EUROPEAN HEMATOLOGY ASSOCIATION

EHA-ISHBT Hematology Tutorial

Self-assessment Case – Session [Haemophilia]

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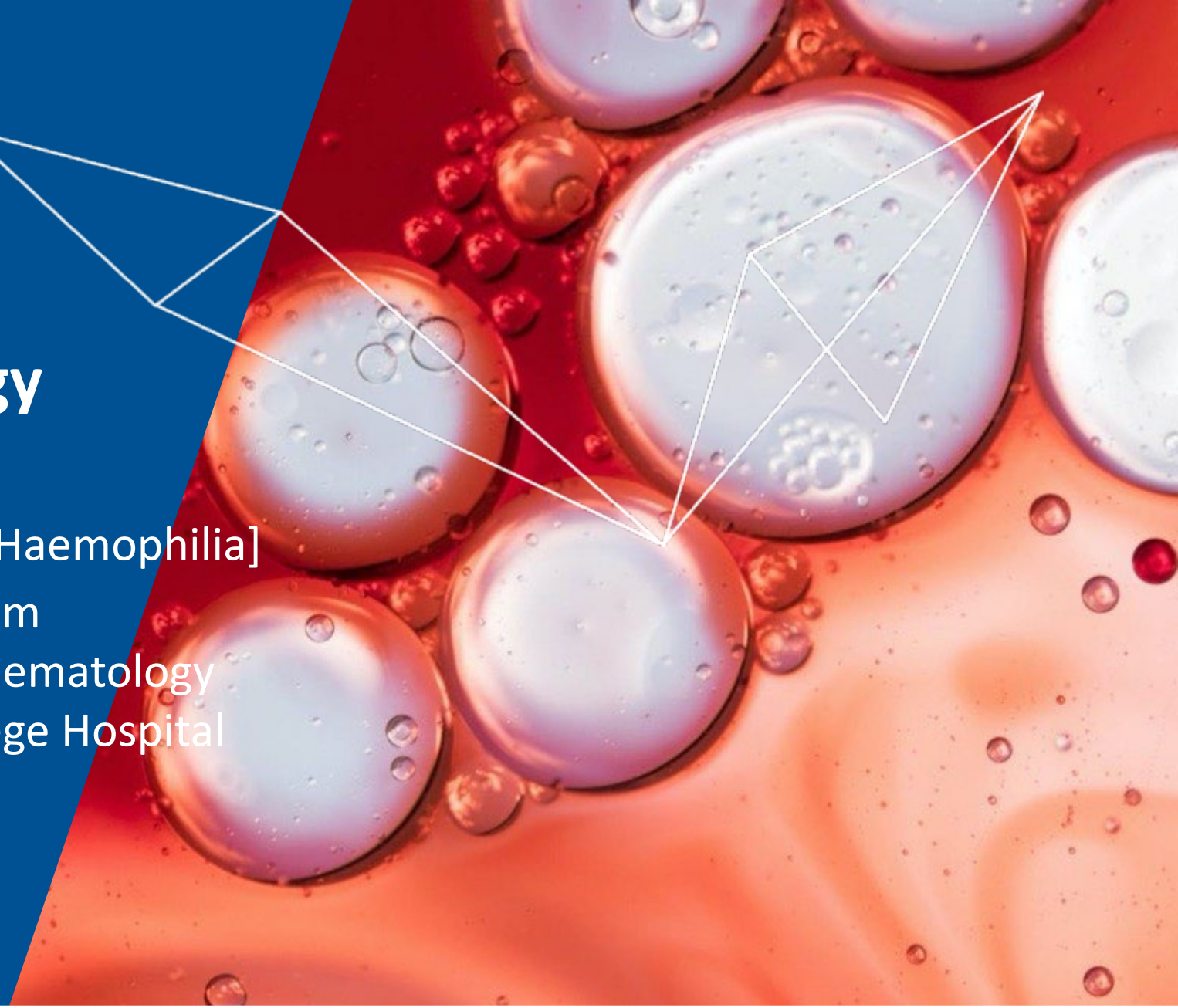

Disclosures

- None

Introduction

- A 40-year-old woman first presented in childhood with recurrent epsitaxis. At initial presentation
- FBC : Normal
- Blood Film: Normal
- PT/APTT: Normal
- Sister had a similar history
- No history of consanguinity

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Questions can be answered by scanning the QR on your phone to access Slido.

For each question you have 15 seconds.

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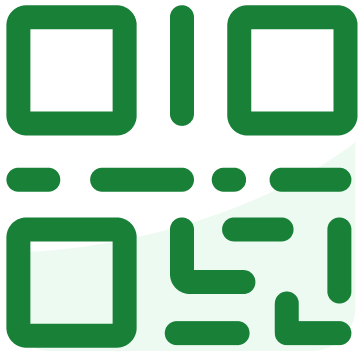

Join at slido.com
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Q1) Which of these inherited bleeding disorders is most likely?

1. Factor XIII deficiency
2. Fibrinogen deficiency
3. Bernard Soulier
4. Glanzmann Thrombasthenia
5. Wiskott-Aldrich Syndrome

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4.41 Which of these inherited bleeding disorders is most likely?

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Q2) What test will you do to confirm the diagnosis

1. PFA-100
2. Light Transmission aggregometry
3. Flow cytometry
4. Genetic testing
5. 2,3 & 4

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4.42 What test will you do to confirm the diagnosis?

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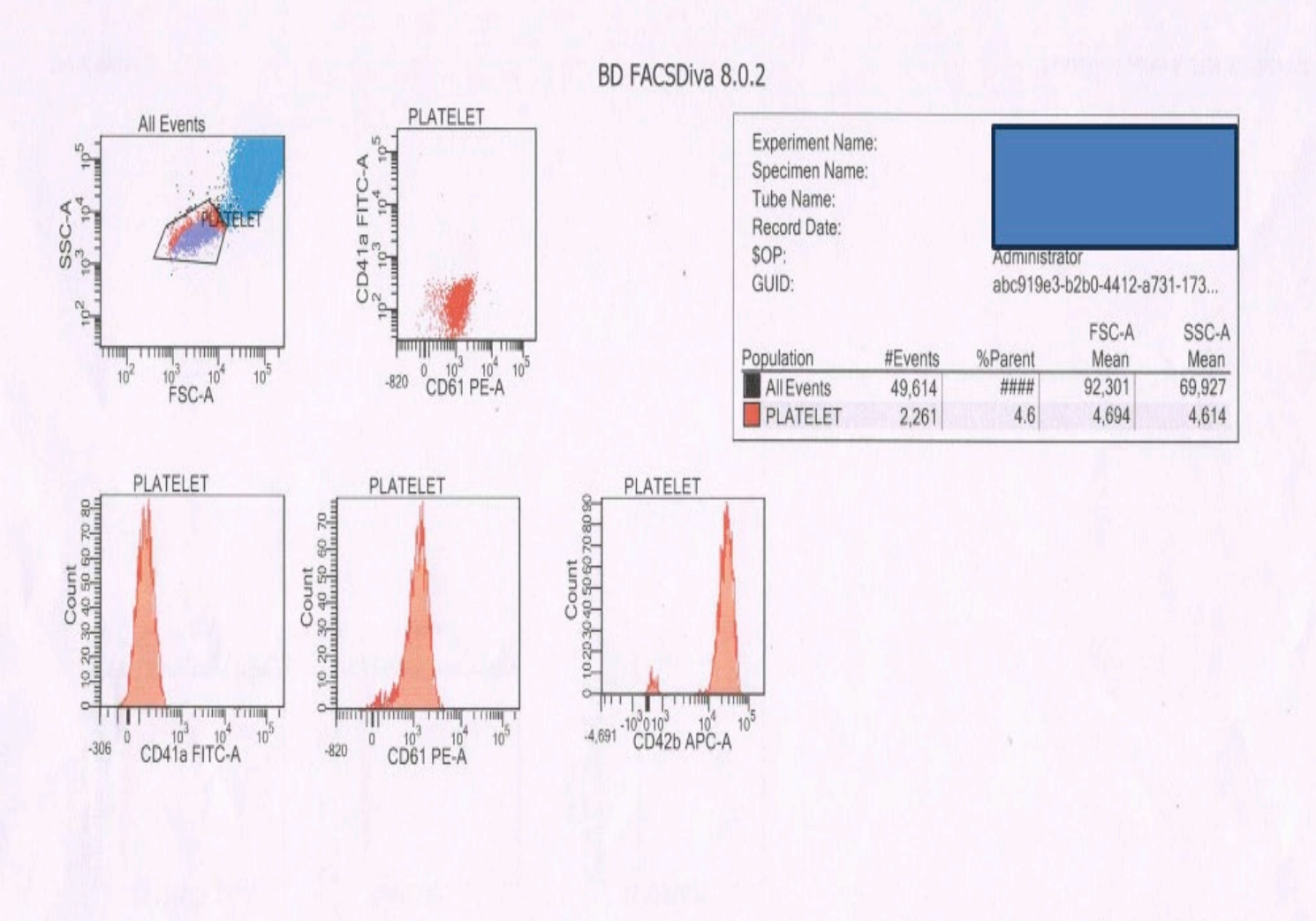
Flow Cytometry



Q-3 What does the flow cytometry show?

1. Absence of CD41 and 61
2. Normal
3. Absence of CD42
4. Absence of CD42 & CD 61
5. Absence of CD 61

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4.43 What does the flow cytometry show?

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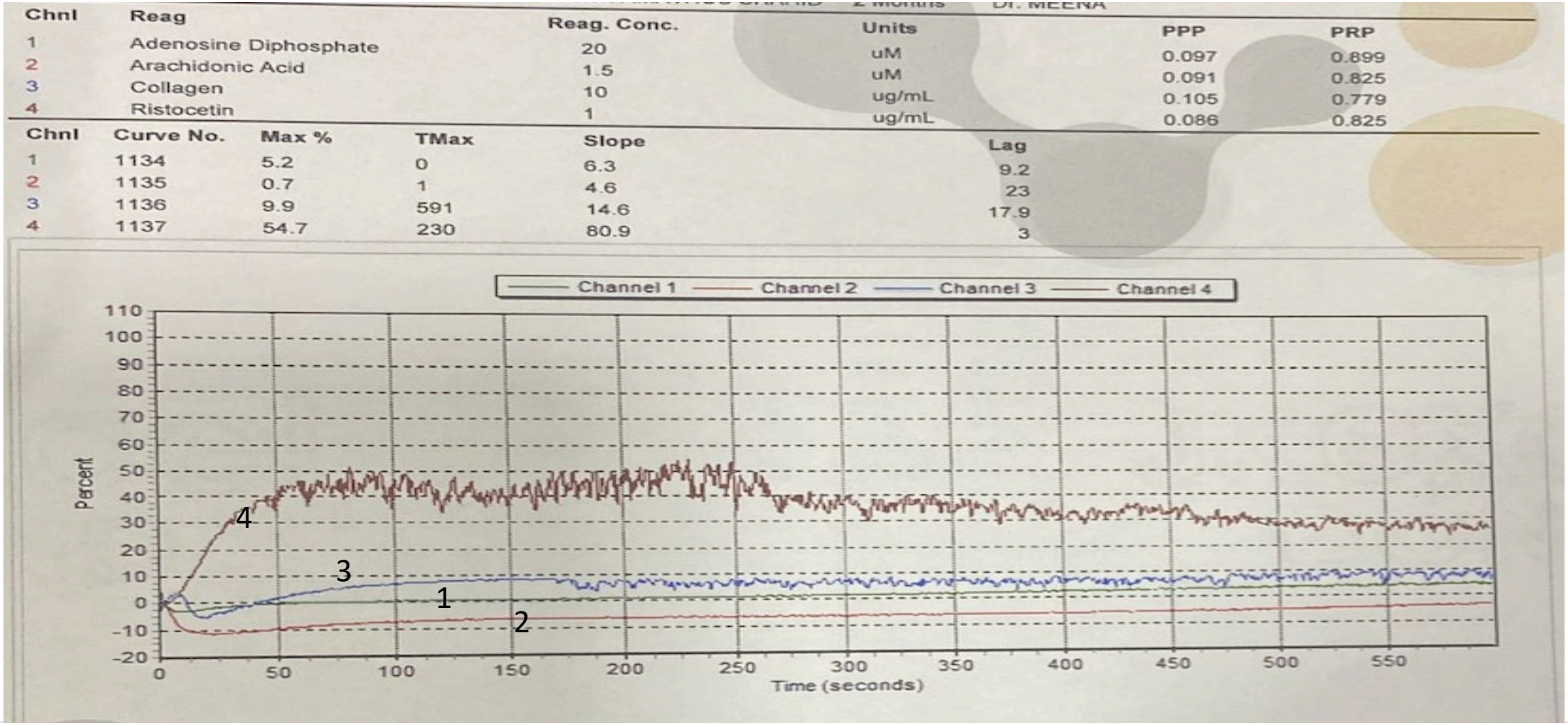
Light Transmission Aggregometry

Chnl	Reag	Reag. Conc.	Units	PPP	PRP
1	Adenosine Diphosphate	20	uM	0.097	0.899
2	Arachidonic Acid	1.5	uM	0.091	0.825
3	Collagen	10	ug/mL	0.105	0.779
4	Ristocetin	1	ug/mL	0.086	0.825

Chnl	Curve No.	Max %	TMax	Slope	Lag
1	1134	5.2	0	6.3	9.2
2	1135	0.7	1	4.6	23
3	1136	9.9	591	14.6	17.9
4	1137	54.7	230	80.9	3



Q4) What does the Light Transmission Aggregometry show?

1. No aggregation to Ristocetin
2. Aggregation to Ristocetin
3. Aggregation to ADP, Arachidonic Acid & Collagen
4. First wave aggregation with ADP, Arachidonic acid, collagen & partial agglutination with Ristocetin
5. Aggregation to Collagen

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4.44 What does the Light Transmission Aggregometry show?

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- She now presents with massive GI bleed with Haemoglobin of 30g/L
- Requiring 2-3 units of PRBC per day
- Endoscopy and colonoscopy is normal
- CT- Angiogram is normal
- Capsule endoscopy shows jejunal ulcers and diffuse mucosal bleed in jejunum
- Gastro-enterologists advise resection of involved jejunum
- Patient agrees for the surgery

Q5- How will you manage the surgery

1. Recombinant factor VIIa (NovoSeven)
2. HLA-matched platelets and recombinant factors VIIa
3. FEIBA
4. Desmopressin
5. Recombinant factor VIIa or FEIBA

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4.45 How will you manage the surgery

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Surgical Plan

- On admission: CBC, U&E, LFT, Coagulation Screen, Group & Save
- 1g IV Tranexamic acid at induction and continue TDS orally/IV for 10 days
- Transfuse 3 units of HLA matched platelets prior to surgery
- Administer Novoseven 90mcg/kg IV bolus, 30 minutes prior to surgery & continue with Novoseven 90mcg/kg IV every 2 hours for the first 48 hours post op
- Transfuse 1 unit of HLA matched platelet on completion of surgery in recovery
- After 48 hours depending on the clinical condition, may be able to reduce the frequency to every 4 hours for further 5 days

Hospital Course

- Patient was given Recombinant Factor VIIa and Cross-matched SDP
- Has uneventful surgery
- Unfortunately, during the surgery was found to have cirrhosis of liver
- Post-op Day 14- she develops jejunal perforation and undergoes emergency laparotomy and Gastro-jejunostomy
- Post-op Day 21- she develops bile leak and undergoes another laparotomy & feeding jejunostomy
- Patients cannot afford any more factors
- What would you do?
- How do you monitor haemostasis?

Q-6 How can you monitor haemostasis

1. TEG or ROTEM
2. Flowcytometry
3. Clinically
4. Global haemostatic Assay + Flowcytometry
5. All of the above

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4.46 How can you monitor haemostasis?

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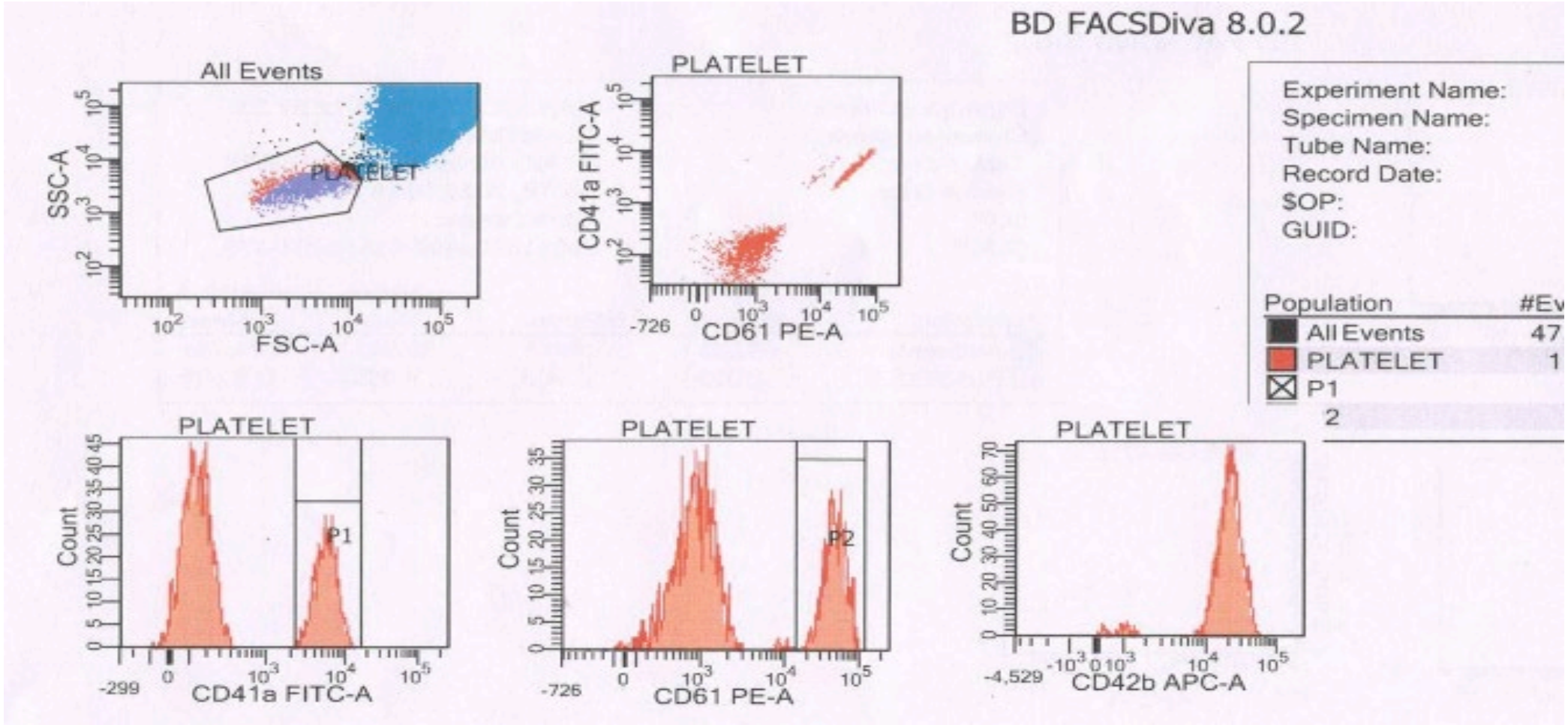
What did we do?

- Literature search
- Decided to proceed with cross-matched platelets after careful discussion with family and surgeons
- Used ROTEM and flow cytometry to guide haemostasis during surgery

Flowcytometry



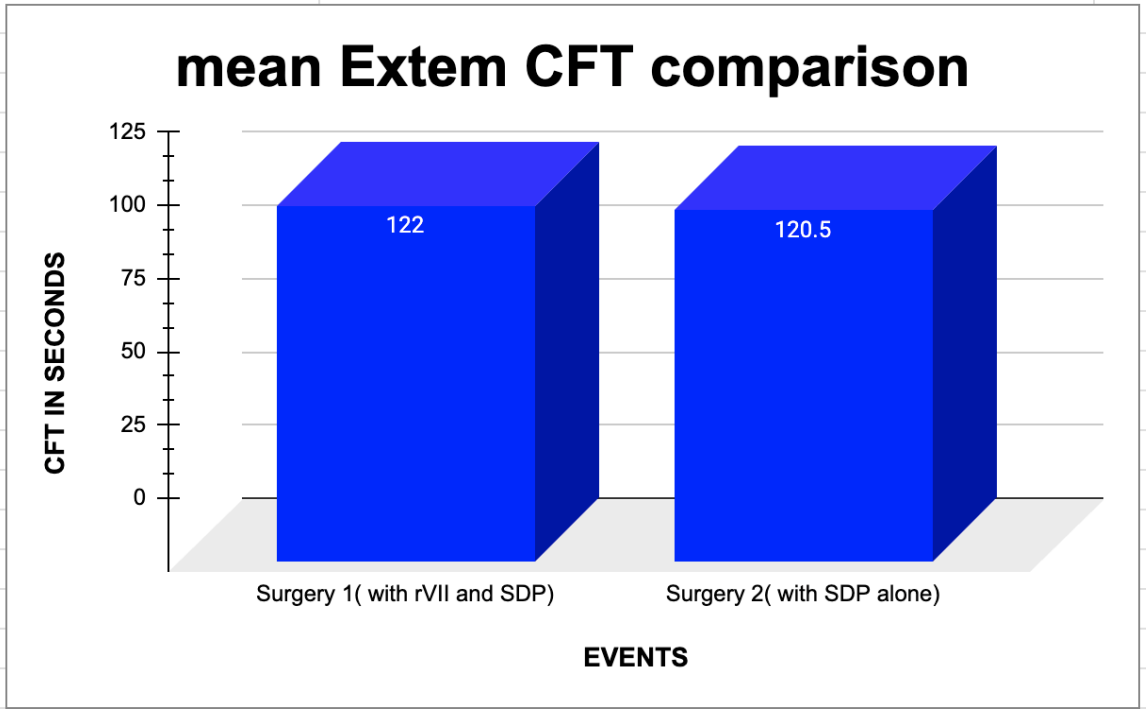
ROTEM

Interpretation of Results obtained from the ROTEM® and TEG® Devices

--- Device ---		
TEG®	**ROTEM®**	**Indicative of...**
Prolonged R Time	**Prolonged Clotting Time [CT]**	Factor deficiency Factor dysfunction Presence of anticoagulants Severe Hypofibrinogenaemia Severe thrombocytopenia
Prolonged K Time	**Prolonged Clot Formation Time [CFT]**	Factor deficiency Thrombocytopenia Platelet dysfunction Hypofibrinogenaemia
Decreased α angle	**Decreased α angle**	Thrombocytopenia Platelet dysfunction Hypofibrinogenaemia
Decreased Maximal Amplitude [MA]	**Decreased Maximal Clot Firmness [MCF]**	Thrombocytopenia Platelet dysfunction Hypofibrinogenaemia
Increased in EPL or LYS30/LYS60	**CLF**	Primary fibrinolysis Secondary fibrinolysis

ROTEM

EVENTS	MEAN EXTEM CLOT FORMATION TIME IN SECONDS(N: 40-85s)
Surgery 1(with rVII and SDP)	122
Surgery 2(with SDP alone)	120.5



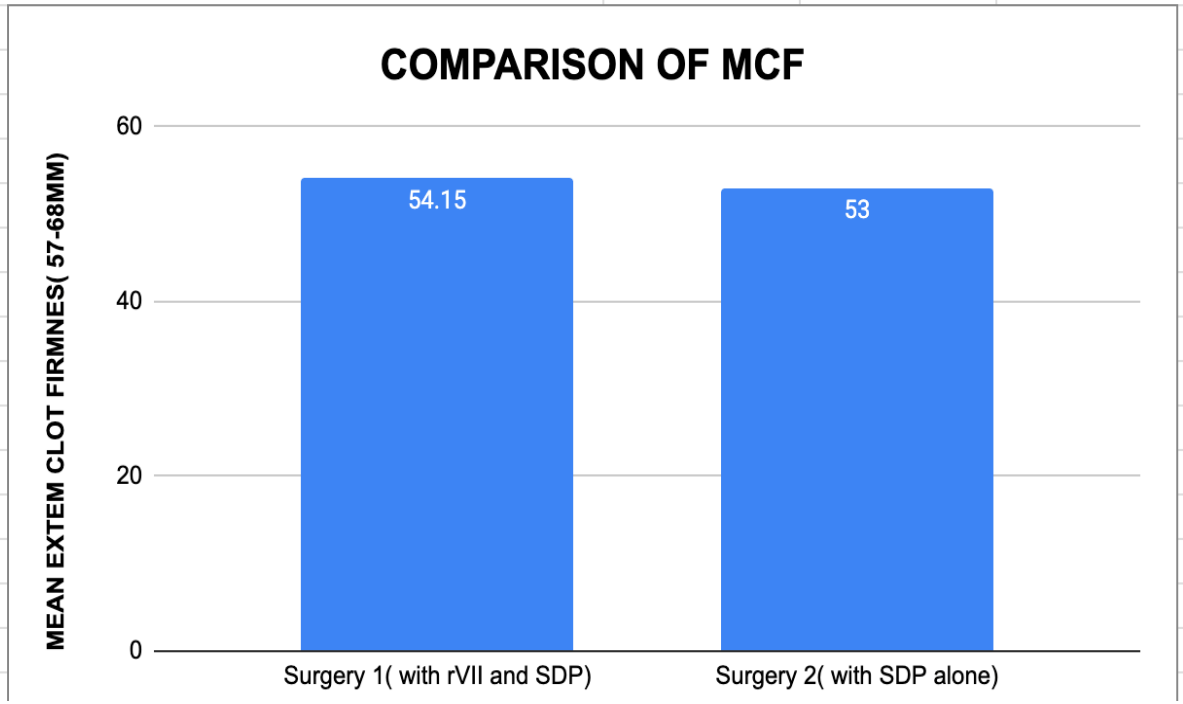
NovoSeven + SDP- 122 S

SDP – 120.5 S

Mean Clot formation time was similar

ROTEM

EVENTS	MEAN EXTEM CLOT FIRMNES(57-68MM)
Surgery 1(with rVII and SDP)	54.15
Surgery 2(with SDP alone)	53



NovoSeven + SDP- 54.15S

SDP – 53 S

Mean Clot firmness time was similar

Discussion

- Glanzmann is a rare autosomal recessive bleeding disorder
- Deficient in fibrinogen receptor GpIIb/IIIa causing defect in platelet aggregation
- Incidence is ~ 1 /1,000,000
- Usually present with muco-cutaneous bleeding
- Managing bleeding is a challenge especially in resource constraint settings
- Combination of assays can be used to monitor haemostasis during surgery

Discussion

- Tranexamic acid is used in mild bleeds
- Severe bleed will need HLA matched platelets and Novo Seven
- ROTEM and Flowcytometry could be used to titrate Novo Seven dosing
- Our experience shows major surgery can be done using only Cross matched platelets with aid of ROTEM and Flowcytometry

References

- Gomez, Keith, et al. "Clinical and laboratory diagnosis of heritable platelet disorders in adults and children: a British Society for Haematology Guideline." *British journal of haematology* 195.1 (2021): 46-72.
- Ganapule A, Jain P, Abubacker FN, Korula A, Abraham A, Mammen J, George B, Mathews V, Srivastava A, Viswabandya A. Surgical procedures in patients with Glanzmann's thrombasthenia: case series and literature review. Blood Coagul Fibrinolysis. 2017 Mar;28(2):171-175.
- Practical Haemostasis
- UpToDate