Platelets: Purpose, Pictures plus Problems

Platelets – The Basics

- Platelets are also called thrombocytes
- Biconvex discoid in shape
- Cytoplasmic fragments of a megakaryocyte
- Platelets do not have a nucleus
- Shed in the bone marrow and found in the peripheral blood
- 1/3 the size of a normal erythrocyte with a ratio of platelet to red blood cell approx. 1:15
- Four zones
  1) Peripheral  2) Sol-gel  3) Organelle  4) Membranous
From Stem Cell to Mature Blood Cells

- Stem Cell to Platelet

Platelet Production is driven by the Hormone, 
**Thrombopoietin** produced in the Kidneys and Liver
Breaking it Down

- **Peripheral Zone**
  - Rich in glycoproteins required for adhesion, activation and aggregation

- **Sol-gel Zone**
  - Rich in microtubules and microfilaments allowing platelets to maintain the discoid shape

- **Organelle Zone**
  - Rich in platelet granules
    - Alpha - contain clotting mediators - Factors V, VIII, Fibrinogen
    - Delta - also called “dense bodies” contain ADP, calcium & serotonin

- **Membranous Zone**
  - Endoplasmic reticulum-derived membranes organized into a dense tubular system responsible for thromboxane A2 synthesis

Let’s Take a Look
Platelets’ Role in Hemostasis

- **Adhesion**
  - Platelets attach to substances outside the interrupted endothelium

- **Activation**
  - Platelets change shape, turn on their receptors and secrete chemical messages

- **Aggregation**
  - Platelets connect to each other through receptor bridges

**Formation of the platelet plug is associated with the activation of the coagulation cascade resulting in fibrin deposition**

---

Looks Like a Horror Movie

**Activated platelets**
Platelet Kinetics

- Megakaryocyte and platelet production is regulated by thrombopoietin, a hormone produced in the kidneys and liver
- Each megakaryocyte produces between 1,000 and 3,000 platelets during its lifetime
- An average of 10 billion platelets are produced daily in healthy adults
- Reserve platelets are stored in the spleen and released when needed by splenic contraction
- Average life span of a circulating platelet is 6-8 days
- Old platelets are destroyed by phagocytosis in the spleen and liver

Platelet Dynamics

- **193** proteins and **301** interactions are involved
- Three stages – Adhesion, Activation, Aggregation
- These stages occur in rapid succession and each continues until the trigger for that stage is no longer present – lots of overlap!!
Come Together

Super Simplified

- **Adhesion**
  - When an endothelial layer is disrupted, collagen and vWF anchor platelets to the subendothelium.
  - Platelet GP1b-IX-V receptor binds with vWF and GPVI receptor binds with collagen

- **Activation**
  - Occurs seconds after adhesion starts
  - Activated platelets secrete the contents of their granules through their canalicular systems to the exterior
  - Morphology of platelet changes and becomes “sticky”

- **Aggregation**
  - Occurs minutes after activation starts
  - Shape changes from curled to straight and becomes capable of binding
Platelet Disorders

- There are several things that can cause problems

  - **Thrombocytopenia** - Not enough

  - **Thrombocytosis** - Too many

  - **Dysfunctional** - Not working correctly

Thrombocytopenia – Not Enough

- Immune Thrombocytopenic purpura (ITP)
- Thrombotic Thrombocytopenic purpura (TTP)
- Chemotherapy induced
- Splenomegaly
- Drug induced
- Aplastic anemia
- Pregnancy associated
- Babesiosis
- Pseudothrombocytopenia

- And it goes on and on and on
## Thrombocytosis – Too Many

### Reactive
- Chronic infection
- Chronic inflammation
- Malignancy
- Post splenectomy
- Iron deficiency
- Acute blood loss

### Myeloproliferative neoplasms
(platelets elevated and dysfunctional)
- Essential thrombocytosis
- Polycythemia vera
- Congenital
- Associated with other myeloid neoplasms

## Dysfunctional – Not Working

### Congenital
- Bernard-Soulier Syndrome – adhesion disorder
- Hemansky-Pudlak Syndrome – activation disorder
- Wiskott-Aldrich Syndrome – aggregation disorder
- Plus many, many more......
  - Granule amount and release disorder
  - ADP receptor defect
  - Storage pool defects

### Acquired
- PNH (Paroxysmal Nocturnal Hemoglobinuria)
- Asthma
- Cancer
- Samter’s Triad (aspirin exacerbated respiratory disease)
Drugs – Just Say “NO”

• Different drugs can affect platelet function in various ways.
  o **Suppress Platelet Function**
    • Aspirin
    • Clopidogrel
    • Cilostazol
  o **Stimulate Platelet Production**
    • Thrombopoietin mimetics
    • Desmopressin
    • Factor VIIa

Aspirin – Just for a Minute

• Aspirin irreversibly disrupts platelet function by inhibiting cyclooxygenase -1 (COX-1) thus preventing normal hemostasis
• Platelets in the presence of aspirin are unable to produce new cyclooxygenase
• Normal platelet function will not return until the use of aspirin has ceased and old platelets are replaced with new ones that haven’t been exposed to aspirin
• Time to return to normal function after discontinuing use of aspirin is about one week
Symptoms of Platelet Disorders

- Excessive bleeding
- Spontaneous bleeding
- Petechiae
- Purpura
- Bleeding gums
- Nose bleed
- G.I. bleed
- Menorrhagia
- Intracranial bleeding
- Thrombosis

Pictures to Ponder
Pictures to Ponder

Purpura

That looks nasty

Nose Bleed

Bleeding Gums
Pictures to Ponder

Taking a Closer Look at ITP

- **Immune (Idiopathic) Thrombocytopenic Purpura**
  - Autoimmune disorder resulting in thrombocytopenia
  - Etiology unknown
    - Acute infection may trigger
    - Increased prevalence in people with systemic autoimmune diseases such as Rheumatoid arthritis and systemic lupus (SLE)
    - Genetic component suspected to predispose
  - Complex, unbalanced immune response
  - Antibodies attach to platelet surface-membrane glycoproteins
  - Platelets bound by these antibodies contain the FC region of the antibody and are cleared by FcyR-bearing macrophages in the reticuloendothelial system (monocytic phagocytic cells in the spleen)
  - Macrophages are highly stimulated which adds to the efficient binding of the coated platelets
**A Picture Says 1000 Words**

- Platelet opsonization occurs = decreased platelets
- And an interesting aside, platelet production also decreased

---

**Treatment of ITP**

- Treatment is based on severity of symptoms and not on platelet count.
- First line therapy for ITP is corticosteroids
  - These suppress the immune system (T and B cell reactivity)
  - Urgent situations require infusions of dexamethasone or methylprednisolone
  - Less severe cases are usually treated with oral prednisone
  - Steroid therapy is reduced as the platelet count increases and patient symptoms stabilize
  - Approx. 75% of patients will experience a relapse during dose reduction or cessation
Other Options for ITP Treatment

- Anti-D (must be Rh positive to be a candidate)
- Immunosuppressants
- Vincristine
- IVIg
- N plate (Romiplostim)
- Splenectomy

TTP – What’s the Difference

- Thrombotic Thrombocytopenic Purpura
  - Thrombotic microangiopathy
  - Platelet consumption resulting in thrombocytopenia
  - Rare disease – only 6 cases per million per year – most acquired but rare congenital
  - Occurs when there is an ADAMTS13 deficiency
    - Autoimmune disease – development of inhibitory antibodies to ADAMTS13 (A Disintegrin And Metalloproteinase with Thrombospondin type 1 motifs, member 13) (Now that’s a long name)
  - Acute, life threatening disease that is a medical emergency
  - Symptoms
    - Thrombocytopenia
    - Hemolytic anemia
    - Confusion
    - Headaches
    - Visual problems
    - Renal impairment
    - Fever

Let’s talk about this
TTP in Layman’s Terms

• VWF (VonWillebrand’s Factor) is a multimeric plasma glycoprotein that recruits platelets to the site of vessel injury
• VWF multimeric size directly relates to its hemostatical activity
  • The bigger it is the more hypercoagulability the VWF multimer
• Regulation of the VWF size is controlled by ADAMTS13
• Deficiency in ADAMTS13 allows VWF multimer to increase in size and in hyperactivity
• Results are unwanted platelet aggregation and platelet rich thrombus formation

Treatment for TTP

• First line treatment for TTP is plasma exchange
  o Plasma exchange removes circulating ADAMTS13 autoantibodies and provides a fresh source of ADAMTS13
  o Decreases mortality from 90% down to 10%
  o During crisis – patient undergoes plasma exchange 2-3 times a day until stable and then once a day until the 2nd day after platelet count is back to normal
  o Continued exchange every 3-4 weeks to prevent relapse
• ADAMTS13
  o No natural inhibitor
  o Long plasma half-life
  o Relatively low levels required to keep VWF multimers in check
• Immunosuppression drugs are used to combat the autoimmune component of the disease
### Chemotherapy Induced Thrombocytopenia

- Chemotherapy-induced thrombocytopenia (CIT) is a common hematologic side effect of both myelosuppressive and ablative therapy.

- CIT has the risk of life-threatening spontaneous hemorrhage.

- CIT necessitates reduction and delays in chemotherapy treatment:
  - Dose and time schedule of chemo drug is scientifically derived to produce the best chance of survival or cure.
  - When dose of therapy is reduced or treatment cycles prolonged, cure rates are lowered.

### What Causes CIT?

- **Chemotherapy works by killing rapid growing cancer cells**
  - Hematopoietic progenitor cells are also rapid growing cells.
  - Chemotherapy interferes with cell production in the bone marrow.

- **Thrombopoietin is the primary regulator of thrombopoiesis**
  - Promotes megakaryocyte differentiation from stem cells.
  - Works in conjunction with other cytokines including interleukin.

- **Interaction between megakaryocytes and bone marrow stromal components are critical for platelet production**
  - Chemotherapy results in myeloaablation of the marrow stroma.
  - Megakaryocytes cannot be produced until the hematopoietic tissue bed repairs and reconstitutes.
Treatment for CIT

• Most common treatment is platelet transfusion
  o Transfusions are a temporary fix until the bone marrow can start producing platelets on its own
  o Dose reduction of chemotherapy or holding chemotherapy will allow the marrow to recover more quickly

• Growth factor drugs used to stimulate production
  o Romiplostim (Nplate)
  o Eltrombopag (Promacta)

---

Thrombocytosis in Iron Deficiency

• Iron Deficiency is the leading cause of anemia
• Microcytic-hypochromic iron deficiency anemia impairs oxygen delivery to the tissues
• Iron deficiency anemia has lower numbers of circulating red cells - less cells to carry the oxygen
• Receptor cells in the kidneys detect low O2 levels
• Kidneys respond by increased secretion of erythropoietin into the blood
• Erythropoietin causes the proerythroblasts in the bone marrow to mature more quickly
  
  Nice, but what does this have to do with platelets????????
**Thrombocytosis in Fe Deficiency**

- **Side effects of Erythropoietin in the bone marrow**
  - There is a degree of homology in the amino acid sequence in erythropoietin and thrombopoietin (the hormone that stimulates platelets)
  - The result is there is also stimulation of the megakaryoblasts by the erythropoietin resulting in an increased production of platelets

- **Reactive Thrombocytosis occurs**
  - The greater the degree of iron deficiency the greater the degree of thrombocytosis
  - Increased chance of thrombosis - can be life threatening

- **Vice Versa**
  - Treatment of the iron deficiency reduces the thrombocytosis and the chance of a thromboembolic event

---

**Case Studies**

Finally, What You’ve Been Waiting For!
Fall in Michigan

48 year old married man with twin 14 year old sons is diagnosed with Pancreatic Cancer – DX 157.0. He has no family history of cancer of any kind. He presented with upper abdominal pain – like an ulcer. CT scan showed a mass on the head of the pancreas and biopsy confirmed adenocarcinoma. Patient is going through first line treatment with Gemcitabine (Gemzar). Treatment plan is 7 cycles of Gemzar and then a recheck of scans and CA19-9 tumor marker.

Note: A cycle is three weeks long. Chemotherapy drug is given on day one and day eight. In addition, laboratory work, including a CBC is done on these days. No drug is given on day fifteen but the patient presents for lab tests and a nurse evaluation.

Weekly CBC’s are drawn to make sure blood counts are within range so drug can be given safely.

Baseline CBC obtained: Cycle 1 – Day 1

WBC, RBC, and PLT all within normal range, the HGB is slightly decreased

<table>
<thead>
<tr>
<th>COMPLETE BLOOD COUNT - Final</th>
<th>Ordered by: 001</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>5.3 x10^3/ul</td>
</tr>
<tr>
<td>RBC</td>
<td>4.48 x10^6/ul</td>
</tr>
<tr>
<td>HGB</td>
<td>13.1 g/dL</td>
</tr>
<tr>
<td>HCT</td>
<td>37.7%</td>
</tr>
<tr>
<td>MCV</td>
<td>84.2 fl</td>
</tr>
<tr>
<td>MCH</td>
<td>29.2 pg</td>
</tr>
<tr>
<td>MCHC</td>
<td>34.7 g/dL</td>
</tr>
<tr>
<td>Plat</td>
<td>205 x10^3/ul</td>
</tr>
</tbody>
</table>

First and second cycles uneventfully - no issues or complications.
Cycle 3 - Day 1

On day one of cycle 3 the CBC is drawn. Patient’s platelet count has dropped to 92,000 which is still within the guidelines to proceed with scheduled treatment.

WBC is within the normal range. RBC, HGB, and PLT are all slightly decreased

<table>
<thead>
<tr>
<th>COMPLETE BLOOD COUNT - Final</th>
<th>Ordered by: 017</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>4.0</td>
</tr>
<tr>
<td>RBC</td>
<td><strong>4.06 Low</strong></td>
</tr>
<tr>
<td>HGB</td>
<td><strong>12.6 Low</strong></td>
</tr>
<tr>
<td>HCT</td>
<td><strong>36.3 Low</strong></td>
</tr>
<tr>
<td>MCV</td>
<td>84.0</td>
</tr>
<tr>
<td>MCH</td>
<td>28.9</td>
</tr>
<tr>
<td>MCHC</td>
<td>34.2</td>
</tr>
<tr>
<td>Plat</td>
<td><strong>92 Low</strong></td>
</tr>
</tbody>
</table>

Cycle 3 - Day 8

On day 8 of cycle 3 a CBC is drawn. Platelet count dropped to 42,000. Per the XN 1000 rules that are in place, the platelet count was reflexed to a fluorescent platelet and the immature platelet fraction (IPF). The IPF value was 0% indicating that either no platelets were being made or platelets were not maturing at a rate rapid enough to be released from the bone marrow early.

WBC, RBC, HGB and PLT are all low. An IPF is zero

<table>
<thead>
<tr>
<th>COMPLETE BLOOD COUNT - Final</th>
<th>Ordered by: 017</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td><strong>2.8 Low</strong></td>
</tr>
<tr>
<td>RBC</td>
<td><strong>3.97 Low</strong></td>
</tr>
<tr>
<td>HGB</td>
<td><strong>10.9 Low</strong></td>
</tr>
<tr>
<td>HCT</td>
<td><strong>30.6 Low</strong></td>
</tr>
<tr>
<td>MCV</td>
<td>83.9</td>
</tr>
<tr>
<td>MCH</td>
<td>28.6</td>
</tr>
<tr>
<td>MCHC</td>
<td>33.4</td>
</tr>
<tr>
<td>Plat</td>
<td><strong>42 Low</strong></td>
</tr>
</tbody>
</table>

Plate count obtained by Fluorescent Flow Cytometry which is specific for platelet mitochondria, the most accurate enumeration methodology

<table>
<thead>
<tr>
<th>IMMATURE PLATELET FRACTION TEST - Final</th>
<th>Ordered by: 017</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMMATURE PLATELET FRACTION</td>
<td><strong>0.0 Low</strong></td>
</tr>
</tbody>
</table>
Action Taken

- Patient’s nurse is proactive and reports the IPF of zero to the physician
- The physician holds that day’s scheduled chemotherapy treatment. The patient is then scheduled to return the very next day for a repeat CBC and nurse evaluation
- Patient is also given instructions not to shave and to call if he has a nose, gum or any other type of bleed
- The patient returns in the morning for the CBC. Platelet count is 6 and IPF is still 0. The patient receives 10 units of platelets
- Patient able to attend his twins’ football game that night

Summary - CIT

- Before having the ability to run and report the immature platelet fraction parameter, this patient would have been given his day 8 chemotherapy treatment. The patient’s platelet count would not have been scheduled to be rechecked until the following Monday, which would have been day 15 of cycle three. The patient would most likely have experienced serious bleeding and would have reported to the Emergency Department. From the E.D. he would have been admitted to the hospital for a platelet transfusion and observation. By running the IPF, the extreme drop in platelets was not only anticipated but it was proactively followed, giving the patient the required transfusion before the active bleed. Not only did the IPF improve the patient’s outcome, it greatly reduced medical dollars by eliminating an Emergency Room visit and a hospital stay.
Case #2  New Consult for Thrombocytopenia

- A 67 year old man presents for evaluation of low platelet level
- Patient has no history of bleeding problems but platelet count from routine physical before having a colon polyp removed reveals a platelet count of 8,000
- Surgery was postponed and patient was referred for a hematology consultation
- History of surgery: tonsillectomy as a child with no known complication or profuse bleeding
- Repeat CBC was done in the Hematologist’s office

Results from the Analyzer

- Platelet = 8,000
- Low platelet count plus
- Platelet clump flag equals
- Slide review needed
Case #2  But Not Really

- Platelet Count from analyzer = 8,000
- But look what is on the slide???

Summary - Pseudothrombocytopenia

- CBC was repeated with collection in a Na Citrate tube in place of the traditional EDTA tube.
- Platelet count from the Na Citrate tube = 278,000
- Pseudothrombocytopenia also called spurious thrombocytopenia
- Phenomenon caused by in vitro agglutination of platelets
- Analyzers cannot differentiate between platelet clumps and individual cells
- Primary causes for this phenomenon
  - EDTA anticoagulant
  - Cold Agglutinins
  - Multiple Myeloma
Case #3 Unexplained Blood Clot

- A 39 year old female presents with a blood clot in her leg
- Patient has a history of iron deficiency due to heavy menorrhagia
- Patient also claims to have bleeding episodes between periods
- Patient takes a minimal dose of oral iron due to problems with constipation when taking increased dose of iron supplements
- History of iron infusions and blood transfusions due to anemia
- Full hematology work up done in office including CBC, Ferritin and Iron/Iron binding

CBC Values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Units</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>5.07</td>
<td>x10^3/ul</td>
<td>4.0 - 11.0</td>
</tr>
<tr>
<td>RBC</td>
<td>3.73</td>
<td>x10^6/ul</td>
<td>3.90 - 5.20</td>
</tr>
<tr>
<td>HGB</td>
<td>5.8</td>
<td>g/dL</td>
<td>12.0 - 16.0</td>
</tr>
<tr>
<td>HCT</td>
<td>24.2</td>
<td>%</td>
<td>36.0 - 47.0</td>
</tr>
<tr>
<td>MCV</td>
<td>62.9</td>
<td>fl</td>
<td>82.0 - 97.0</td>
</tr>
<tr>
<td>MCH</td>
<td>18.8</td>
<td>pg</td>
<td>27.0 - 33.4</td>
</tr>
<tr>
<td>MCHC</td>
<td>28.9</td>
<td>g/dL</td>
<td>32.5 - 35.5</td>
</tr>
<tr>
<td>Plat</td>
<td>646</td>
<td>cells</td>
<td>130 - 400</td>
</tr>
<tr>
<td>Neut%</td>
<td>52.7</td>
<td>%</td>
<td>38 - 70</td>
</tr>
<tr>
<td>Lymph%</td>
<td>33.1</td>
<td>%</td>
<td>20 - 45</td>
</tr>
<tr>
<td>MONO%</td>
<td>8.9</td>
<td>%</td>
<td>2 - 14</td>
</tr>
<tr>
<td>EOS%</td>
<td>3.9</td>
<td>%</td>
<td>0 - 5</td>
</tr>
<tr>
<td>BASO%</td>
<td>1.2</td>
<td>%</td>
<td>0 - 2</td>
</tr>
<tr>
<td>Immature Gran %</td>
<td>0.2</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Nucleated RBC %</td>
<td>0.0</td>
<td>%</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>
This Supports Iron Deficiency

<table>
<thead>
<tr>
<th>Result</th>
<th>Value (Previous)</th>
<th>Units</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>FERRITIN - Final</td>
<td>Ordered by: 030</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ferritin</td>
<td>&lt;5.0 Low</td>
<td>Ng/mL</td>
<td>10 - 120</td>
</tr>
<tr>
<td>IRON/IRON BINDING - Final</td>
<td>Ordered by: 030</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IRON</td>
<td>12 Low</td>
<td>ug/dl</td>
<td>37 - 145</td>
</tr>
<tr>
<td>TIBC</td>
<td>441 High</td>
<td>ug/dl</td>
<td>250 - 400</td>
</tr>
<tr>
<td>Iron Sat Percent</td>
<td>3 Low</td>
<td>%</td>
<td>15 - 50</td>
</tr>
<tr>
<td>VITAMIN B12 / FOLATE - Final</td>
<td>Ordered by: 030</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B12</td>
<td>452</td>
<td>pg/ml</td>
<td>200 - 1100</td>
</tr>
<tr>
<td>Folate</td>
<td>10.1</td>
<td>Ng/mL</td>
<td>0 - 20</td>
</tr>
</tbody>
</table>

www.chcwm.com

Cross Over Stimulation

- So, remember me?

Stimulation of Megakaryoblasts by erythropoietin resulting in increased platelet production and increased chance of a thrombotic episode

www.chcwm.com
Follow Up

- Significant anemia consistent with iron deficiency
- In addition, fatigue, headaches and dyspnea
- 2 units of PRBC’s given
- Strongly recommend a GYN consultation for possible hysterectomy
- New FDA approved IV iron preparation called Injectafer will be given in one week
- Will recheck CBC in 2 weeks
- And if you’re wondering, IPF is normal at 2.4%

Two Weeks Later

- Hemoglobin goes up and platelet count goes down
Case #4 Unexplained Thrombocytopenia

- A 29-year-old woman presents to her physician with unexplained bruising and petechiae.
- Patient states recent viral illness (had the flu for 4 weeks).
- Past history of thrombocytopenia at age 2 that resolved spontaneously with no intervention and was attributed to ITP.
- LDH is slightly elevated at 420 U/L.
- Initial CBC reveals platelet count of 14,000 and IPF (immature platelet fraction) of 46%.
- IPF indicates bone marrow is working – not a production problem!
- Are platelets being consumed or destroyed?????
Diagnosis and Treatment

• Due to medical history and rapid onset of thrombocytopenia following a recent viral infection this is most likely recurrence of ITP
• Lack of evidence of end organ damage lowers the suspicion for TTP
• Extremely low platelet count along with very high IPF reflects common findings in ITP (IPF in TTP would not be as high)
• Initial therapy was 1 mg/kg dosing of prednisone. After no significant improvement in 48 hours of starting the corticosteroid, IVIG was added with a 1 g/kg X2 day course
• Platelet count responded appropriately and count increased to 114,000.
• Patient to continue on 90 mg prednisone and follow up with weekly CBC checks.

5 Days – Later Following Treatment

<table>
<thead>
<tr>
<th></th>
<th>Final</th>
<th>Ordered by: 017</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COMPLETE BLOOD COUNT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>6.56</td>
<td>x10^3/ul</td>
</tr>
<tr>
<td>RBC</td>
<td>3.86</td>
<td>x10^6/ul</td>
</tr>
<tr>
<td>HGB</td>
<td>10.9</td>
<td>g/dL</td>
</tr>
<tr>
<td>HCT</td>
<td>34.3</td>
<td>%</td>
</tr>
<tr>
<td>MCV</td>
<td>85.7</td>
<td>fl</td>
</tr>
<tr>
<td>MCH</td>
<td>31.2</td>
<td>pg</td>
</tr>
<tr>
<td>MCHC</td>
<td>32.0</td>
<td>g/dL</td>
</tr>
<tr>
<td>Plat</td>
<td>114</td>
<td>x10^3/ul</td>
</tr>
<tr>
<td>Neut%</td>
<td>6.27</td>
<td>%</td>
</tr>
<tr>
<td>Lymph%</td>
<td>0.15</td>
<td>%</td>
</tr>
<tr>
<td>MONO%</td>
<td>0.09</td>
<td>%</td>
</tr>
<tr>
<td>EOS%</td>
<td>0.01</td>
<td>%</td>
</tr>
<tr>
<td>BASO%</td>
<td>0.00</td>
<td>%</td>
</tr>
<tr>
<td>Immature Gran%</td>
<td>0.03</td>
<td>%</td>
</tr>
<tr>
<td>Nucleated RBC%</td>
<td>0.00</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>IMMATURE PLATELET FRACTION TEST</strong></th>
<th>Final</th>
<th>Ordered by: 017</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMMATURE PLATELET FRACTION</td>
<td>17</td>
<td>%</td>
</tr>
</tbody>
</table>

Much Better

Still working but not as hard
**Case #5**  Blast from the past - 2005

- 19 year old female presents to the Emergency Department with a headache - states for over a week
- In addition, nausea, vomiting, fatigue and confusion
- CBC reveals a HGB=5.8g/dl and platelet count =1,000
- Patient was jaundiced and bilirubin was 4.4 mg/dl
- Blood smear showed microspherocytes and schistocytes
- Coombs test was negative
- Bone Marrow biopsy was performed and peripheral smear sent to pathologist for review. Results consistent with consumption and a clinical diagnosis of TTP

**The Test Confirms TTP**

- **ADAMTS13 Activity Test  < 5 L%** (normal range >67)
- This range of ADAMTS13 is high risk and associated with an increased risk for recurrent clinical episodes of TTP

[Diagram of normal subject and patient with Thrombotic Thrombocytopenic Purpura]
### Treatment

- Patient was treated with plasma exchange, steroids and was given PRBC’s
  - Plasma exchange 3 times a day for the first week
  - Then plasma exchange 1 time a week for ten weeks
  - Steroids - Solu-Medrol 250 mg IV
  - 2 units of PRBC’s
  - Daily CBC’s until normal and then 1x week for 1 year

### Fast Forward to 2015

- 29 year old female seen for thrombocytopenia, platelet count at initial visit = 9,000 with an IPF = 19%
- Microangiopathic hemolytic anemia, Hgb=6.4 and elevated LDH (LDH =1138)
- Peripheral smear compatible with the diagnosis of recurrent TTP
- Patient has history of TTP – 2005 – treated successfully with plasmapheresis
- Complicating factor – patient is 19 weeks pregnant
- Patient has had two miscarriages in the past, possibly related to her TTP
Here We Go Again

<table>
<thead>
<tr>
<th>COMPLETE BLOOD COUNT - final edit</th>
<th>Ordered by: 017</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>5.1</td>
</tr>
<tr>
<td>RBC</td>
<td>2.17</td>
</tr>
<tr>
<td>HGB</td>
<td>6.4</td>
</tr>
<tr>
<td>HCT</td>
<td>20.1</td>
</tr>
<tr>
<td>MCV</td>
<td>92.6</td>
</tr>
<tr>
<td>MCH</td>
<td>29.4</td>
</tr>
<tr>
<td>MCHC</td>
<td>31.8</td>
</tr>
<tr>
<td>Plat</td>
<td>9</td>
</tr>
</tbody>
</table>

Platelet count obtained by Fluorescent Flow Cytometry methodology which is specific for Platelet Mitochondria, providing the most accurate enumeration.

Neut% | 49.5 | % | 38 - 70 |
Lymph% | 36.0 | % | 20 - 45 |
MONO% | 12.3 | % | 2 - 14 |
EOS% | 1.8 | % | 0 - 5 |
BASO% | 0.2 | % | 0 - 2 |
Immature Gran % | 0.2 | % | |
Nucleated RBC % | 0.0 | % | <1 |

MMATURE PLATELET FRACTION TEST - Final edit | Ordered by: 017 |

IMMATURE PLATELET FRACTION | 19 | % | 0.9 - 7.0 |

Moving Too Fast

- Patient begins daily plasmapheresis X2
- TTP is a high risk factor in pregnancy
- Due to complications, baby is delivered by cesarean section at 24 weeks
- Baby boy is born and is only 11” long and weighs 1 lb, 6 oz. He is admitted to neonatal intensive care unit
- Mom continued to have plasmapheresis after delivery but is tapered down to 3 times weekly
- Mom’s platelet count is stable at 296,000
- At 5 weeks, baby boy stable & up to 1 lbs, 12 oz. He will remain in NICU for several months, but he is making good progress
My Embarrassing Bruise

Fell off the step stool looking for the previous picture

At least I didn’t break my neck – and I did find the picture

www.chcwm.com