AN UNUSUAL CASE REPORT OF POST-TRANSFUSION PURPURA

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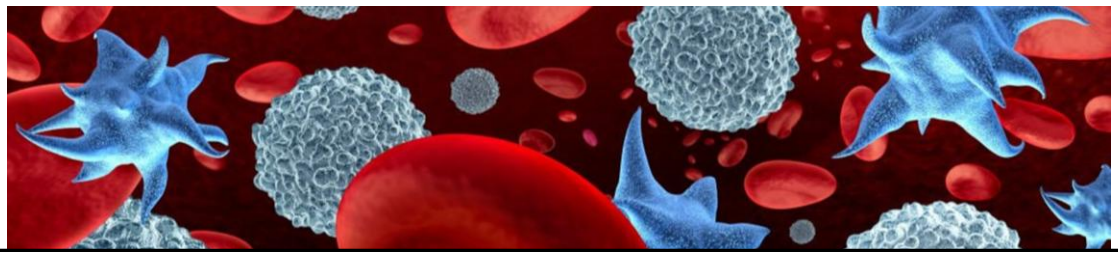
OBJECTIVES

1. Characterize the rare adverse condition of post-transfusion purpura (PTP).
2. Discuss the development of alloantibodies to human platelet antigens (HPAs).
3. Describe diagnosis, treatment, and management strategies for controlling PTP.



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WHAT IS POST-TRANSFUSION PURPURA (PTP)?

- Rare but serious clinical condition; common in multiparous females, multi-transfused patients
- Delayed transfusion reaction that occurs 5 - 10 days after transfusion
- Characterized by sudden drop in platelet count ⟶ THROMBOCYTOPENIA ⟶ BLEEDING!!!
- Mediated by antibodies to human platelet antigens (HPA); Anti-HPA-1a is most common
- Typically self-limiting; platelet counts recover in about 20 days
- Treatment includes high-dose intravenous immunoglobulin (IVIg), steroids, plasma exchange
- Diagnosis based on recent transfusion and identification of platelet-specific antibodies
  - ➢ Must differentiate from other causes of thrombocytopenia

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OTHER CAUSES OF THROMBOCYTOPENIA

DIC	HIT	Malignancy	ITP
Consumption of clotting factors & plts	AutoAb to heparin treatment	Spleen sequesters platelets	Broadly reacting autoAb
Clotting and bleeding	Platelets are mistakenly attacked	Lymph nodes, liver, and spleen become enlarged	Platelets are mistakenly attacked
Test clotting factors and bleeding time	Test for autoAb and Ab to heparin	Use imaging studies to confirm organomegaly	Test for autoAb vs platelet-specific Ab

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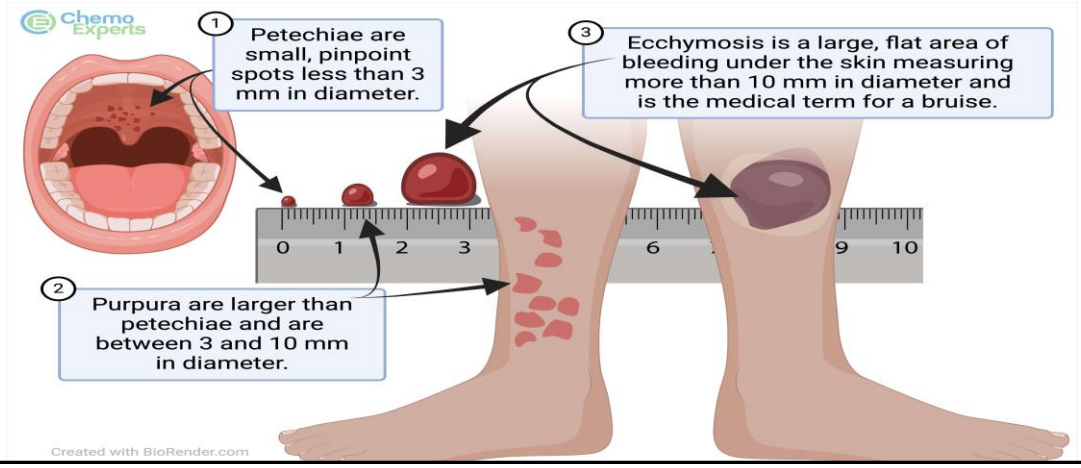
HOW DO WE KNOW A PATIENT IS THROMBOCYTOPENIC?

- Evidence of clotting issue and bleeding: mucosal bleeding, petechiae, purpura, ecchymosis



https://www.chemoexperts.com/bleeding-into-the-skin-petechiae-purpura-ecchymosis.html

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CASE DESCRIPTION

- 69-year-old man, Chicago IL
- History: coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), ST-elevation myocardial infarction (STEMI), stenting to coronary artery 6 days prior to current presentation
- Current condition: patient presents in refractory cardiogenic shock secondary to STEMI; stable, scattered ecchymosis, Hgb = 8.7 g/dL
- Initial treatment plan: extracorporeal membrane oxygenation (ECMO), pRBC transfusion

Owczarzak, L., Alrifai, T., Shivi, J., Dehghan-Paz, I. (2024). https://amjcaserep.com/abstract/full/idArt/942949

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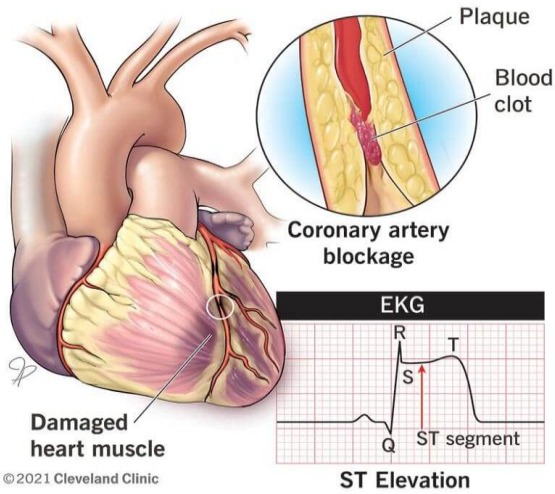
A FEW EXPLANATIONS...

- Coronary artery disease (CAD): arteries in the heart become narrowed or blocked completely
- Chronic obstructive pulmonary disease (COPD): progressive condition of damage and inflammation inside the airways
- ST-elevation myocardial infarction (STEMI): severe heart attack due to blockage and blood clot in coronary artery; ST refers to the ST segment on electrocardiogram (ECG)



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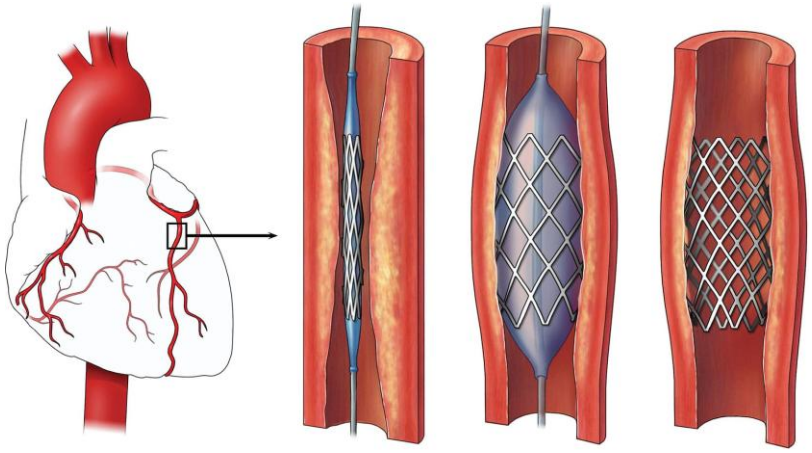
CORONARY STENTING



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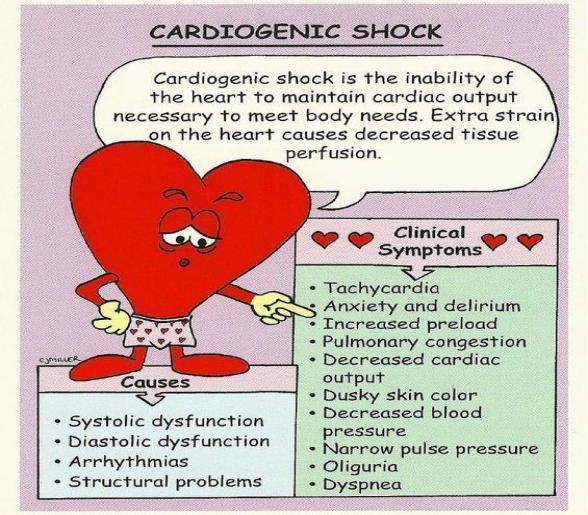
WHAT IS REFRACTORY CARDIOGENIC SHOCK?

- Cardiac and circulatory failure resulting in organ hypoperfusion - heart is unable to pump enough blood to meet the body's oxygenation needs
- Our patient experienced this 6 days after coronary stenting
- Required extra corporeal membrane oxygenation (ECMO)



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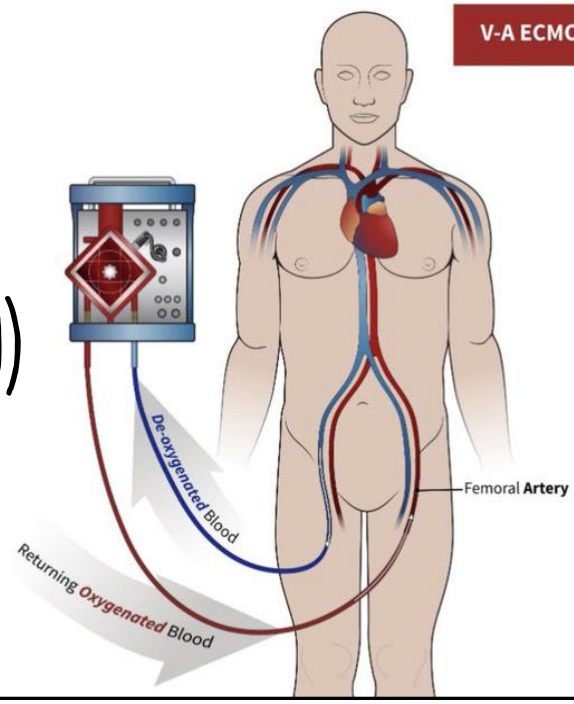
EXTRA CORPOREAL MEMBRANE OXYGENATION (ECMO)

- Temporary mechanical circulatory support
- Extracorporeal gas exchange



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EXTRA CORPOREAL MEMBRANE OXYGENATION (ECMO)

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CASE CONTINUES WITH PROFOUND THROMBOCYTOPENIA

- Patient hemoglobin was 8.7 g/dL upon admission (RR: 13.5 - 17.5 g/dL)
- Perioperative bleeding during ECMO cannulation
- Hemoglobin drops to 8.3 g/dL, patient receives transfusion of 1 unit of leuko-reduced pRBCs
- On day 4 of admission, platelet count plummets from 147,000/uL to <2,000/uL
- Patient receives 2 units of pRBCs and 2 units of apheresis platelets
- Hematuria from indwelling Foley catheter, oozing from femoral cannula

Owczarzak, L., Alrifai, T., Shivi, J., Dehghan-Paz, I. (2024). https://amjcaserep.com/abstract/full/idArt/942949

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DIFFERENTIAL DIAGNOSIS AND FURTHER WORKUP

DIC	HIT	Malignancy	ITP or PTP
PT/INR	AutoAb	Imaging revealed normal liver and spleen	Recent transfusion
Fibrinogen	DAT		ECMO

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SUSPICION OF POST-TRANSFUSION PURPURA (PTP)

- Patient was started on dexamethasone 40 mg daily for 4 days
- Intravenous immunoglobin (IVIg) 1g/kg daily for 2 days
- Supportive transfusion of 4 units of platelets
- Now time to hunt down the offending antibody

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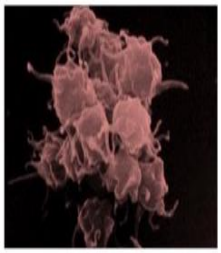
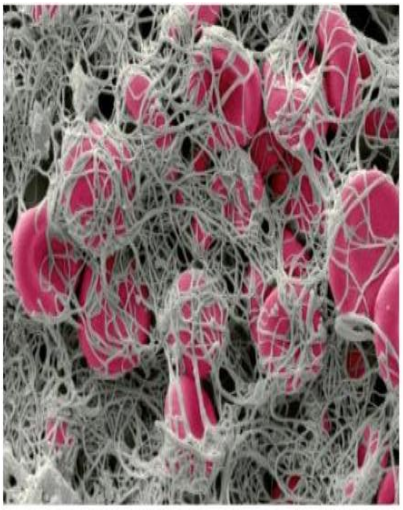
LET'S TAKE A CLOSER LOOK AT PLATELETS

- Annucleate discoid cells
- Fragments of megakaryocyte
- Once activated, will adhere to damaged blood vessel, cross-link with fibrinogen to form a fibrin clot
- May also play roles in inflammation, innate, and adaptive immune responses
- 150,000 - 400,000 per uL





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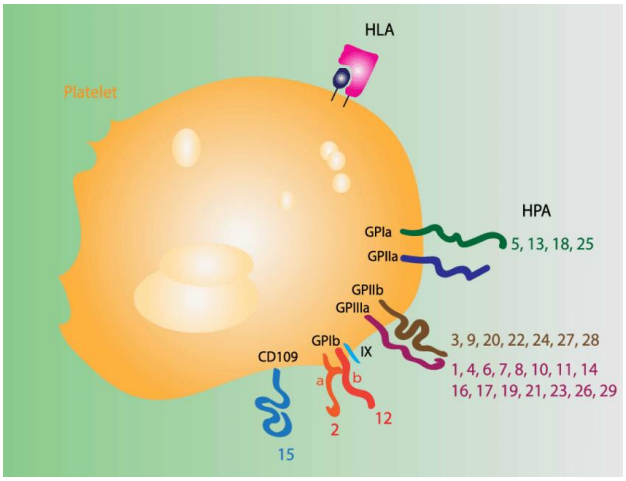
HUMAN PLATELET ANTIGENS (HPAS)

- Protein antigens on the surface of platelets
- Mediate platelet activity in hemostasis
- Bind collagen, fibrin, fibrinogen, von Willebrand factor (vWF)
- 35 HPAs on 6 platelet glycoproteins:

GPIa, GPIIb, GPIIIa, GPIbα, GPIbβ, CD109



Curtis, B. R. and McFarland, J.G. (2013). https://onlinelibrary.wiley.com/doi/epdf/10.1111/vox.12085

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HUMAN PLATELET ANTIGENS (HPAS)

- Each person has a unique platelet antigenic profile based on what genes are inherited
- 12 antigens exist in biallelic groups: HPA-1, HPA-2, HPA-3, HPA-4, HPA-5, HPA-15
- Expressed in polymorphic forms caused by single nucleotide polymorphism (SNPs)
- Numbered by order of discovery, with higher frequency antigen designated "a" and lower frequency antigen designated "b"

Curtis, B. R. and McFarland, J.G. (2013). https://onlinelibrary.wiley.com/doi/epdf/10.1111/vox.12085

Versiti - Human Platelet Antigen (HPA) Database

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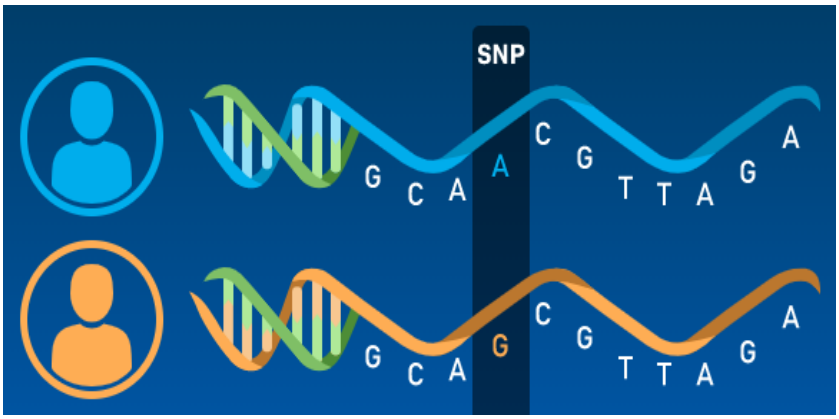
SINGLE NUCLEOTIDE POLYMORPHISMS (SNP)



HPA - 5a

HPA - 5b

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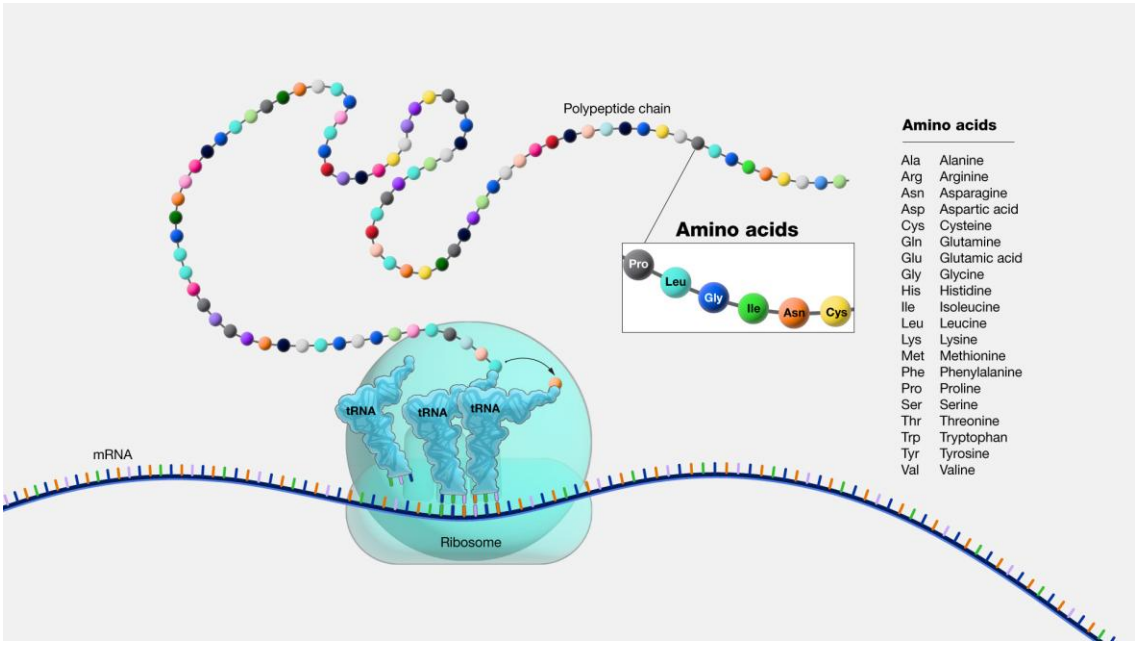

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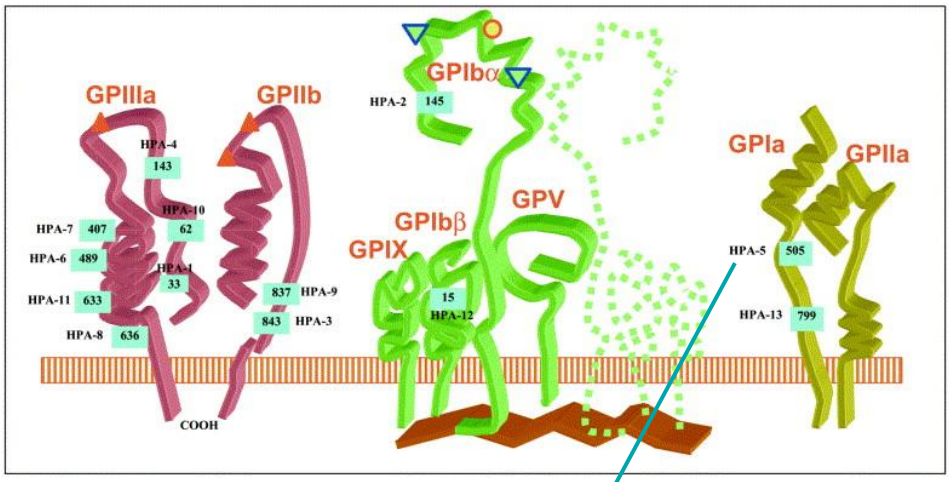

The platelet antigen, HPA-5, is expressed on glycoprotein Ia (GPIa) at position 505 on the amino acid chain
If the amino acid at position 505 is Glutamic acid, the antigen is HPA-5a
If the amino acid at position 505 is Lysine, the antigen is HPA-5b

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Antigen Group	Antigens on platelets	Allele frequency			Nucleotide change	Amino acid change
		Caucasian (%)	African (%)	Asian (%)		
HPA-1a ***HPA-1b***	1a 1a/1b 1b	72 26 2	90 10 0	100 0 0	T196C	Lysine – Proline
HPA-2a ***HPA-2b***	2a 2a/2b 2b	84 14 1	71 29 0	95 5 0	C524T	Threonine – Methionine
HPA-3a ***HPA-3b***	3a 3a/3b 3b	37 48 15	68 32 0	59.5 40.5 0	T2621G	Isoleucine – Serine
HPA-4a ***HPA-4b***	4a 4a/4b 4b	>99.9 <0.01 <0.01	100 0 0	99.5 0.5 0	G526A	Arginine – Glutamine
HPA-5a ***HPA-5b***	5a 5a/5b 5b	88 20 1	82 18 0	98.6 0.4 0	G1648A	Glutamic acid – Lysine
HPA-15a ***HPA-15b***	15a 15a/15b 15b	35 42 23	65 35 0	53 47 0	A2108C	Tyrosine – Serine

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SO HOW DO PEOPLE FORM ANTIBODIES TO PLATELETS?

Autoimmune

- Native (self) platelets attacked by mistake
- Loss of tolerance to self-antigens

Alloimmune

- Non-native (non-self) platelets stimulate antibody formation
- Pregnancy or transfusion

Drug-induced

- Certain medications can trigger formation of antibodies against platelets

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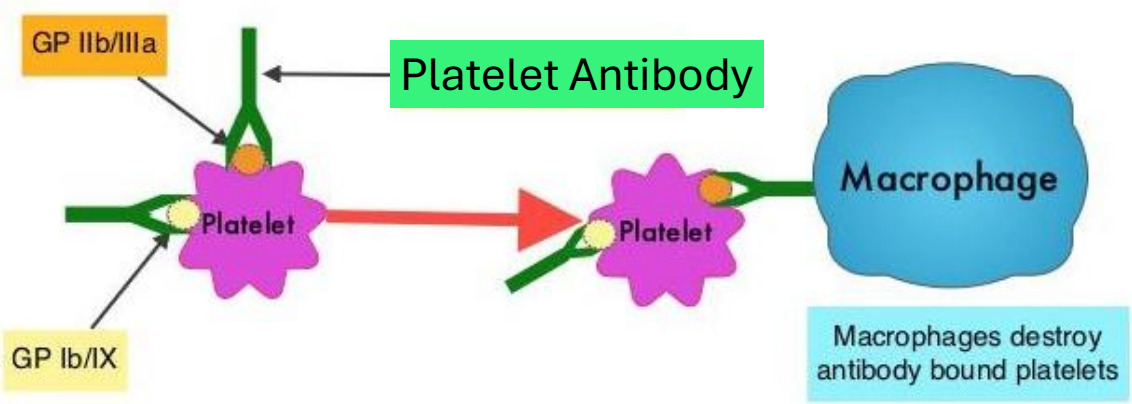
IMMUNE MEDIATED PLATELET DESTRUCTION



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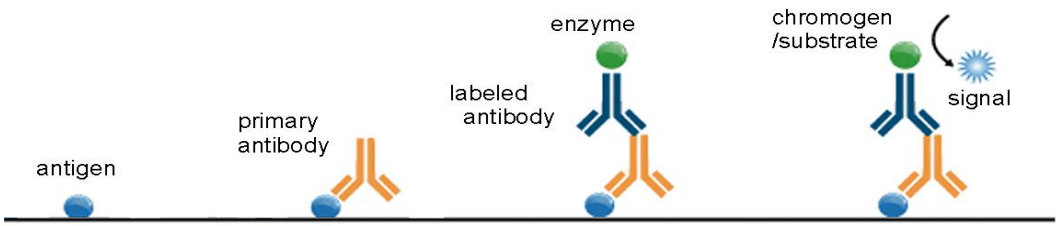
INITIAL TESTING FOR PLATELET ANTIBODIES

- Sample drawn 12 hours after onset of PTP
- Initial screening by ELISA using patient serum (red top)



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INITIAL TESTING FOR PLATELET ANTIBODIES

- Initial screening sent to American Red Cross Reference Lab
- Was negative for our patient

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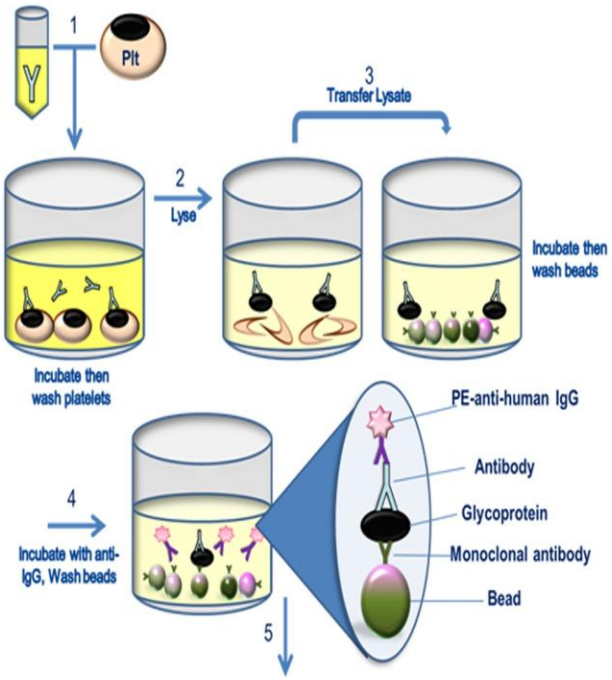
POST-TRANSFUSION PURPURA PANEL TESTING

- Sample drawn 3 days after PTP onset
- Monoclonal antibody immobilization (MAIPA)
- Platelet antibody bead array (PABA)
- Whole platelet flow cytometry assay
- PCR for genotyping patient's platelets



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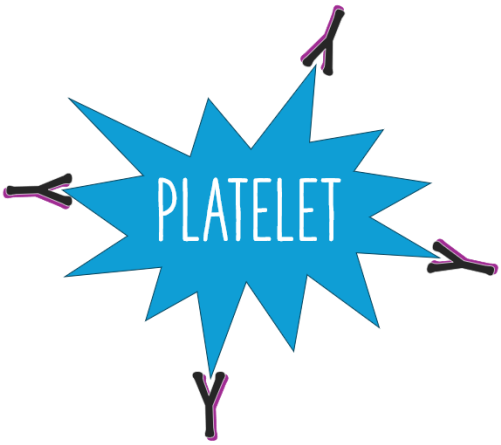
PANEL TEST RESULTS FOR OUR PATIENT



- PABA results: Anti-HPA-5b
- Patient genotype: HPA 5a/5a

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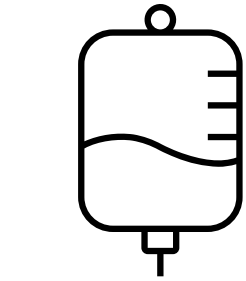

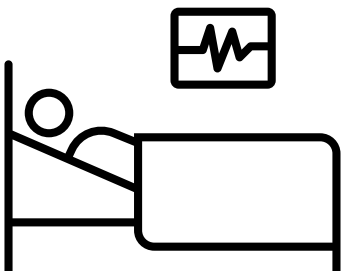

PATIENT CASE RESOLUTION

- Patient remained hospitalized for about 12 days
- Treated with dexamethasone x4 days and IVIg x2 days
- Received an additional 4 units of apheresis platelets
- Platelet counts recovered to > 100,000/uL by day 7
- Platelet count was 225,000/uL when discharged
- No recurrence of thrombocytopenia or transfusion since

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WHAT MAKES THIS CASE SO UNUSUAL

1 Patient was male with no prior transfusion history

- 95.5% of documented PTP cases are female
- Multiple pregnancies expose females to foreign platelet antigens, causing alloantibody formation
- Can be problem for mom if she needs platelet transfusion
- Can be problem for baby if antibody crosses placenta

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WHAT MAKES THIS CASE SO UNUSUAL

2 Onset of thrombocytopenia occurred more rapidly than usual

- Prior reports of PTP note severe thrombocytopenia occurring within 5 - 10 days after initial transfusion
- This patient: 4 days after index transfusion and 12 hours after second transfusion

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WHAT MAKES THIS CASE SO UNUSUAL

3 Characteristic bruising and bleeding was practically absent

- Most PTP cases report characteristic petechiae, purpura and significant mucocutaneous bleeding, often hemorrhaging
- Risk of mortality is 20% in most cases
- This patient: subtle hematuria and mild catheter oozing

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WHAT MAKES THIS CASE SO UNUSUAL

4 Culprit antibody, anti-HPA-5b, is somewhat novel

- 80-85% of PTP cases are caused by anti-HPA-1a
- Incidence of PTP caused by anti-HPA-5b is rare
- Very few people even have HPA-5b antigen

Antigen Group	Antigens on platelets	Allele frequency		
		Caucasian (%)	African (%)	Asian (%)
HPA-5a	5a	88	82	98.6
HPA-5b	5a/5b	20	18	0.4
	5b	1	0	0

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WHAT WE CAN LEARN FROM THIS CASE

- Not everything reads the book!
- Diagnosis of PTP requires high clinical suspicion based on patient presentation *AND* transfusion history
- Detectable levels of antibodies may lag behind symptom onset and laboratory evidence of thrombocytopenia
- Rapid diagnosis and management can reduce mortality risk, control outcomes, and mitigate recurrence of PTP with future transfusions

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THANK YOU FOR LISTENING!!!

What should we talk about next time?
Let me know on the evaluation!
Or contact me at
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Kristin Butler
LSU Health Shreveport

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