It’s a bird, It’s a plane, No It’s a…

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Saint Luke’s Hospital of Kansas City
SAINT LUKE’S HEALTH SYSTEM

Community Blood Center
Save a Life. Right Here, Right Now.

It's a Bird, It's a Plane, No It's a…

- 55 year old woman admitted 11/23/2015 for colon cancer that metastasized to her liver
  - History of 3 pregnancies
- Surgery was performed 11/23 to remove masses
  - Exploratory laparotomy led to right hepatic lobectomy
  - 10 hour surgery
- Lab values prior to surgery:
  - PLT 180 TH/uL (140-400)
  - Hgb 12.3 g/dL (12.0-15.0)

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- Given three packed cells during surgery and a couple units of plasma later that evening
- Surgery goes well, Hgb and PLT counts are monitored for next several days
- 11/23 Post-Op Hgb 11.4/PLT 215,000
- At midnight Hgb 8.5/PLT 115,000

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- 11/24 0440 Hgb 7.3 and PLT 98,000
  - Transfused 2 RBCs and 1 PLT
- After transfusion Hgb 9.6 and PLT 70,000
  - Transfused 2 thawed plasma and 1 PLT

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- Nothing else transfused after 11/24 and patient values start rising
  - 11/25 Hgb 8.3/PLT 65,000
  - 11/26 Hgb 8.7/PLT 80,000
  - 11/27 Hgb 9.6/PLT 111,000
  - 11/28 Hgb 10.4/PLT 157,000
  - 11/29 Hgb 10.1/PLT 146,000

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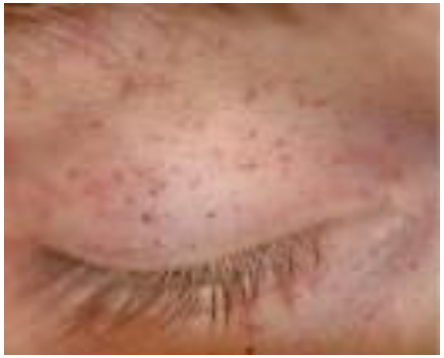
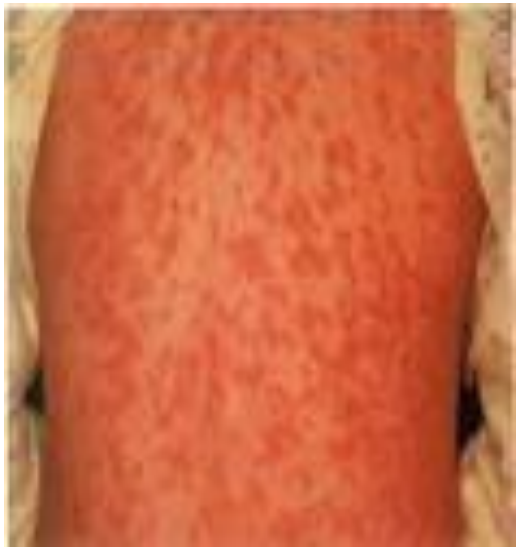
- 11-30 Hgb 10 g and PLT count 1,000
  - Patient bleeding from nose
  - Petechiae on arms, legs, thighs and trunk
  - Couldn’t move patient because would start bleeding





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- What could have caused a sudden drop in the platelet count?
  - Hematology/oncology consult on the case
    - ITP - Idiopathic thrombocytopenic purpura?
    - Medication related (Zosyn, famotidine, heparin)?
    - Autoimmune response from platelet transfusion?
- Sample obtained and sent to Community Blood Center for investigation into possible platelet antibody

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- At CBC
  - Sample received 11-30 for investigation of autoimmune thrombocytopenia
    - Platelet antibody screen and platelet bound IgG
  - Platelet count was 2,000
  - Platelet count was too low to get a monolayer so no platelet bound IgG performed
  - Platelet antibody screen was positive
    - Reactive 8/8 with Capture P solid phase adherence assay
    - ELISA assay showed HLA antibody and reactivity with 2 of 2 glycoprotein IIb/IIIa carrying the HPA-1a antigen

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- Human Platelet Antigens (HPA)
  - 34 HPA expressed on 6 different glycoproteins
    - GPIIb
    - GPIIIa
    - GPIa
    - GP1bα
    - GPIbβ
    - CD109
  - Six biallelic systems covering 12 antigens
    - HPA-1, -2, -3, -4, -5, -15
  - 22 other other HPA are low frequency or rare antigens

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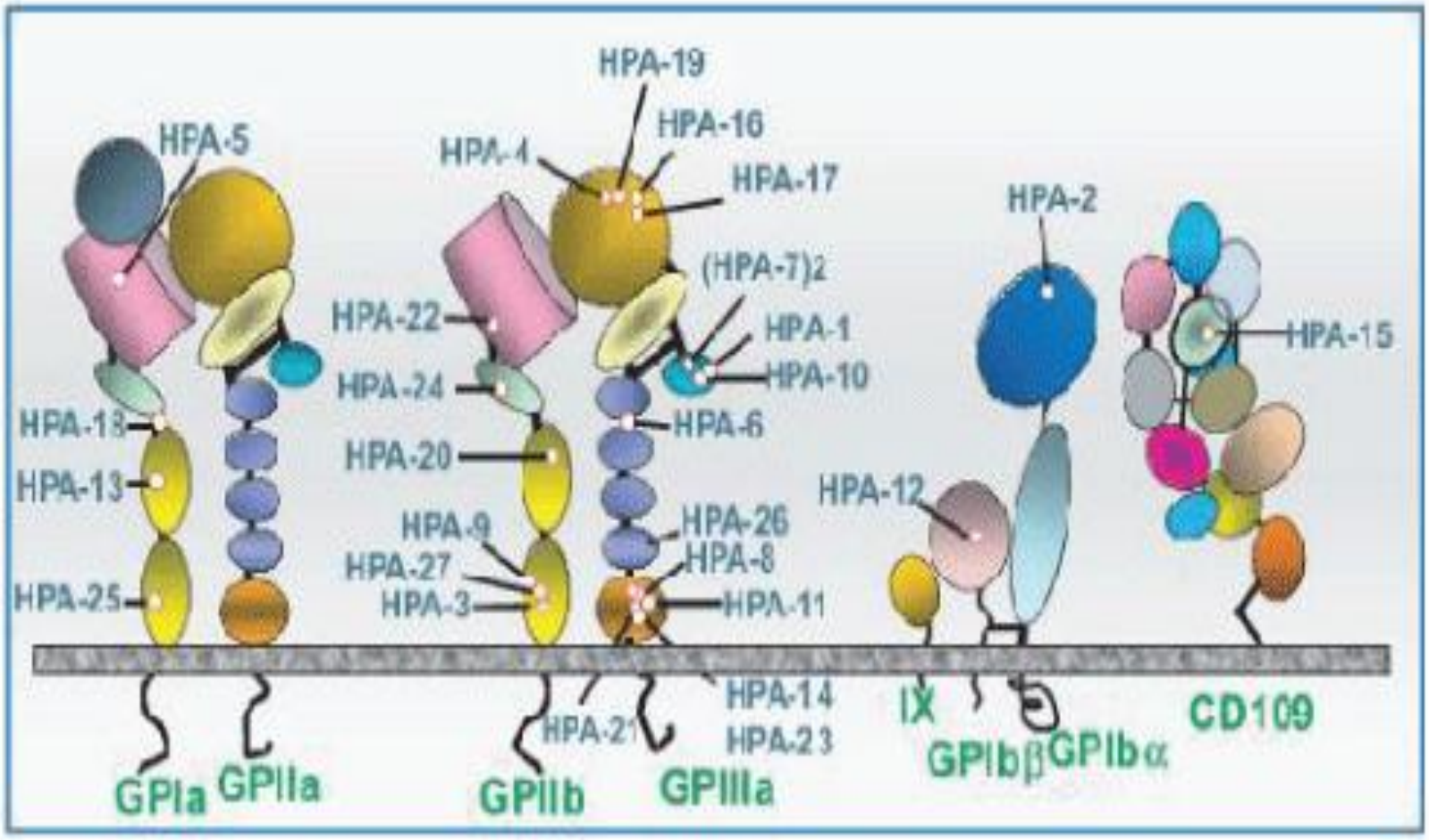
Platelet glycoproteins



New York Blood Center

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- GPIIb/IIIa
  - Most abundant molecule on surface of platelets
  - 20 of 34 HPAs reside on GPIIb/IIIa
  - Receptor for ligands important in mediating hemostasis and inflammation
- GPIb/V/IX, GPIa/IIa and CD109 express remaining 14 HPAs

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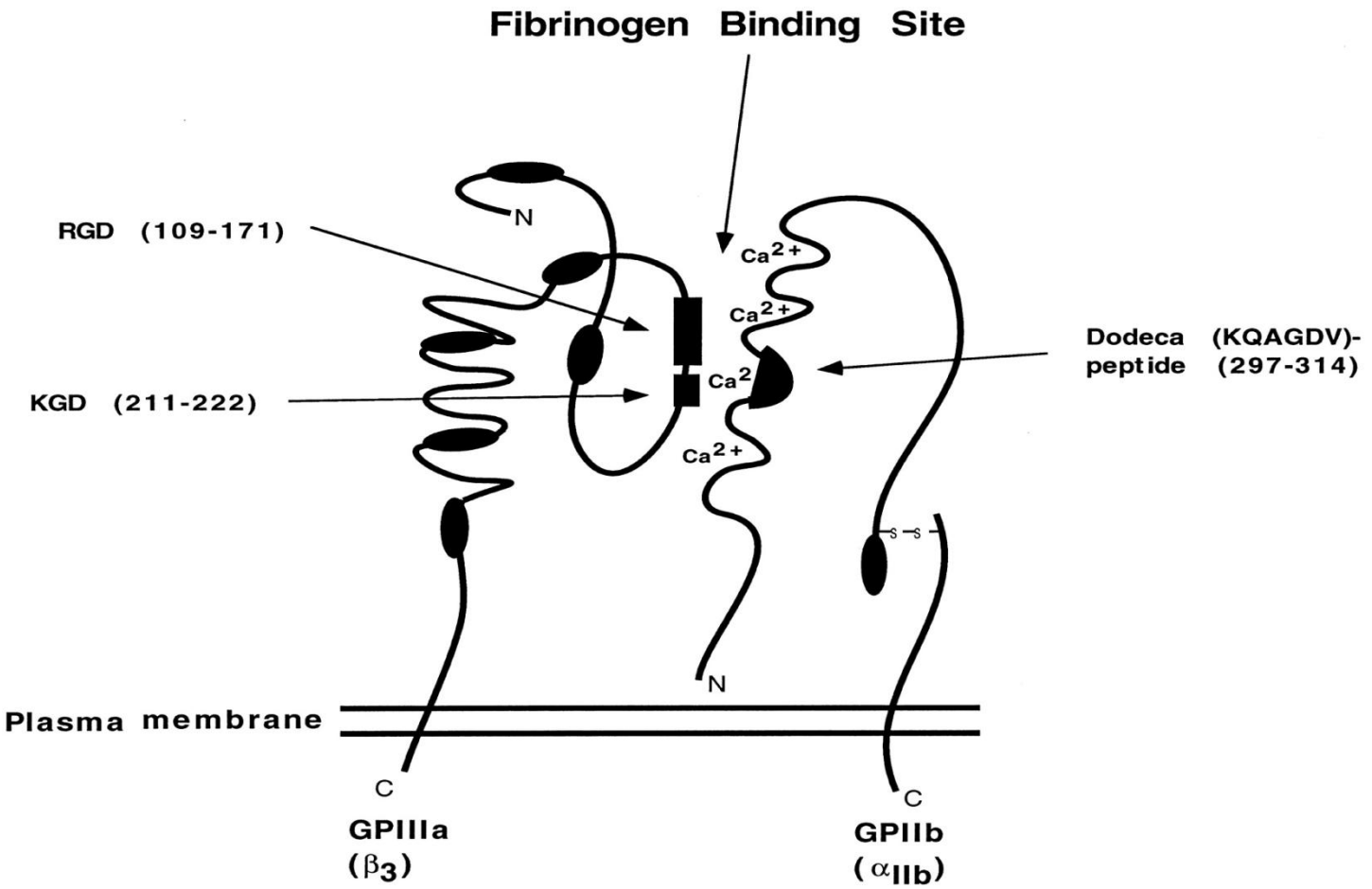
- GPIIb/IIIa



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- HPA-1a
  - Incidence of HPA-1a negative phenotype in Caucasians is ~2%
  - Anti-HPA-1a most common cause of neonatal immune thrombocytopenia (NAIT) in Caucasians and African ancestry
    - 85% of NAIT cases

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- Sample sent to NYBC for HPA-1a genotyping
  - Patient was HPA-1a negative
- What do these test results and history suggest as a possible diagnosis???
- Patient was transfused 11-23 and 11-24 with red cells, platelets and plasma

PTP- post transfusion purpura

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- PTP is a rare syndrome characterized by development of dramatic severe self limiting thrombocytopenia and bleeding
  - Purpuric rash, bruising, mucosal bleeding, gastrointestinal and urinary tract bleeding
  - Duration of thrombocytopenia in untreated patients is about 14-21 days
- Occurs 2-14 days after transfusion of blood products in patient's previously sensitized by pregnancy or transfusion
  - PTP is an anamnestic response

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- Most commonly associated with transfusion of RBCs
  - Also associated with platelets and plasma
- 30% of patients have major hemorrhage and mortality rate is 10-20%
- PTP caused by alloimmunization to human platelet specific antigens
  - Most often HPA-1a (90% of cases) alone or in combination with abys to other platelet antigens on glycoprotein IIb/IIIa
  - Other antibodies reported to cause PTP:
    - HPA-1b, HPA-3a, HPA-3b, HPA-4a, HPA-5a, HPA-5b
- Incidence of 1 in 50,000 to 100,000 transfusions

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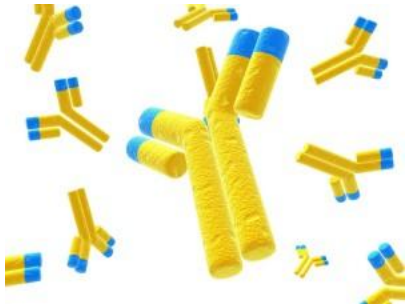
- Typically occurs in multiparous women but also reported rarely in men
  - Female to male ration is 5:1
- Patients who develop anti-HPA-1a often share certain HLA genotypes: HLA-B8 or HLA-DRB3*0101 and HLA-DQB1*0201
  - Similar to that seen in NAIT
- Platelet antibody destroys transfused and autologous platelets



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- Differential diagnosis includes consideration of other causes of thrombocytopenia:
  - Autoimmune thrombocytopenia
  - Drug induced thrombocytopenia
  - Disseminated intravascular coagulation
  - Heparin induced thrombocytopenia
  - Thrombotic thrombocytopenia purpura
- Diagnosis confirmed by clinical presentation and detection of platelet specific alloantibodies
  - Platelet genotype is helpful

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- 3 theories why autologous plts destroyed
  - Immune complexes bind to platelets through Fc receptor causing destruction of platelets
  - Donor derived soluble plt glycoprotein adsorbed onto autologous platelets making them susceptible to immune destruction
  - Immune response includes autoimmune component along with alloantibodies
    - Causes both autologous and transfused antigen negative platelet destruction
    - Most support for this theory

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- Treatment
  - High dose IVIG (2g/Kg) alone or in combination with corticosteroids
    - Usually results in plt count >100,000 in 3 -5 days
    - 85% response rate
    - Mechanism of action of IVIG is thought to be due to:
      - Anti-idiotype antibodies
      - Fc receptor blockage
      - Nonspecific binding of IG to platelet surface and/or
      - Acceleration of IgG catabolism
  - Plasma exchange may be helpful in patients who do not respond to IVIG

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- Treatment
  - Splenectomy for those that do not respond
  - Tx of antigen negative plts may be used in acute phase to help control bleeding but have decreased survival also
    - Plt count will not go up and stay up

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- Prevention
  - Recurrence of PTP after subsequent RBC transfusion is uncommon but has been reported
  - Recommend RBC and platelet products from corresponding antigen negative donors on subsequent transfusions
    - Value of this is unclear
  - Washed red cells may offer some protection against recurrence
    - Reports of PTP occurring after deglycerolized rejuvenated or washed red blood cells
  - UK report described decrease in PTP cases after implementation of universal RBC leukoreduction

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- HPA-1a negative products
  - Rare incidence of ~ 2%
  - How do you test for them?
    - Screen products at time of donation for HPA-1a
      - Serologically
        - No commercial antisera available
        - Must have source of anti-HPA-1a
        - Hard to find pure anti-HPA-1a without HLA antibodies also present
      - Molecular
        - Utilize DNA from donor
        - CBC actively screens for HPA-1a negative donors

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- How do you get HPA-1a negative products
  - Screen for HPA-1a negative platelets
    - Limited amount of products donated in a day
    - May take several days of random screening
  - Some centers maintain donor lists of HPA-1a donors
    - Call donors in to donate
      - Must schedule donors
      - Wait for release from processing
  - Import HPA-1a negative platelets from other providers

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- Recap on patient:
  - Previously has had a normal platelet count – drops from surgery
  - Given two units of platelets 11/24/2015
  - Platelet count remains normal for the next 5 days
  - Sudden drop occurs on day 6 11/30/2015
    - Petechiae and nose bleeds
  - CBC confirms platelet antibody – HPA-1a antibody

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- Treatment plan for patient:
  - Order for IVIG 50g dose of 1000 mg/kg once a day from 11/30-12/2
  - Zosyn and famotidine discontinued 11/30 in case medication related
  - Afrin for nose bleeds (eases congestion and sinusitis)
  - Transfuse HPA-1a negative platelets but want to avoid giving platelets as this may lead to further immune response
    - Recommended to transfuse only during bleeding episodes
  - Washed RBCs should be given
  - Avoid plasma transfusions to avoid subsequent events

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- 11/30 HPA-1a negative plt ordered from CBC to have on hand in the event of bleeding and/or a of PLT <10,000
- 12/1 Hgb 8.6/PLT 5,000
- 12/2 Hgb 9.7/PLT 7,000 @ 0030
  - Doing well in AM, healing at surgical sight; no nose bleeds – Afrin spray continued
- 12/2 Hgb 9.2/PLT 1,000 @ 2038
  - Bleeding during bowel movement, blood in urine, vaginal bleeding @ 2000
  - HPA-1a negative PLT transfused at 2130

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- 12/3 @ 0024 Hgb 8.4/PLT 5,000
  @ 0902 Hgb 9.0/PLT 39,000
- 12/4 @ 0102 Hgb 8.5/PLT 1,000
  - HPA-1a platelet ordered and given 12/4 @ 2247
  - Discovered 50 g dose of IVIG was incorrect for patients weight and 110 g dose of 1000mg/kg given 12/4 and discontinued after one dose – total of 4 IVIG doses
- 12/5 Hgb 7.2/PLT 18,000
- 12/5 1 saline washed HPA-1a negative RBC ordered from CBC to have on hand
  - Unit not given expired
- 12-5 HPA-1a negative PLT ordered from CBC
  - None available. CBC calling in donors to donate

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- 12/6 Hgb 7.0/PLT 8,000
- 12/7 Hgb 7.2/PLT 12,000
- 12/8 Hgb 6.3/PLT 45,000
- Platelet count increasing while hemoglobin drops
  - One washed HPA-1a negative RBC is ordered and transfused 12/8 1500
  - 12/9 @ 0201 Hgb 8.0/PLT 60,000
- Further platelet transfusions cancelled as count is up

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- Patient outcome
  - Pt hemodynamically stable (HgB 9.0 & PLT 139) and discharged 12/9 @ 1819
  - Seen again in ED for post-surgical staph infection and admitted 12/14
    - Hepatic fluid collection
    - Augmentin given for infection then discharged 12/17 – no transfusions needed

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- Patient continually followed by Oncology for the next few months
- Lab work drawn a minimum of 2X a month
  - Platelet count and hemoglobin remain stable and continue to rise
  - No symptoms of bleeding
- Office visit about once a month

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- Waiting for patient to fully recover from surgery and infections to continue with cancer treatment

- 3/22/2016
  - Hgb 11.0 and PLT count 198,000 and patient states they now feel ready to move forward with chemotherapy treatment for next 4 months

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- Women with history of PTP may be at increased risk for having a pregnancy affected by neonatal alloimmune thrombocytopenia (NAIT)
  - Increased risk of PTP in women who have previously had children with NAIT has not been reported

Official Lab Ninja

Designated Blood Bank Brain

PTP will not prevail!!

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Objectives

- Discuss the clinical manifestations associated with post transfusion purpura
- Discuss the testing required to diagnose post transfusion purpura and the common antibodies associated with post transfusion purpura
- List the recommended treatment for post transfusion purpura and recommendations for blood products for transfusion