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The Coagulation System in End-Stage Liver Disease

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Nothing to disclose

Coagulation System in ESLD

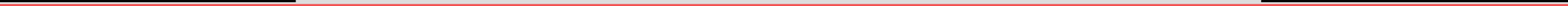
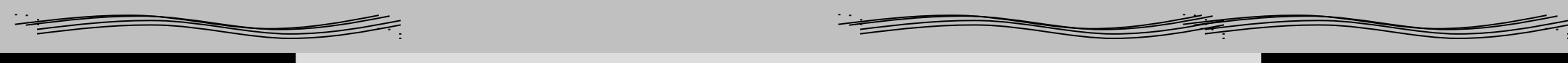
- Coagulation imbalance in plasma ?
 - Risk of venous thrombosis ?
 - Risk factors for bleeding ?
 - Evaluation of coagulation system ?
-

Tissue

Extracellular
Matrix

Endothelium

Blood



Tissue



The diagram illustrates the interaction between a platelet and a tissue surface. The top half is a light gray area labeled 'Tissue', and the bottom half is a red area labeled 'Blood'. A black horizontal line represents the tissue surface. A yellow oval labeled 'Platelets' is positioned at the interface. To its right, two stacked yellow rectangles are labeled 'FvW' (top) and 'FVIII' (bottom). Wavy black lines above the tissue surface represent collagen fibers.

Platelets

FvW

FVIII

Blood

Tissue

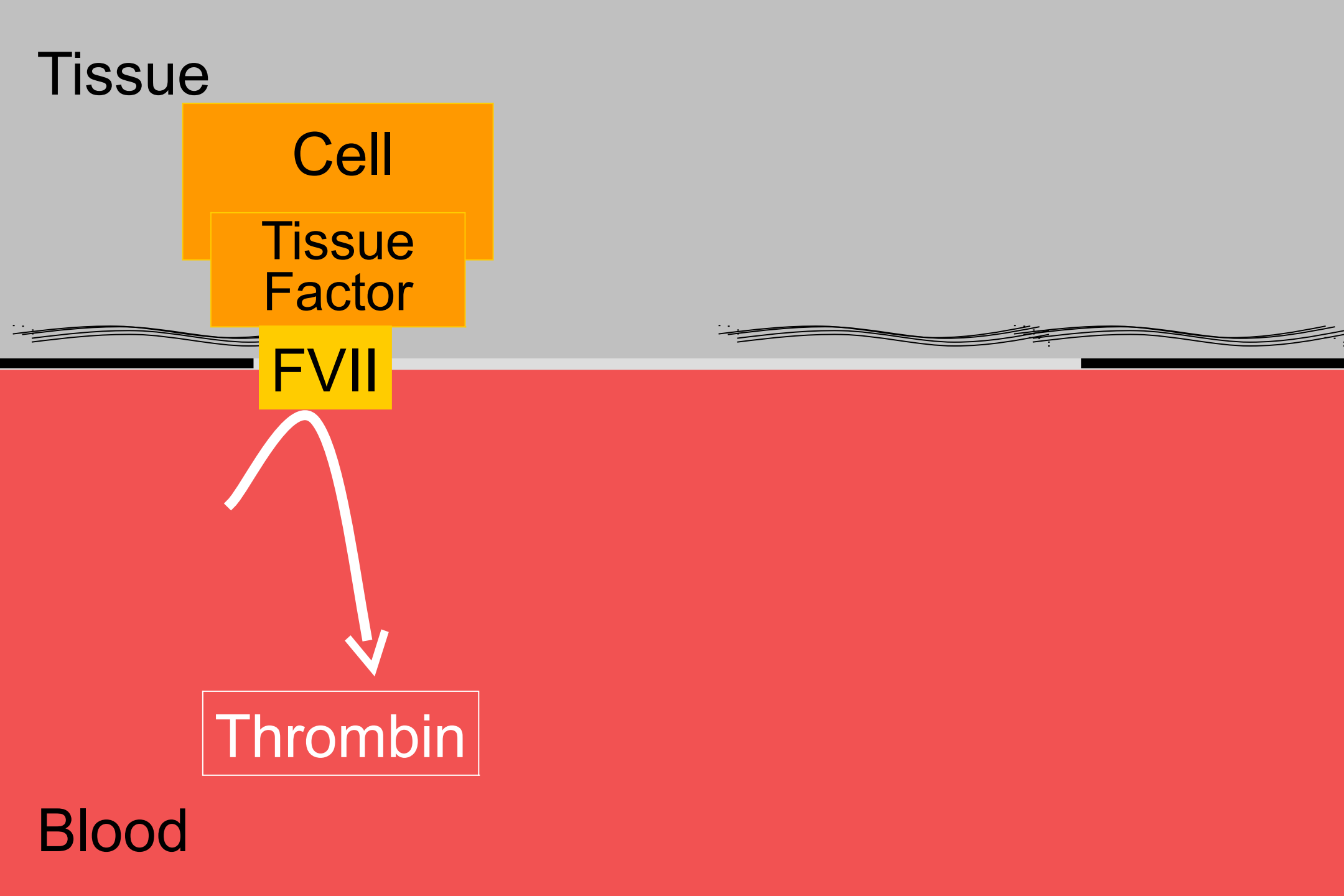
Cell

Tissue
Factor

FVII

Thrombin

Blood



Tissue

Cell

Tissue
Factor

FVII

Platelets

FvW

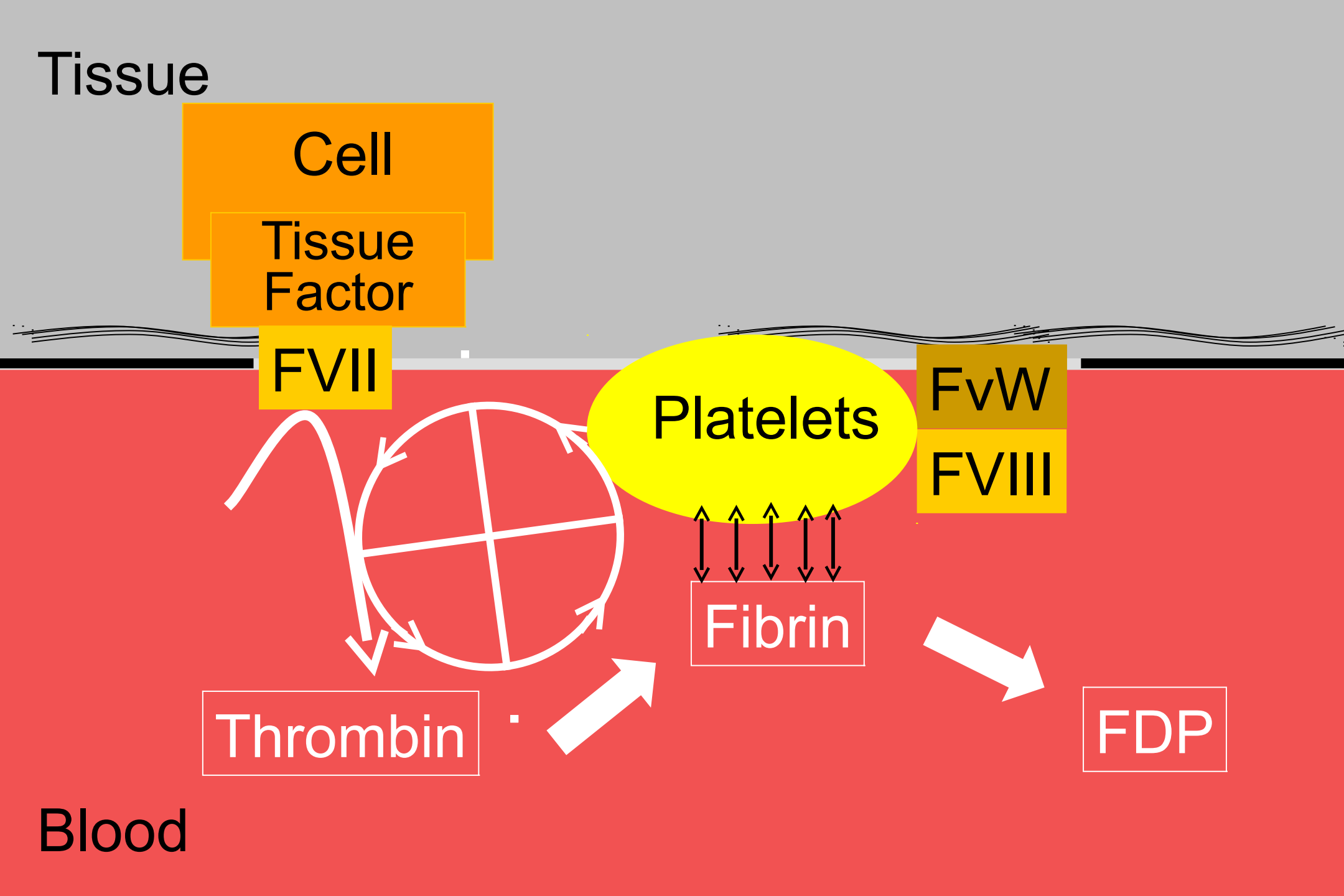
FVIII

Fibrin

Thrombin

FDP

Blood



Tissue

Cell

Tissue
Factor

FVII

Platelets

FvW

FVIII

Fibrin

Thrombin

FDP

Blood

Thrombocytopenia – Prevalence

Platelets	Cirrhosis (%)	Non-Cirrhotic CLD (%)	OR
< 40,000	11	0.9	
< 100,000	383	11.5	
< 150,000	657	8.4	

Bashour, Am J Gastroenterol 2000
Active alcoholism and ongoing sepsis excluded

Thrombocytopenia and ESLD

- Splenic sequestration
 - Decreased survival (platelet bound IgG)
 - Inappropriate thrombopoiesis/thrombopoietin
-

Thrombocytopenia and ESLD

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Increased factor VIII and vW factor

Increased platelet coverage of collagen coated plates

Thrombocytopenia and ESLD

When Platelets $> 75,000/\mu\text{L}$

- Not a risk factor for gastrointestinal bleeding
- An index of the severity of liver disease
- Increased risk of portal vein thrombosis with Eltrombopag

Lisman, J Hep 2002. Caldwell, Hepato 2006.
Senzolo, World J Gastro 2006. Afdhal, NEJM 2012, & Gastro 2014

Tissue

Cell

Tissue
Factor

FVII

Platelets

FvW

FVIII

Thrombin

Fibrin

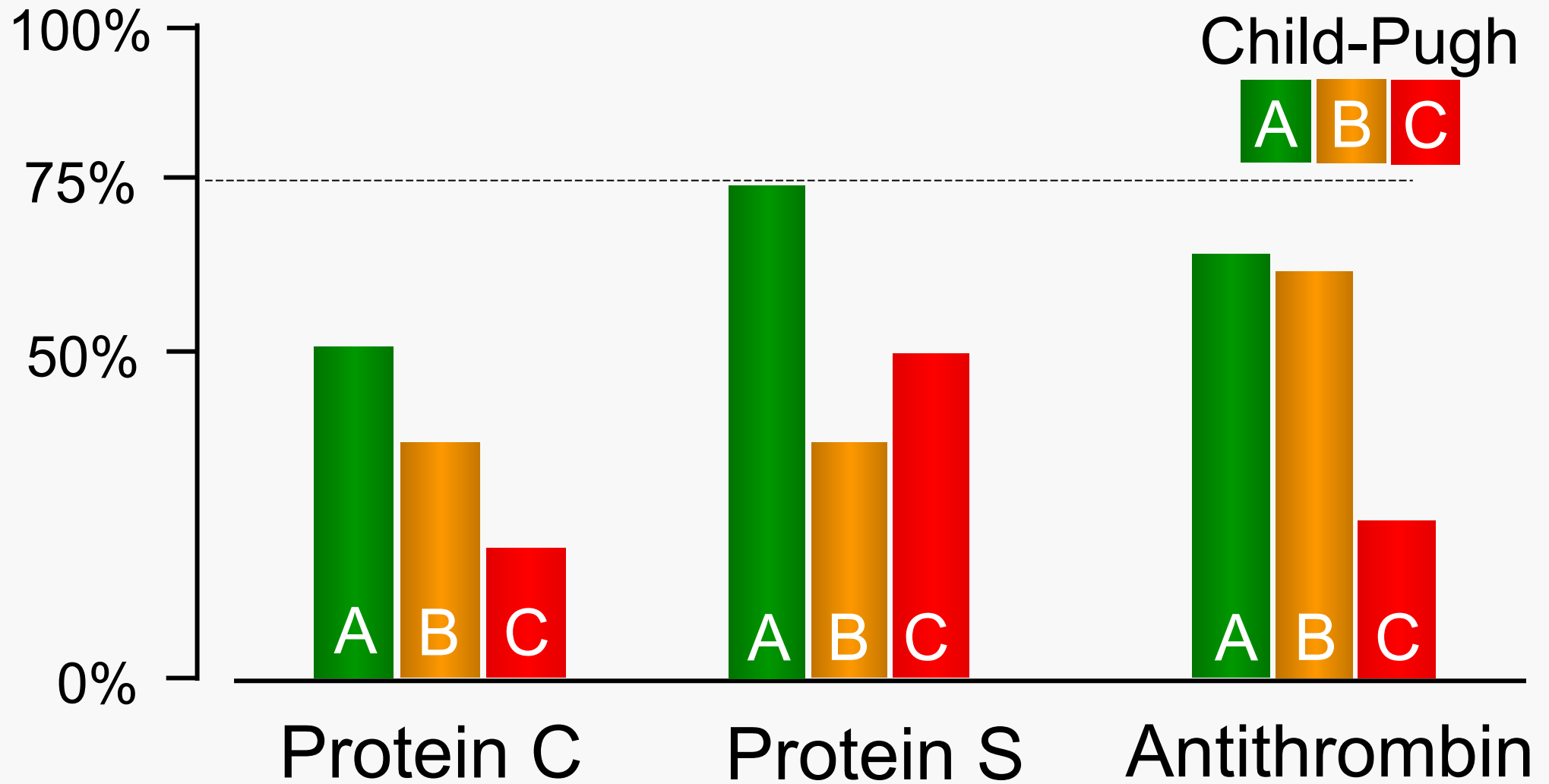
FDP

Blood

Coagulation System in ESLD

- Anticoagulant: ↓F1, II, V, VII, IX, X
 - Procoagulant
 - ↑ Tissue factor
 - ↑ FVIII
 - ↓ clearance of activated factors
 - ↓ protein C, protein S, antithrombin
-

Coagulation Inhibitors in Cirrhosis



Coagulation System in ESLD

- Anticoagulant: ↓F1, II, V, VII, IX, X
 - Procoagulant
 - ↑ Tissue factor
 - ↑ FVIII
 - ↓ clearance of activated factors
 - ↓ protein C, protein S, antithrombin
-

Coagulation System in ESLD

- Anticoagulant: ↓F1, II, V, VII, IX, X
 - Procoagulant
 - ↑ Tissue factor
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 - ↓ clearance of activated factors
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In plasma :

- Maintained thrombin generation
- Increased resistance to thrombomodulin

Coagulation System in ESLD

- Hypercoagulable imbalance in plasma
 - Risk of venous thrombosis ?
 - Risk factors for bleeding ?
 - Evaluation of coagulation system ?
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Coagulation System in ESLD

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Northup, AJG 2006. Soogard, AJG 2009.

Coagulation System in ESLD

- Hypercoagulable imbalance in plasma
- Increased risk of venous thrombosis

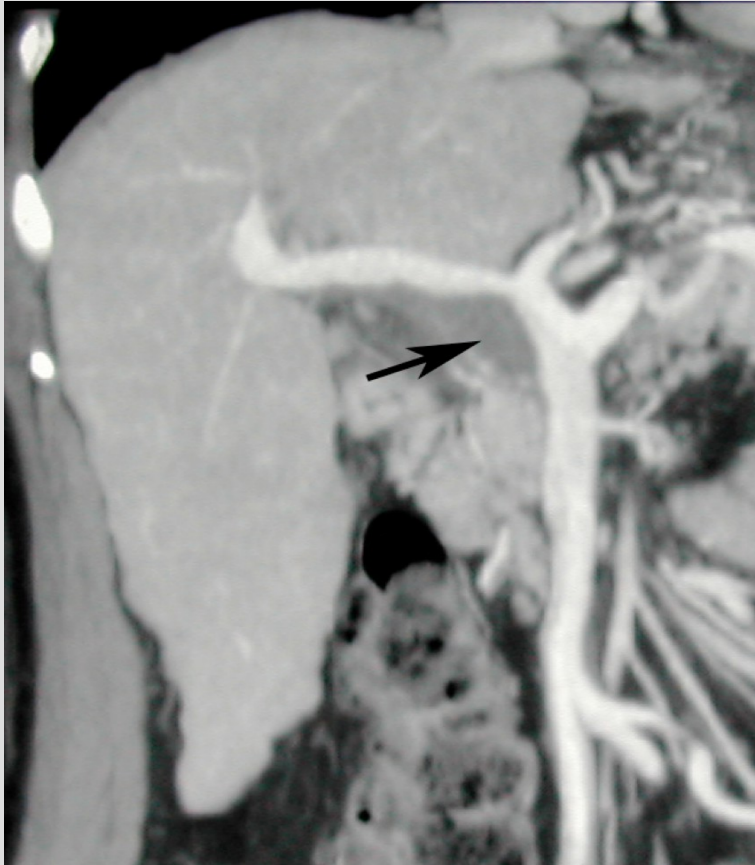
- A prothrombotic state
- Anticoagulation therapy apparently well tolerated

Northup, AJG 2006. Soogard, AJG 2009.

Amitrano, J Clin Gastro 2010. Francoz, Gut 2005.

Senzolo, Liver Int 2012. Delgado, Clin Gastro Hepato 2012

Extrahepatic Portal Vein Thrombosis in Cirrhosis



Partial PVT	Occlusive PVT
10% (5-16)	3% (1-4)
Spontaneous regression	
40% (31-71)	

Coagulation System in ESLD

- Hypercoagulable imbalance in plasma
- Increased risk of venous thrombosis
- **Risk factors for bleeding ?**
- Evaluation of coagulation system ?

Northup, AJG 2006. Soogard, AJG 2009.

Coagulation System in ESLD

- Hypercoagulable imbalance in plasma
 - Increased risk of venous thrombosis
 - **Portal hypertension main risk factor for bleeding**
 - Evaluation of coagulation system ?
-

Prediction of bleeding risk in ESLD

- Predictive : Low platelet counts (how low ?)*
- Not predictive:
 - Coagulation factor levels and INR
 - Bleeding time
- Unclear
 - Closure time (PFA100)
 - Clot lysis time
 - Thromboelastography

*75,000/ μ L safe

Prophylaxis and Treatment for Bleeding

Negative RCTs* - Desmopressin
- Recombinant factor VIIa

No RCT - Platelet transfusion
- Fresh frozen plasma
- Coagulation factor concentrates
- Aprotinin
- Aminocaproic or tranexamic acid

* In a context of variceal bleeding

AEs Associated with Therapy for Bleeding

Blood products	<ul style="list-style-type: none">- Exacerbation of bleeding- Volume overload
Platelets	<ul style="list-style-type: none">- Lung injury
TPO agonists	<ul style="list-style-type: none">- Portal vein thrombosis
rFactor VIIa	<ul style="list-style-type: none">- Thrombosis
Aprotinin	<ul style="list-style-type: none">- Thrombosis- Kidney injury
Desmopressin	<ul style="list-style-type: none">- Thrombosis- Water retention/hyponatremia

Coagulation System in ESLD

- Hypercoagulable imbalance in plasma
 - Risk of venous thrombosis ?
 - Portal hypertension main risk factor for bleeding
 - **Evaluation of coagulation system**
-

Evaluation of Coagulation

- Poor relevance of classical coagulation tests
 - Unclear relevance of newer tests (thrombin generation, thromboelastography)
 - VKA-related INR inappropriate
 - ESLD-related INR unavailable
-

Coagulation in ESLD patients

1. Cirrhosis is a mild prothrombotic state.
 2. Bleeding is not related to hypocoagulability.
 3. Coagulation-directed therapy not supported by available data.
 4. Anticoagulation therapy can be considered.
 5. Evaluation of bleeding risk still a challenge.
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In patients with platelets $> 75,000/\mu\text{L}$

