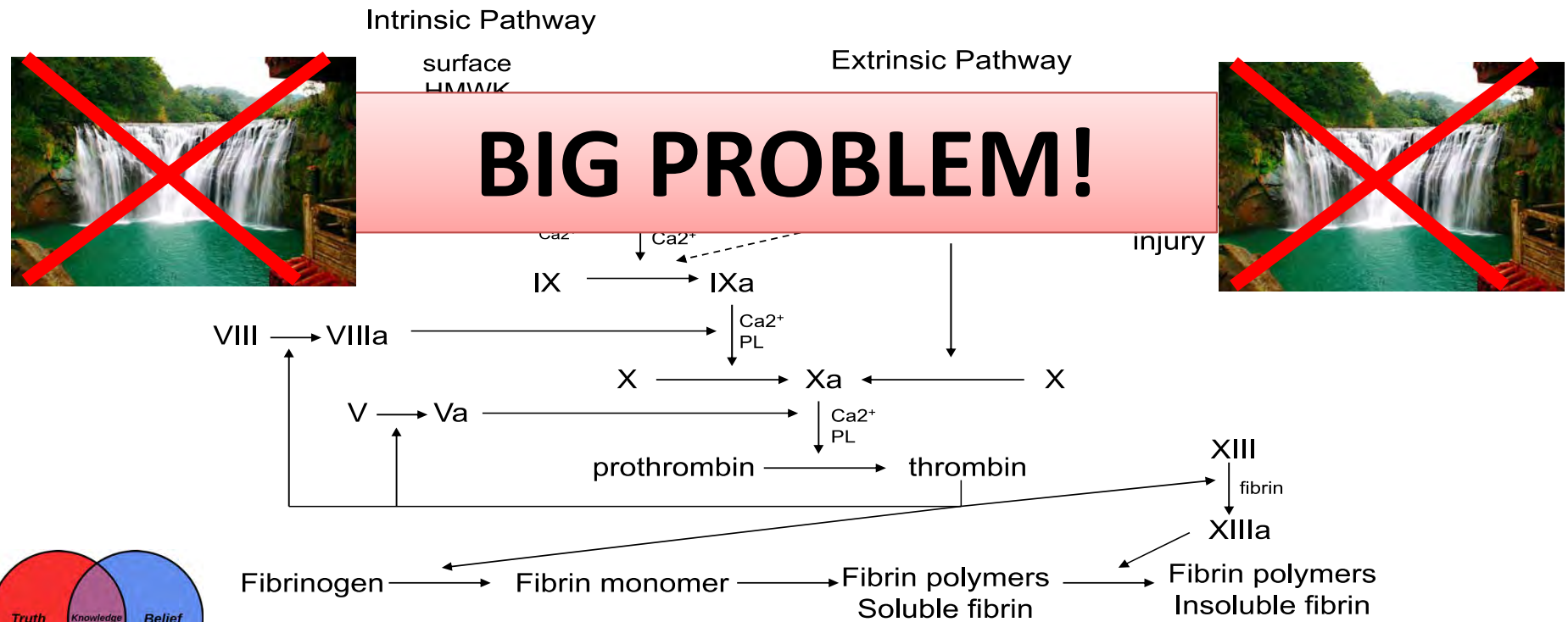


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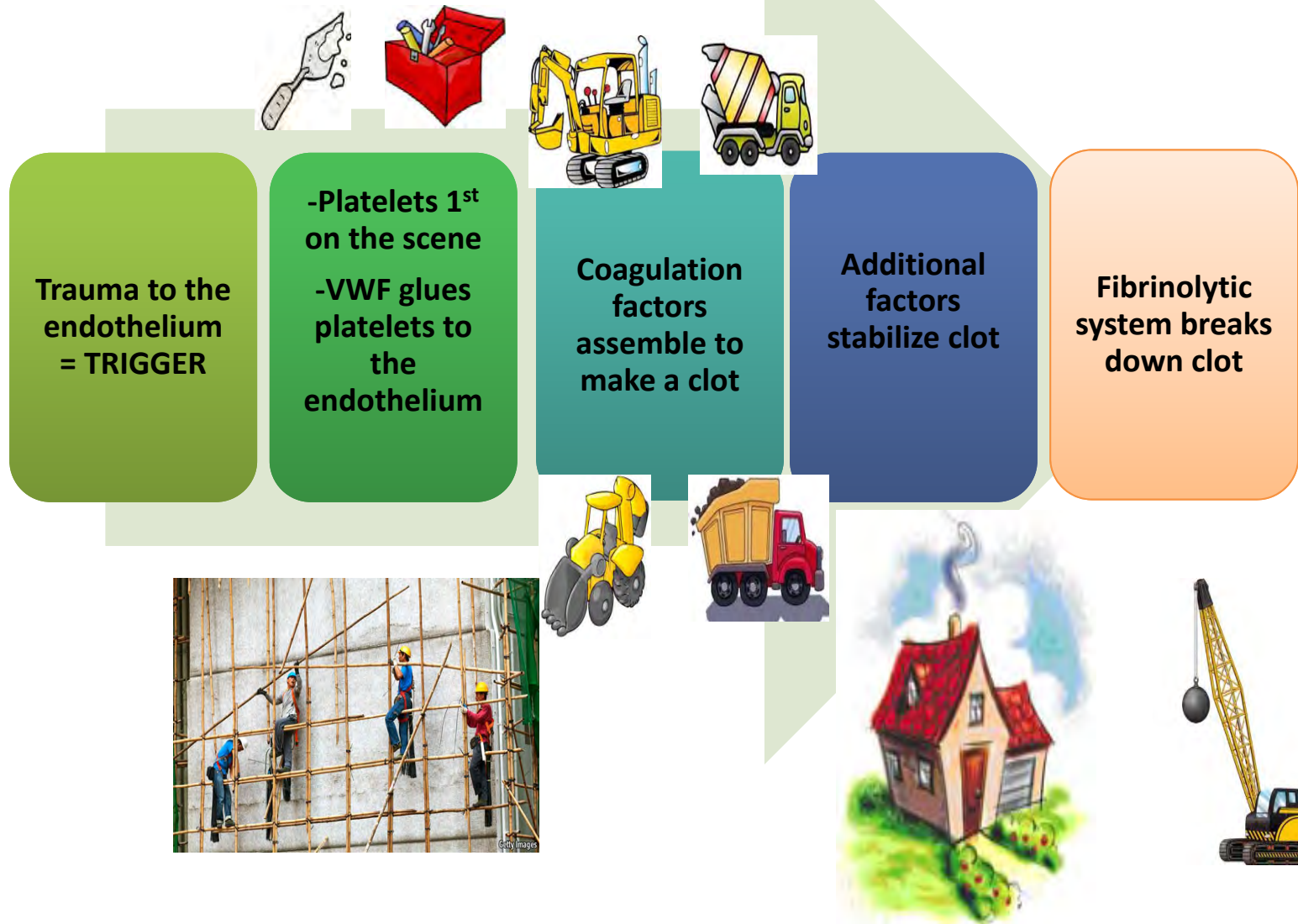
Objectives

- Brief review of hemostasis
- Brief review of acute coagulopathy of trauma
- Review of testing limitations for standard lab tests
- Review lab triggers for transfusion of RBCs and components in setting of MH

Updated Coagulation Cascade

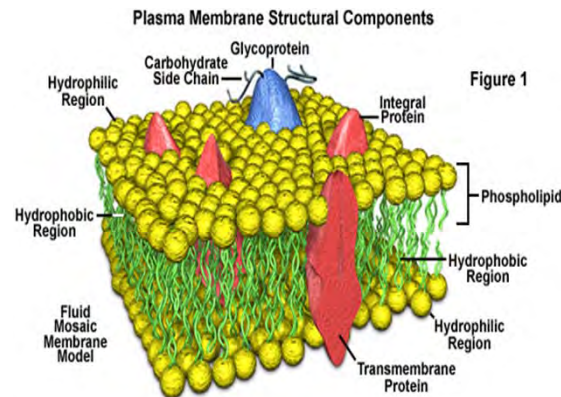


Hemostasis Simplified



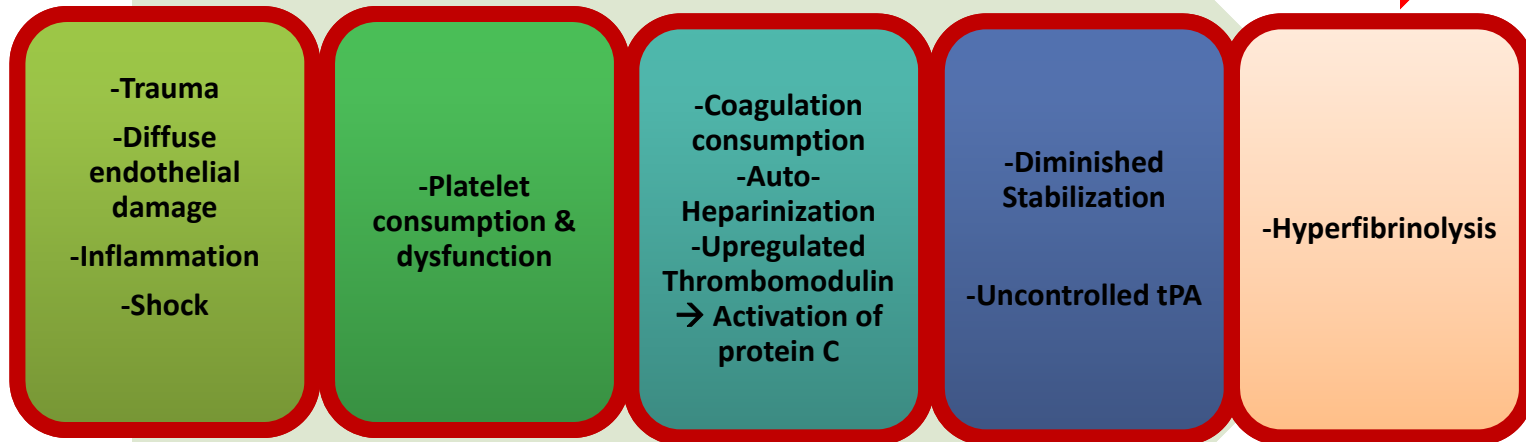
Coagulation is Localized to the Cellular Surface

- Occurs on membranes with exposed phospholipids
 - Phosphatidyl serine
 - Phosphatidyl ethanolamine
- Exposed phospholipids are not found on resting cells



Hoffman, M. & Monroe, D.M. *Thrombosis and haemostasis* **85**, 958-965 (2001).

Coagulopathy of Trauma Simplified



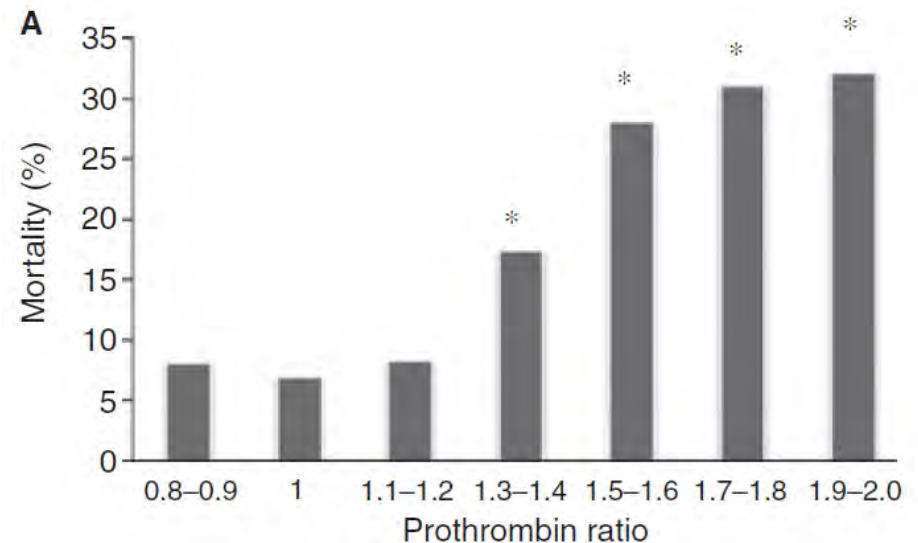
Acute Coagulopathy of Trauma is Bad

Retrospective cohort study of 1088 trauma patients

- Coagulopathy defined as: PT>18 s, aPTT>60 s, or TT>15 s
 - 24% met this definition on arrival before resuscitation
 - 46% mortality rate with coagulopathy vs. 11% mortality rate without (p<0.001)

Retrospective cohort study of 3646 trauma patients

- Those with a prothrombin time ratio (PTr) > 1.2 had higher mortality and transfusion requirements than patients with a normal PTr
 - Mortality: 22.7% vs. 7.0% (p< 0.001)
 - Packed red blood cells: 3.5 vs. 1.2 units (p< 0.001)



What is the role of the Hematology (Routine & Coagulation) Lab in a MHP?

- For effective management, it is necessary to understand *why* the patient is currently bleeding
- Is the bleeding **coagulopathic** or **surgical** in nature?
- If the patient has coagulopathic bleeding – is this due to:
 - Platelet deficiency or dysfunction?
 - Reduced thrombin generation?
 - Clot instability?
 - Hyperfibrinolysis?
 - Acidosis?
 - Hypothermia?



The Ideal Coagulation Laboratory Test

- The ideal laboratory test in the face of a MH would provide an **accurate, reliable** and **rapid** assessment of the patient's **in vivo hemostatic capacity**
- **The ability of our contemporary coagulation tests to comply with these requirements must be questioned**
- **Important to understand what a test was originally designed to measure and what it has been validated to measure**

Categories of Lab Tests

- Two broad categories of laboratory tests that are useful in the assessment of massive hemorrhage

1. Static assays



1. Dynamic assays

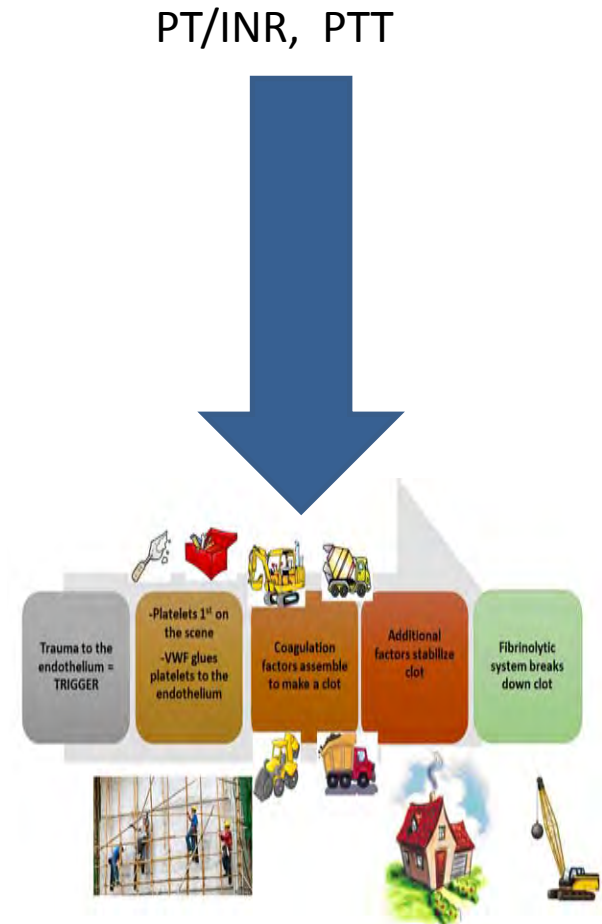


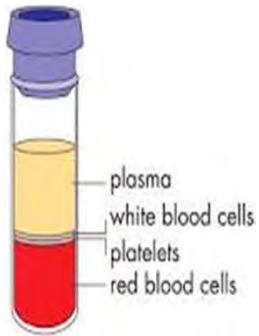
Static Assays

- Complete blood cell count (CBC)
- Prothrombin time (PT)
- Activated partial thromboplastin time (aPTT)
- Fibrinogen
- Thrombin time (TT)

Basic Clot Based Tests

- Prothrombin Time (PT)
 - International Normalized Ratio (INR)
- Activated Partial Thromboplastin Time (PTT)
- END RESULT = CLOT FORMATION



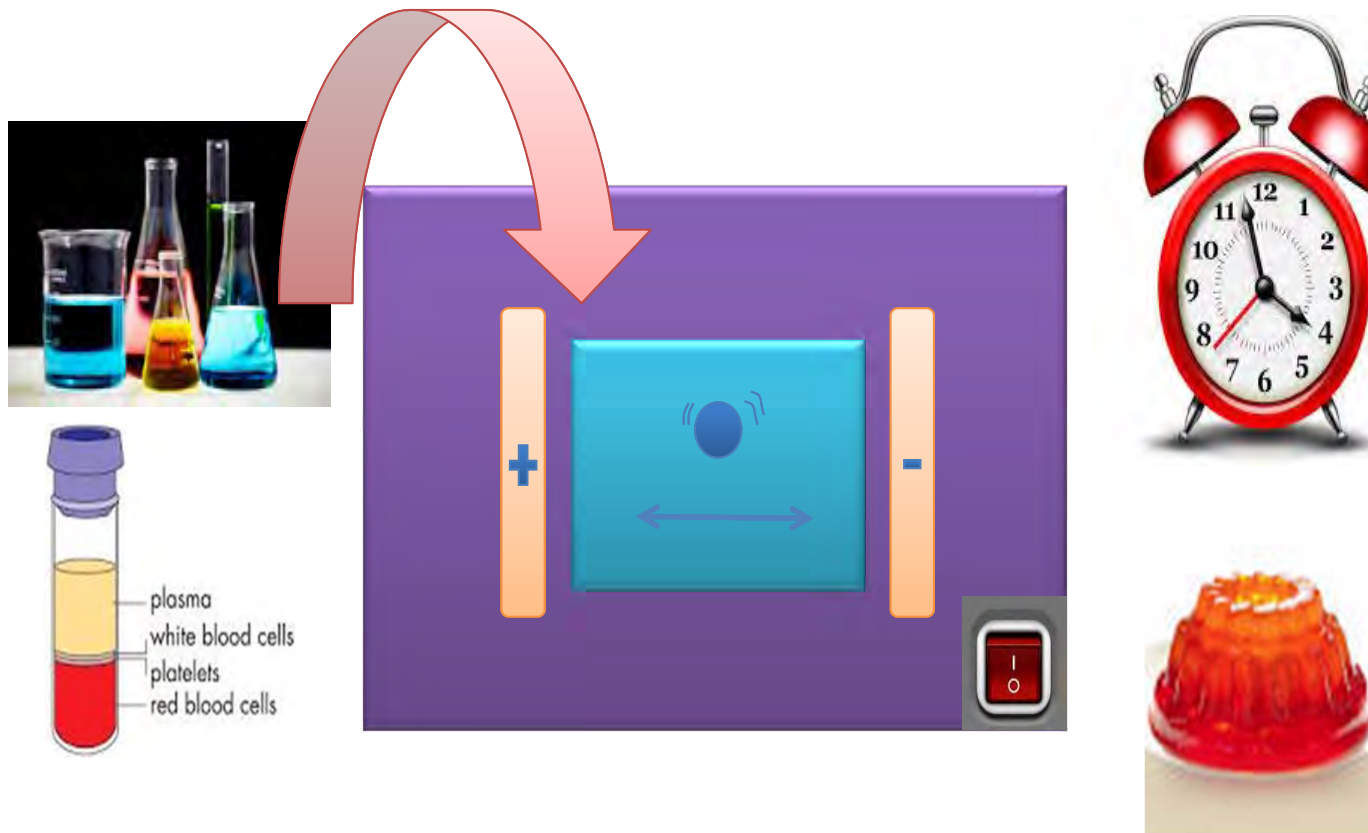


Throw out the Cell-Based Model!

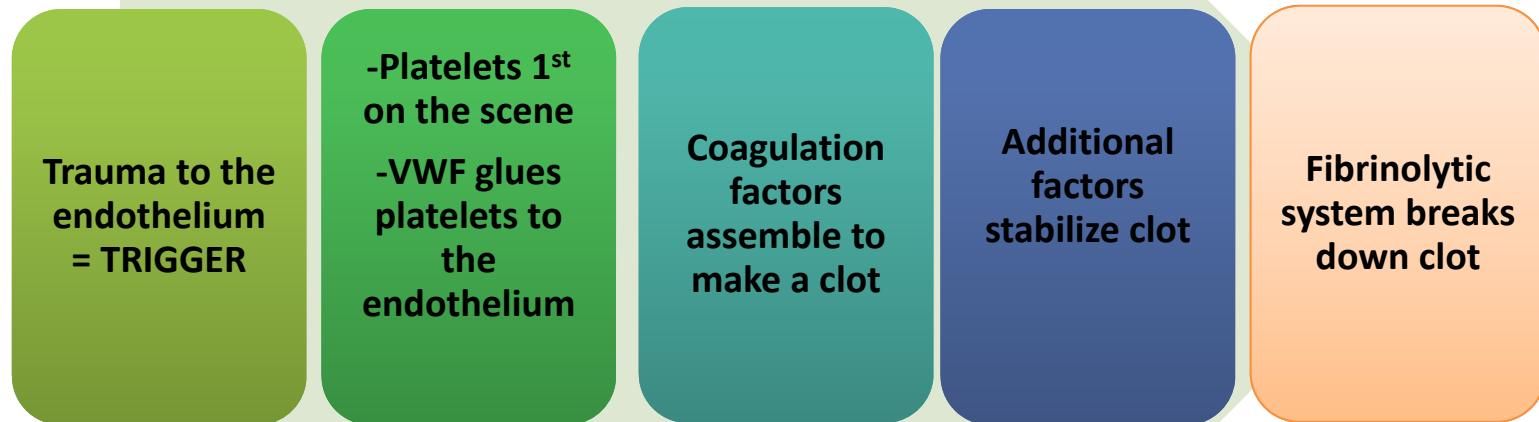


- The PTT and PT measure the time to clot formation of the sample in a test tube in the presence of their respective clot-driving reagents
 - assess only a small component (<5%) of thrombin generation
- Both tests are automated and run on platelet poor patient plasma
- PPP acts as the in vitro representation of the patient's hemostatic capacity
- Therefore, there is a mechanistic disconnect between in vivo and in vitro hemostasis even **prior to placement of the sample on the analyzer**

What is the principle of Clot-Based Assays?



Hemostasis Simplified: Static Assays



CBC

PTT
PT/INR
Fibrinogen

Origin & Evidence

Static Assays in setting of MH

- **PT/INR**

- Effective at determining the amount of warfarin that is present in steady state
- Was not designed to be a dynamic measure of the hemostatic system
- INR > 1.2 = BAD

- **aPTT**

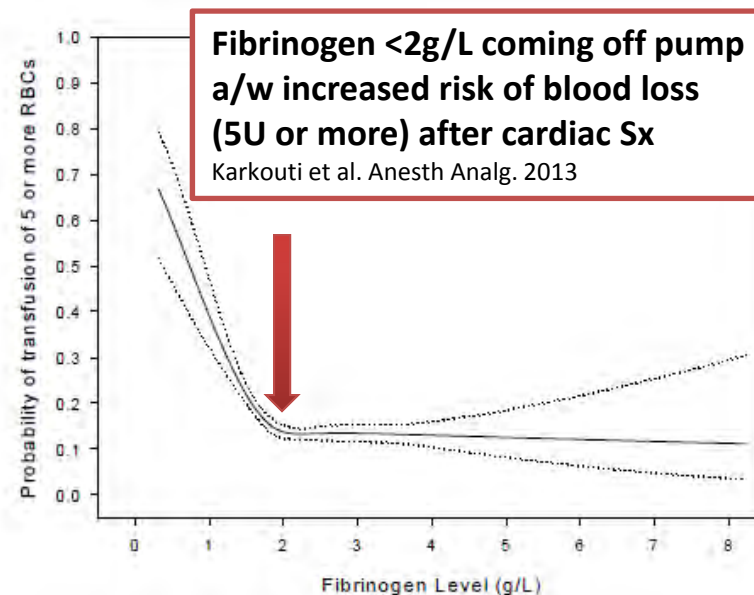
- Initially design
- Attuned to me
- May detect les

- **TT**

- Nothing publis

- **Fibrinogen**

- No quality stu
- fibrinogen detection method in setting of MH
- Decreased fibrinogen on arrival at the ED = independent predictor of MT requirement and death in severely injured patients
- Critically low threshold has not been well-established in trauma (?1, ?1.5, ?2)



operatively

less than 30-35%

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Based on the Evidence: Static Assays in setting of MH

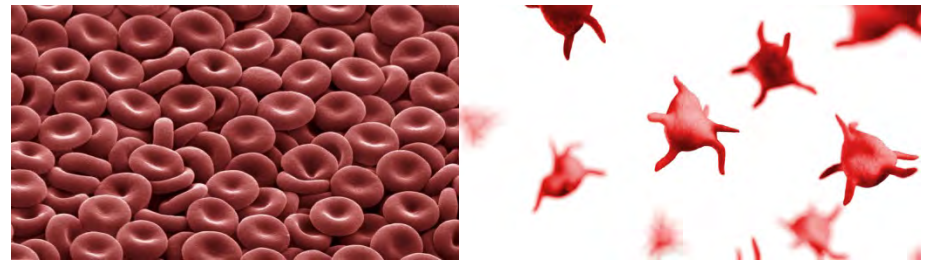
- Fluctuations in the levels of the static studies may not correlate with in vivo bleeding diatheses
- Their proper interpretation is relatively unknown
- Their employment is entirely extrapolated from their use in other much more stable clinical environments
- Clot based assays are run on platelet poor plasma, which abrogates the setting of in vivo hemostasis
- There is a fixed delay in the performance of the tests that further negatively affect their clinical relevance in the acute setting

Toulon, P., et al. *Thrombosis and haemostasis* 101, 394-401 (2009).
Dzik WH et al. *Crit Care*,15(6):242 (2011).

The CBC

- **Hemoglobin**

- Low hemoglobin is an **indicator of severe bleeding associated with coagulopathy**
- Acute anemia ***may*** have a negative effect on **hemostasis rheology**
 - Possibly less platelet margination, activation, support of thrombin generation
- RCTs that have evaluated Hb thresholds for transfusion in critically ill patients have consistently found that restrictive strategies (Hb 70-90) are **as safe or safer** than liberal strategies (Hb>90)
 - Not studied in MH patients



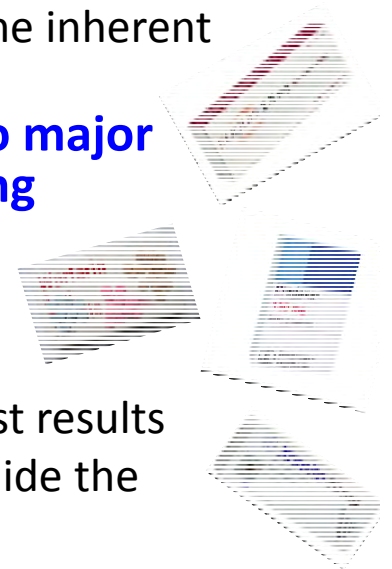
- **Platelet count**

- No assessment of platelet function
- Maintaining a platelet count >50-100 ***seems*** important to minimize risk of microvascular and diffuse bleeding in a variety of settings
- Up front administration of platelets in patients who are not yet thrombocytopenic is controversial
- The association between lower platelet counts and mortality applies to platelet counts within the normal range
- Platelet count alone is a weak indicator of platelet transfusion need bc it ignores platelet function

Conclusions:

Static Assays in setting of MH

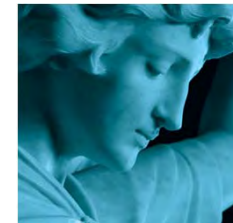
- Paucity of good quality evidence supporting transfusion targets in the setting of MH
 - BUT coagulopathy IS associated with BAD things (INR>1.2, fibrinogen <2)
- **A few practical conclusions can be drawn:**
 - 1. We cannot rely on a single test result – test early and hourly**
 - A trend may be more clinically meaningful as this controls for the inherent variability
 - 2. A normal initial coagulation screen indicates that there is no major coagulation factor defect and possibly/probably no inhibiting anticoagulant present**
 - Small glimpse of thrombin generation; do not be fooled
 - 3. Decisions should be based on the clinical picture**
 - Acute events are likely to unfold prior to the achievement of test results
 - But that doesn't mean that you shouldn't order tests to help guide the direction of care



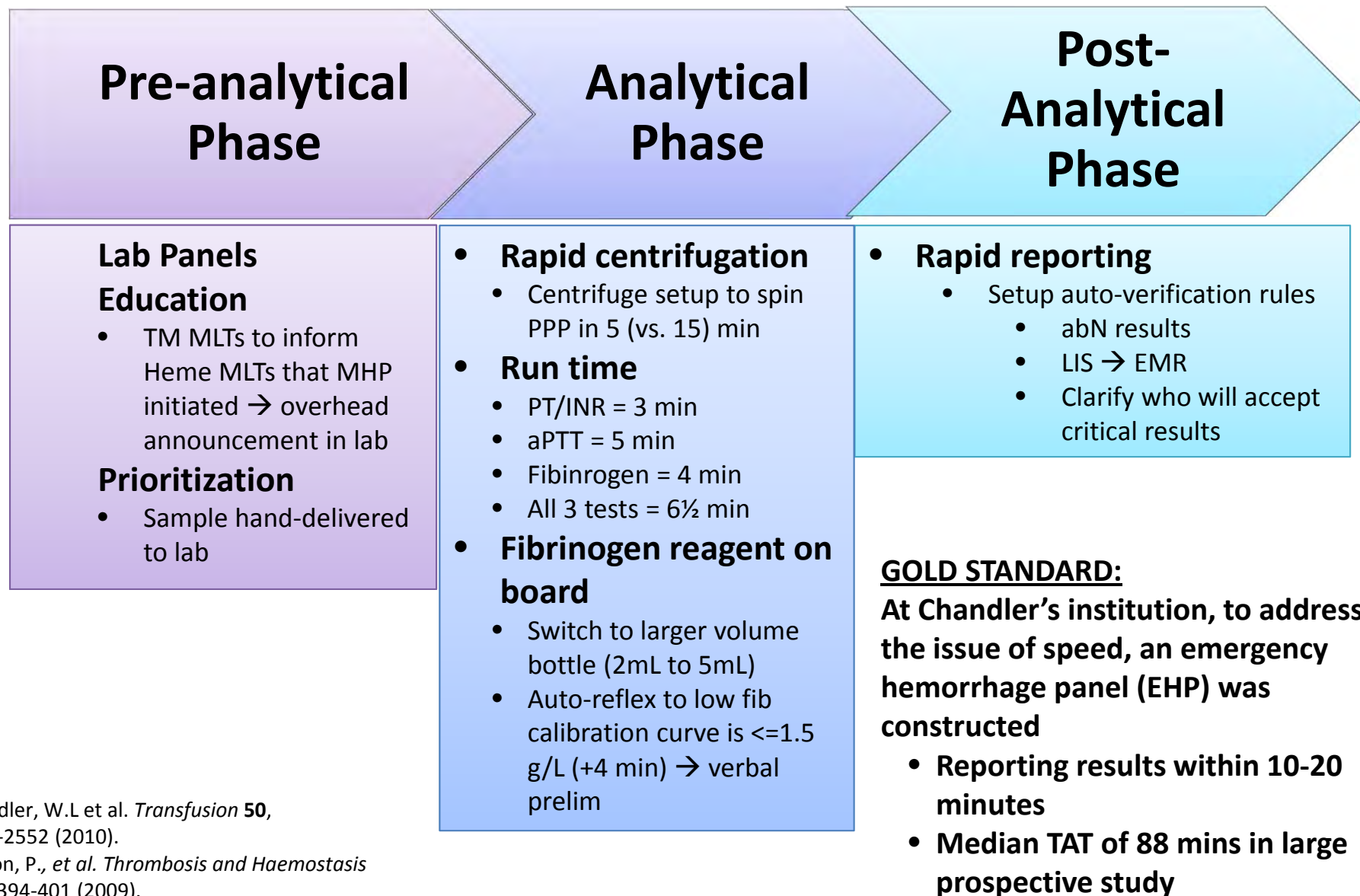
Is there anything that we can do to make the Static Assays Better?



- Speed is critical in the case of MH
- Slow testing may be of no clinical benefit if the result arrives too late
- Accuracy is important, however the focus should be on **accuracy sufficient to make clinical decisions within the shortest possible time frame**



Improving Turn-Around Time



Chandler, W.L et al. *Transfusion* 50, 2547-2552 (2010).

Toulon, P., et al. *Thrombosis and Haemostasis* 101, 394-401 (2009).

Take Home: Targets Simplified

TRUTH:

We know what test results are BAD.
We don't know what our transfusion targets should be.

BLEEDING

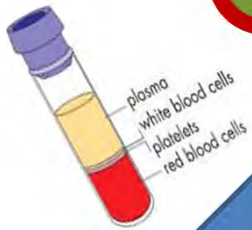
- Trauma
- Diffuse endothelial damage
- Inflammation
- Shock

- Platelet consumption & dysfunction

- Coagulation consumption
- Auto-Heparinization
- Upregulated Thrombomodulin
→ Activation of protein C

- Diminished Stabilization
- Uncontrolled tPA

- Hyperfibrinolysis

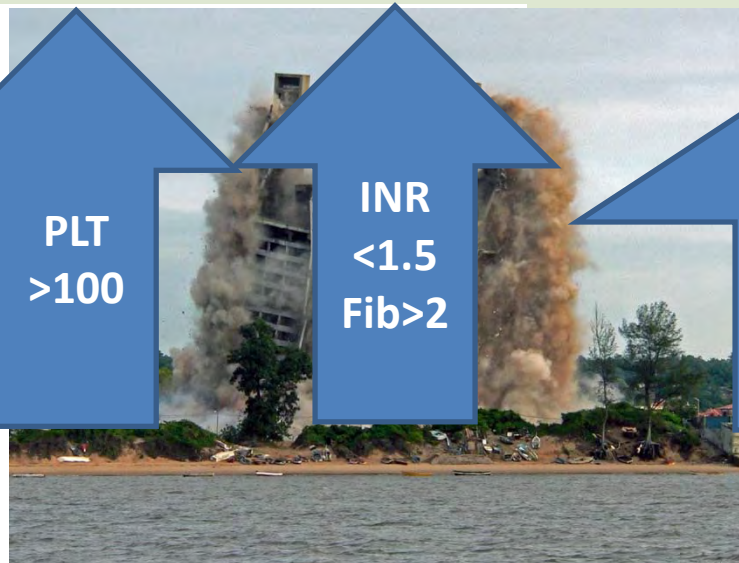


Hb
>70

PLT
>100

INR
<1.5
Fib>2

TXA



Objectives Revisited

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Thank you

Questions?

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