CASE PRESENTATION: A HEALTHY GIRL WITH BRUISES

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CASE: HISTORY

- 4Y/O girl, previously healthy, presented with
- Day 1: low grade fever and vomiting, consult at a private hospital was managed with anti-
- Next day: developed bruises on lower extremities
- Day 4: Bruises worsened, coagulation profile done, showed elevated INR, prolonged APTT referred to SKMC ED.
- **Denies:** Epistaxis, Gum Bleeding, joint swelling or changes in the urine color, hx of thrombotic events

FURTHER HISTORY

- No Hx of ingestion of drug or poison, exposure to pesticides, insect bites , no vaccination over the last two months
- No significant past medical & surgical History
- No known allergies
- Family History: Parents non consanguineous. Parents healthy not on any maintenance medication
- No known family history of bleeding or hypercoagulable states .

PHYSICAL EXAMINATION

- **Vitals: T: 36.7 C, HR:114 bpm, RR:22, O2 saturation: 98% on room air, BP: 91/53**
- **General**: No acute distress**, not pale, no icterus**
- **Respiratory**: Lungs are clear to auscultation
- **Cardiovascular: Distinct S1, S2 , No murmur, normal peripheral perfusion**
- **Gastrointestinal**: Soft, Non-tender, Non-distended.
- **Integumentary: Warm, Pink, Bilateral posterior and lateral extremities red to purple bruises**

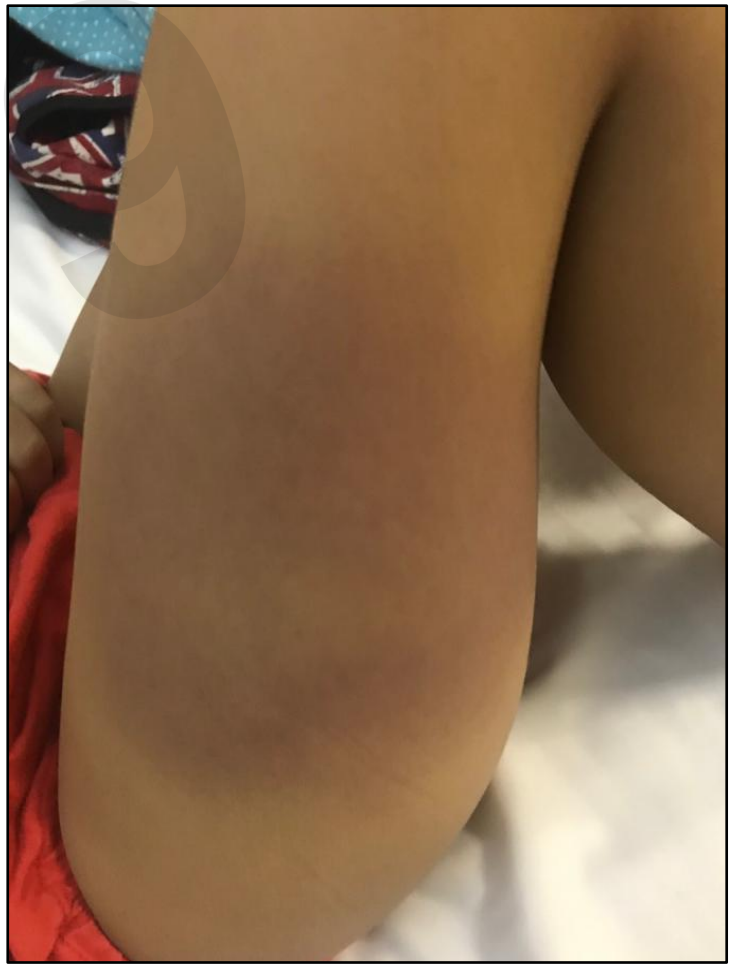


Figure 1: Right lateral thigh at admission

DIFFERENTIAL DIAGNOSIS

- ITP
- Viral induced
- Medication induced: Warfarin, Heparin
- DIC
- Purpura due to hypercoagulability: Acquired vs Congenital
  - Congenital (Protein C & S)
  - Acquired antiphospholipid

INVESTIGATIONS

- What to look for?

INVESTIGATIONS (1)

WBC	7.8x 10^9	4.5-10 x 10^9
RBC	5.39 x10^9	4.8-9.3 x 10^9
Hgb	120 g/dL	115-135
Platelet	235 X10^9	150-450
CRP	16.07	<= 10

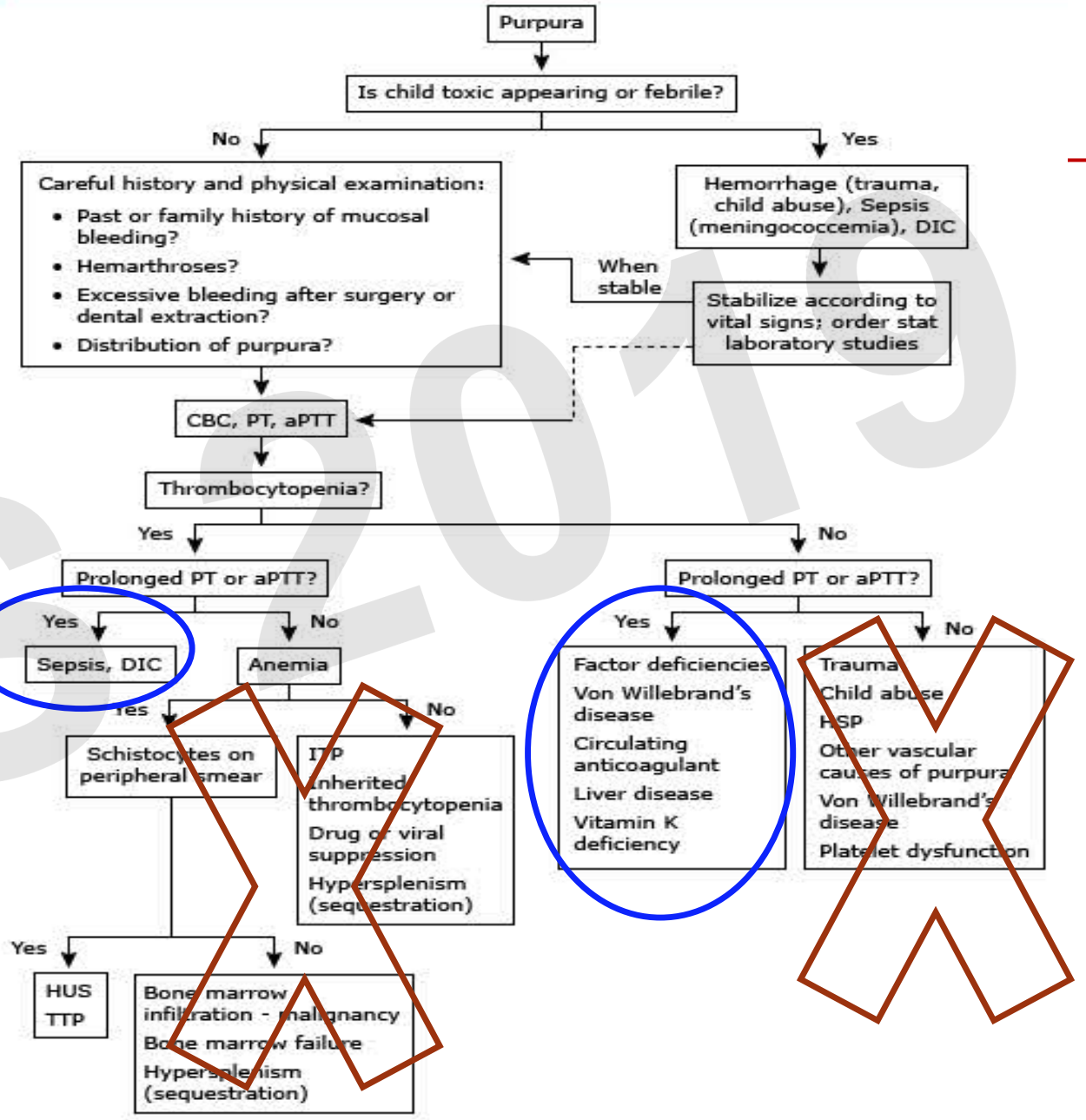
PT	38.2 sec (H)	12.0-15.0
INR	3.7 sec (H)	0.7-1.1
APTT	58.3 sec (H)	27.7-42.1
Thrombin time	59.4 sec (H)	12-14

INVESTIGATIONS (2)

Mixing study APTT, incubated	39.50
PT- Mix 50:50 Incubation	15.5sec
PT- Mix 50:50 No Incubation	14.9 secs

D-Dimer	>20 (H)	<0.50mg/dL

Pediatric purpura algorithm



PROVISIONAL DIAGNOSIS

- DIC
- Purpura due to hypercoagulability: Acquired vs Congenital
  - Congenital (Protein C & S)
- Factor Deficiency
- Vitamin K Deficiency

QUESTION 1: WHAT WOULD THE NEXT STEP BE IN MANAGEMENT?

A. Investigate and observe
B. Vitamin K (I.V)
C. Fresh frozen plasma (FFP)
D. Heparin
E. Cryoprecipitate

BACK TO THE PATIENT: WHAT WAS DONE?

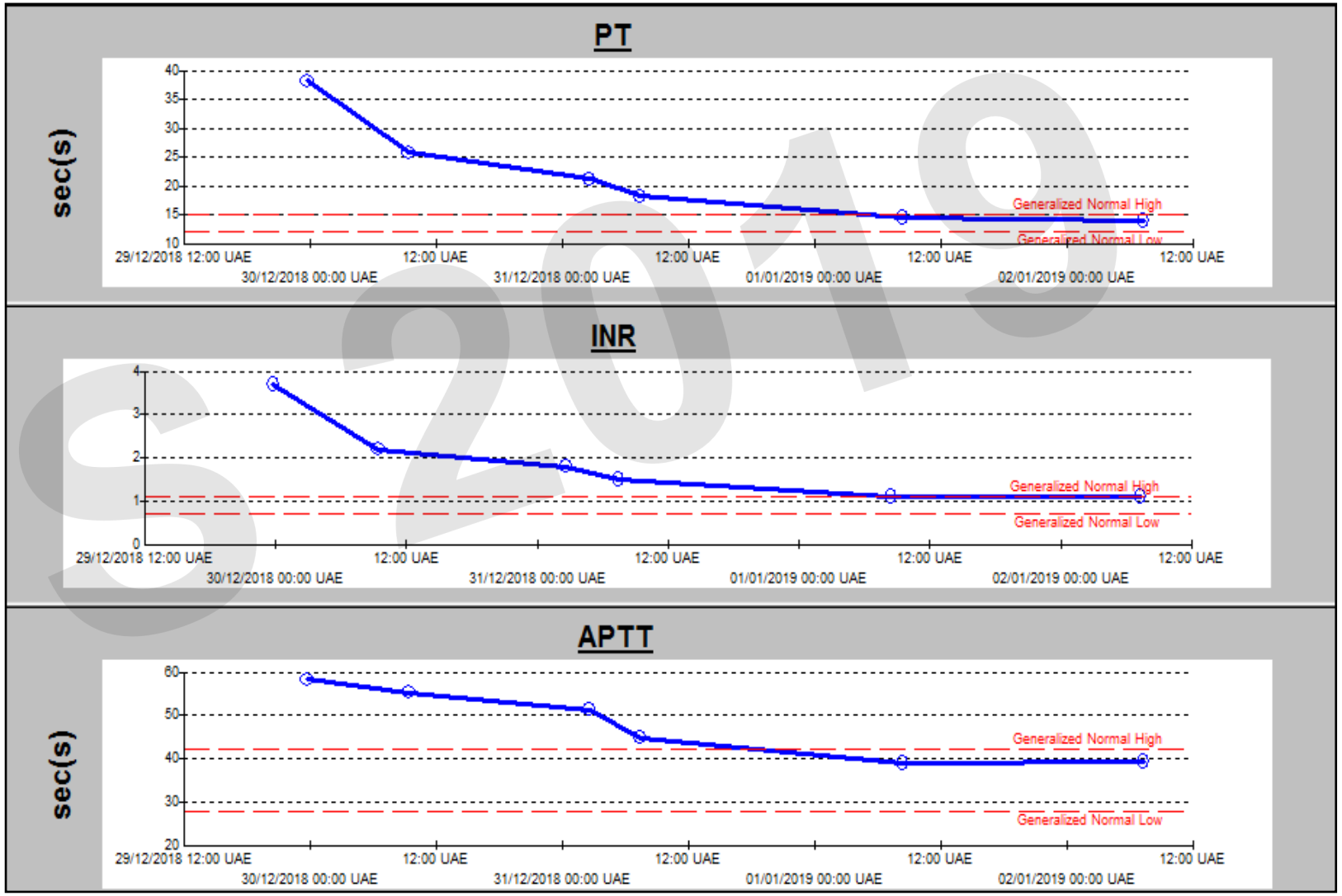
A. Investigate and observe
B. **Vitamin K (I.V)**
C. Fresh frozen plasma (FFP)
D. Heparin
E. Cryoprecipitate

MANAGEMENT (1) VITAMIN K

PT	25.8 sec	38.2 sec (H)	12.0-15.0 sec
INR	3.5 sec	3.7 sec (H)	0.7-1.1 sec
APTT	55.3 sec	58.3 sec (H)	27.7-42.1 sec
Thrombin time	59.4 sec	59.4 sec (H)	12-14 sec

Fibrinogen	0. 4 (L)	2.0- 4.0 gm/dL
D-Dimer	>20 (H)	<0.50mg/dL

Management (2): FFP



Management (2): FFP

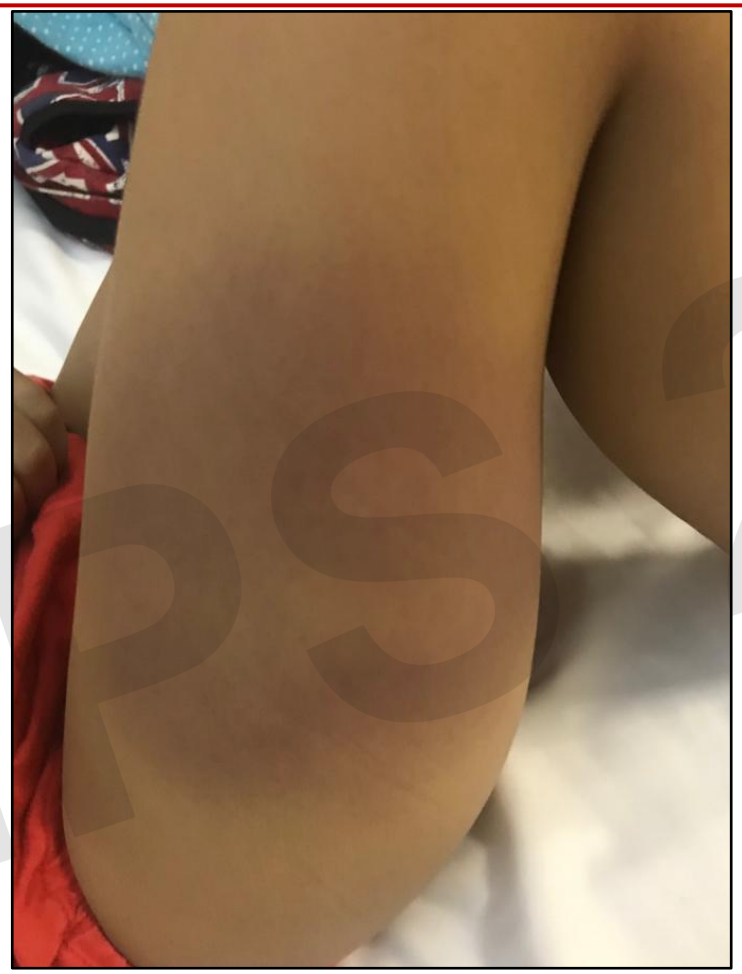


Figure 1: Right lateral thigh at admission

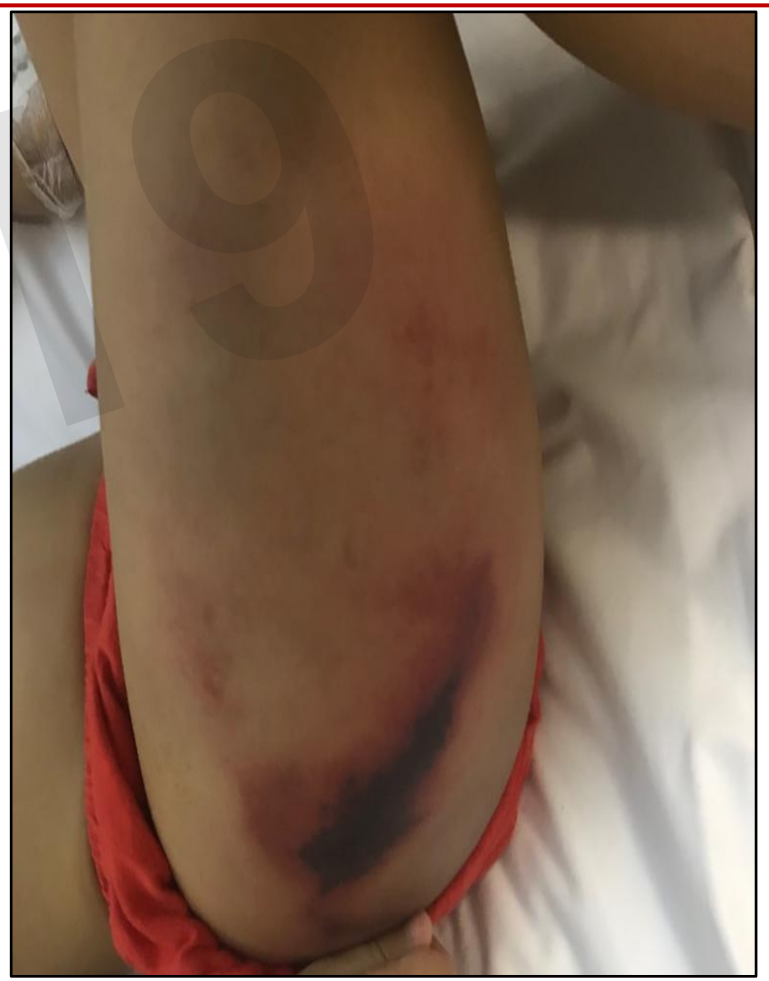


Figure 2: Right lateral thigh 12 hours post FFP

DIAGNOSIS

Purpura Fulminans

What is the cause?

PURPURA FULMINANS

- PF is a life-threatening disorder of acute onset characterized by cutaneous hemorrhage and necrosis caused by DIC
- Three distinct categories can be identified:
  - Acute infectious: Neisseria, Staphylococcus, Pneumococcus and Haemophilus
  - Genetic Deficiency ANTICOAGULANT protein C and protein S
  - Idiopathic

Hoffman: Hematology: Basic Principles and Practice, 5th ed.

WHAT FURTHER INVESTIGATIONS DO TO ?

Investigation (3):

- ✓ Additional
  - Factor assay
  - Protein C
  - Protein S

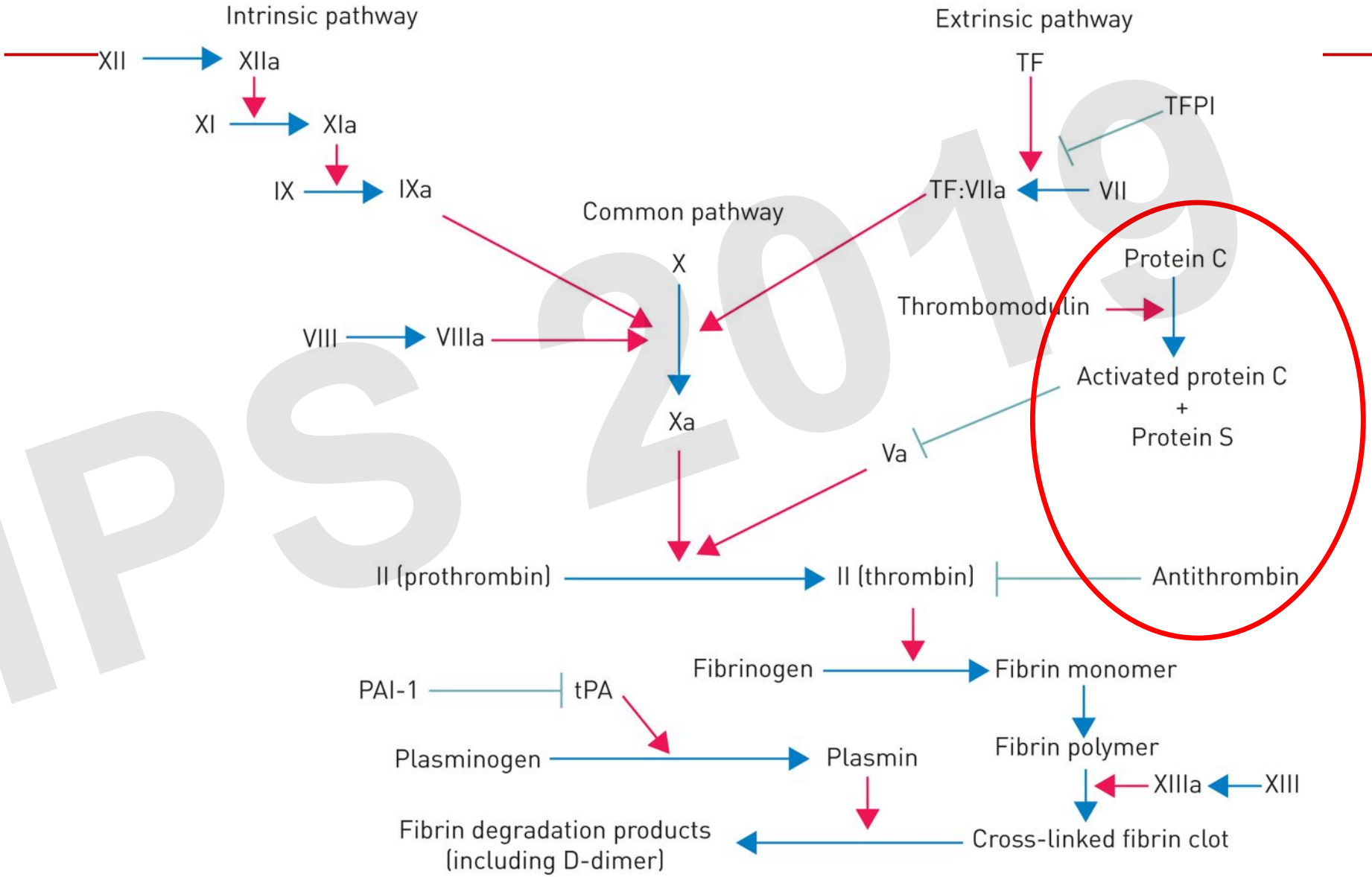
Factor II	74.0%
Factor VII	65.0%
Factor VIII	54.0%
Factor IX	103.0%
Factor XI	101.0%
Antithrombin III	101.0%
Protein C Act	**30.0%**
Protein S Act	**<10%**

Doppler Ultrasound ruled out thrombosis of major vessels

DIAGNOSIS

Purpura Fulminans due to protein S deficiency

CASCADE



CAUSE OF DEFICIENCY OF PROTEIN S

- Genetic
  - **Neonatal purpura fulminans (homozygous PC or PS deficiency)**
  - Heterozygotes generally are not symptomatic until the 3rd and 4th decades
- Acquired
  - Liver disease
  - DIC
  - Vitamin K deficiency

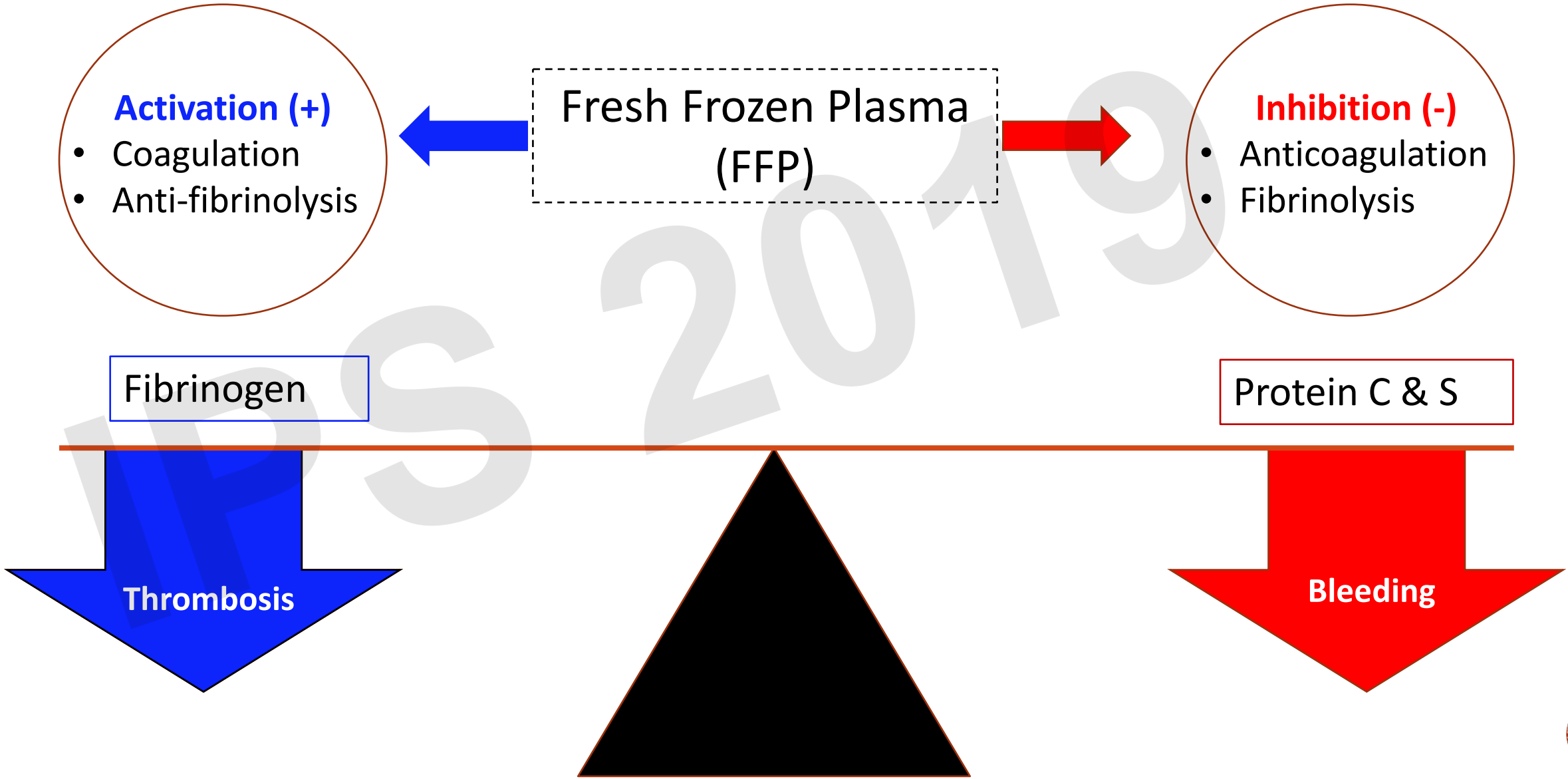
Hoffman: Hematology: Basic Principles and Practice, 5th ed.

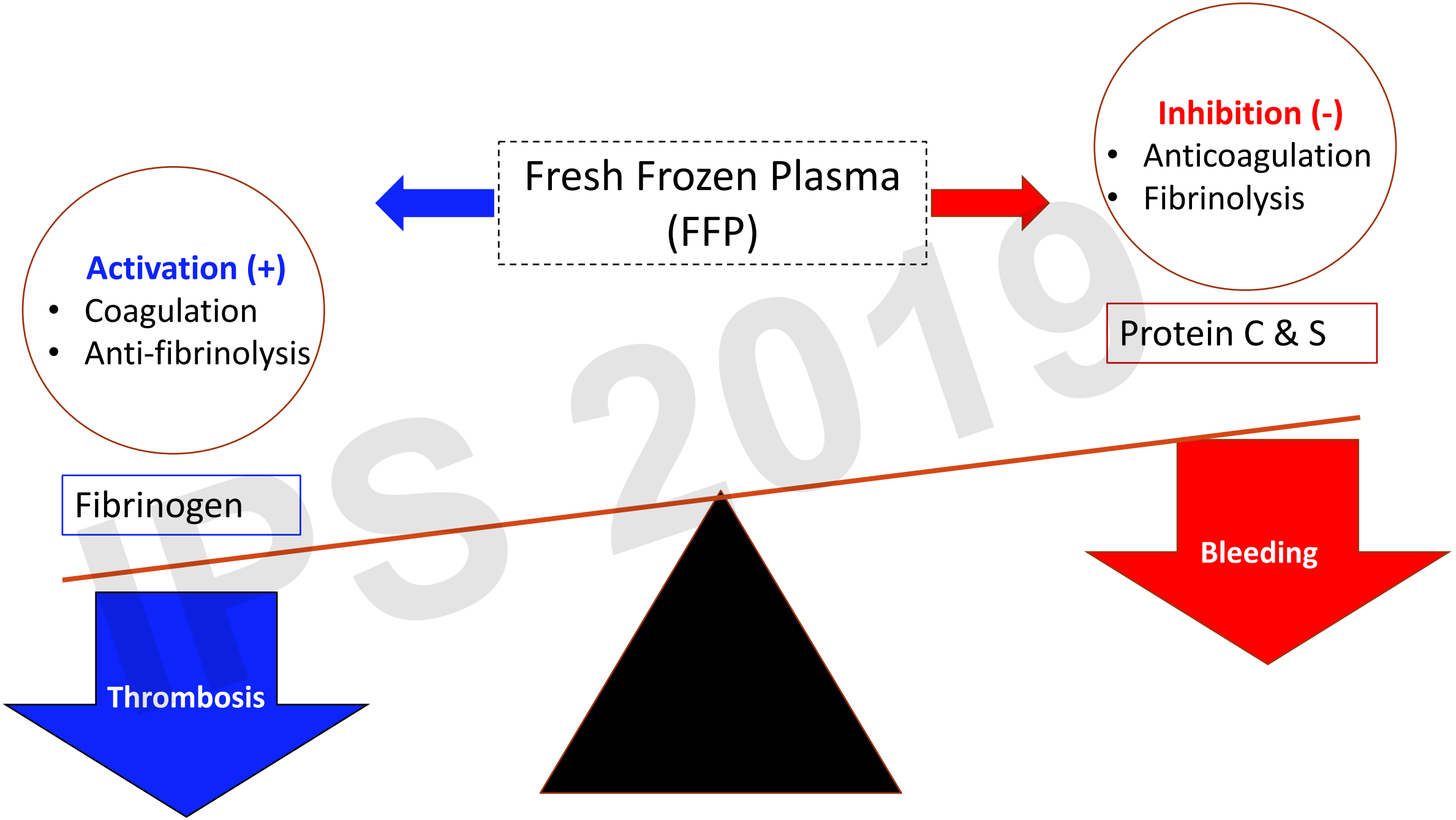
CLINICAL FEATURES OF PATIENTS WITH INHERITED DEFICIENCIES OF PROTEIN S

- **Venous thrombosis (>90% of cases)**
  - Deep vein thrombosis of the lower limbs
  - Pulmonary embolism
  - Superficial thrombophlebitis
  - Mesenteric vein thrombosis*
  - Cerebral vein thrombosis*
- **Frequent family history of thrombosis**
- **Frequent recurrences**

Back To The Patient

What happened on administering FFP ?




Fresh Frozen Plasma (FFP)
Activation (+)
• Coagulation
• Anti-fibrinolysis
Inhibition (-)
• Anticoagulation
• Fibrinolysis
Protein C & S
Fibrinogen
Thrombosis
Bleeding

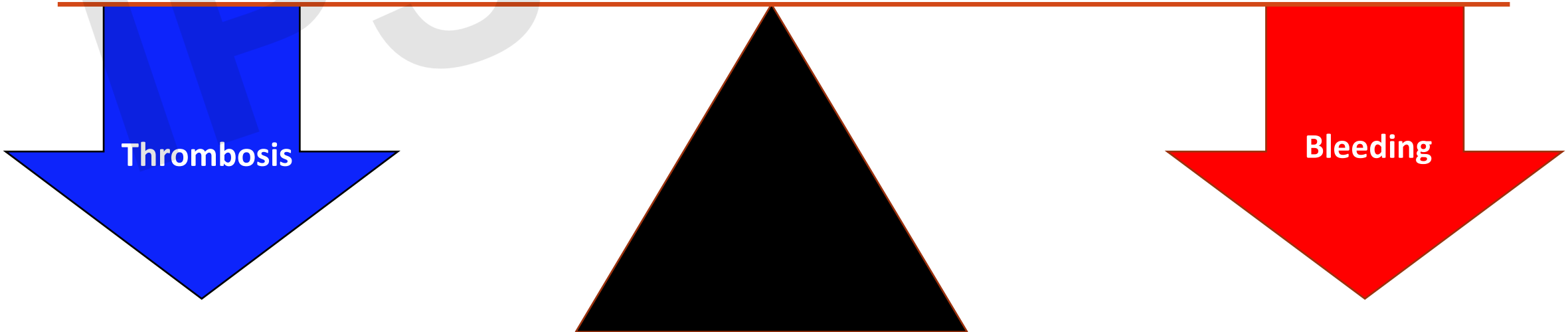
Back To The Patient

What is the solution?

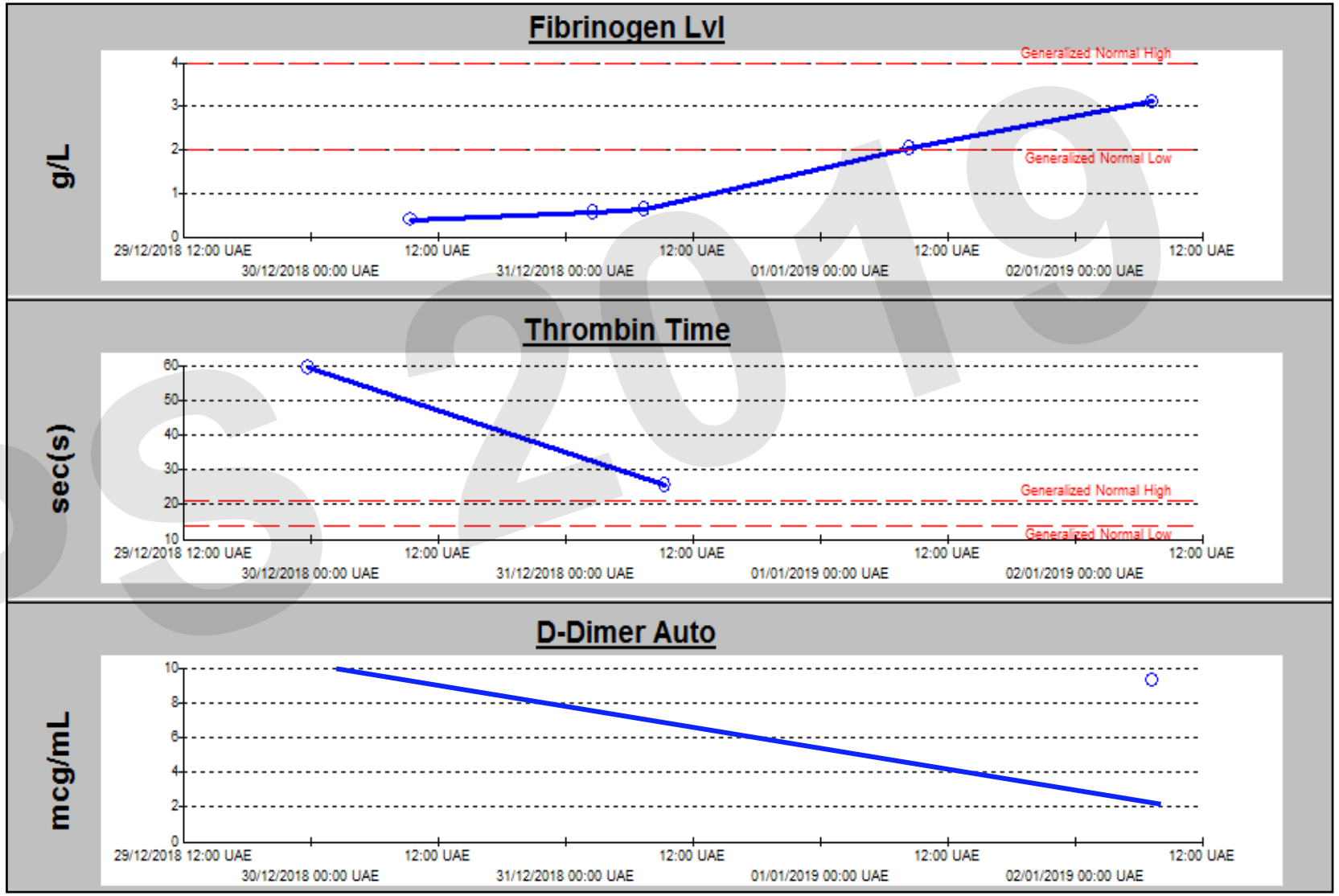
Activation
- Coagulation
- Antifibrinolysis

Inhibition
- **Anticoagulation**
- Fibrinolysis

LMWH



Management (2): Fresh Frozen Plasma with Heparin



1 MONTH FOLLOW UP

Skin lesion healed completely

Protein S 10%

Parents Protein C & S level within normal

Genetic Testing (Awaiting result)

Continue on LMWH for 3 months

D-dimer considered surrogate endpoint for monitoring disease

CONCLUSIONS:

- Purpura Fulminans may be the presenting symptom in patient with Protein S deficiency

- Purpura Fulminans is a hematological emergency presenting with necrosis of the skin and Disseminated Intravascular coagulopathy

CONCLUSIONS

- FFP should be used to replete consumed coagulation and anti-coagulation factors, particularly Protein C and S

- Immediate heparinization, concurrently with FFP may limit mortality as well as morbidity

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