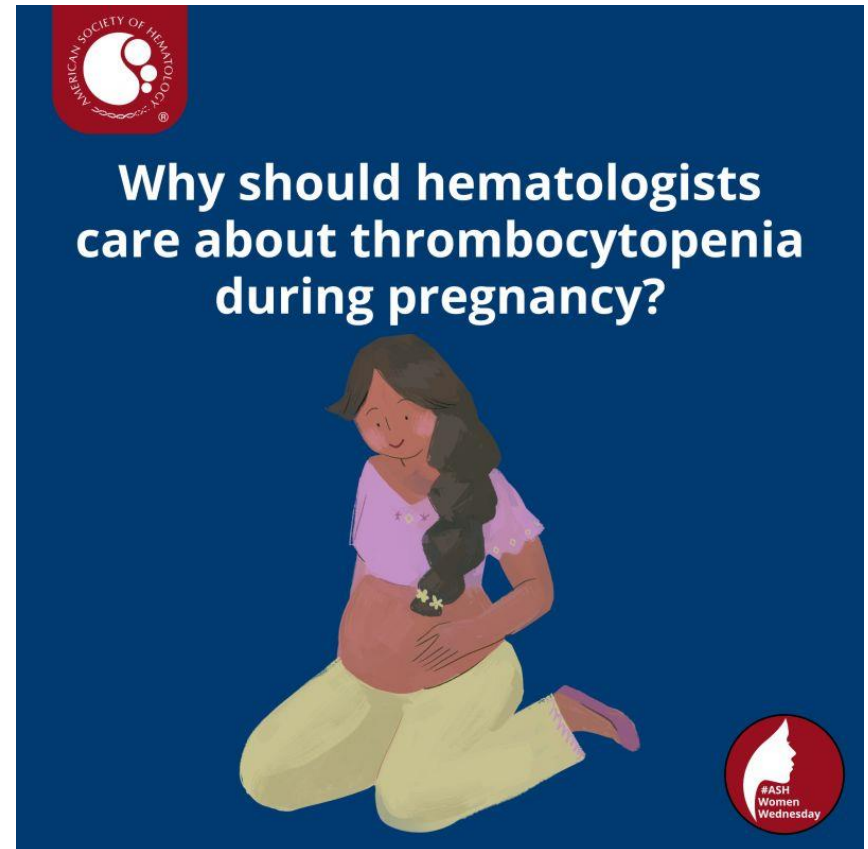


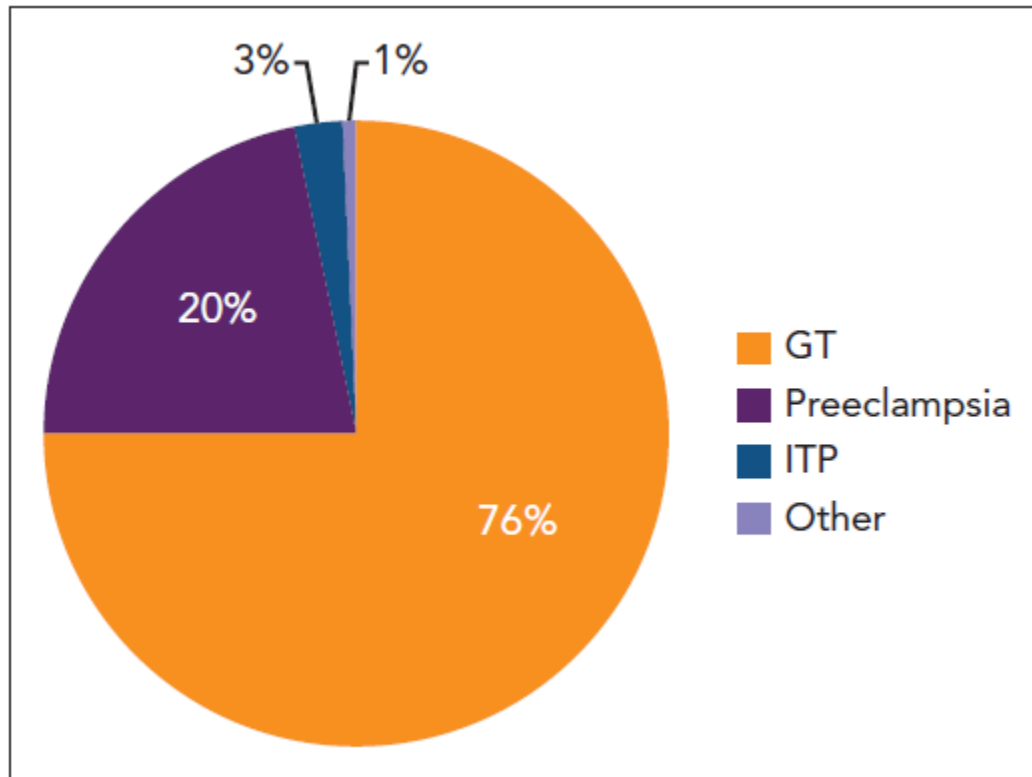
# ***Thrombocytopenia in pregnancy***

***Basic principals and clinical cases***

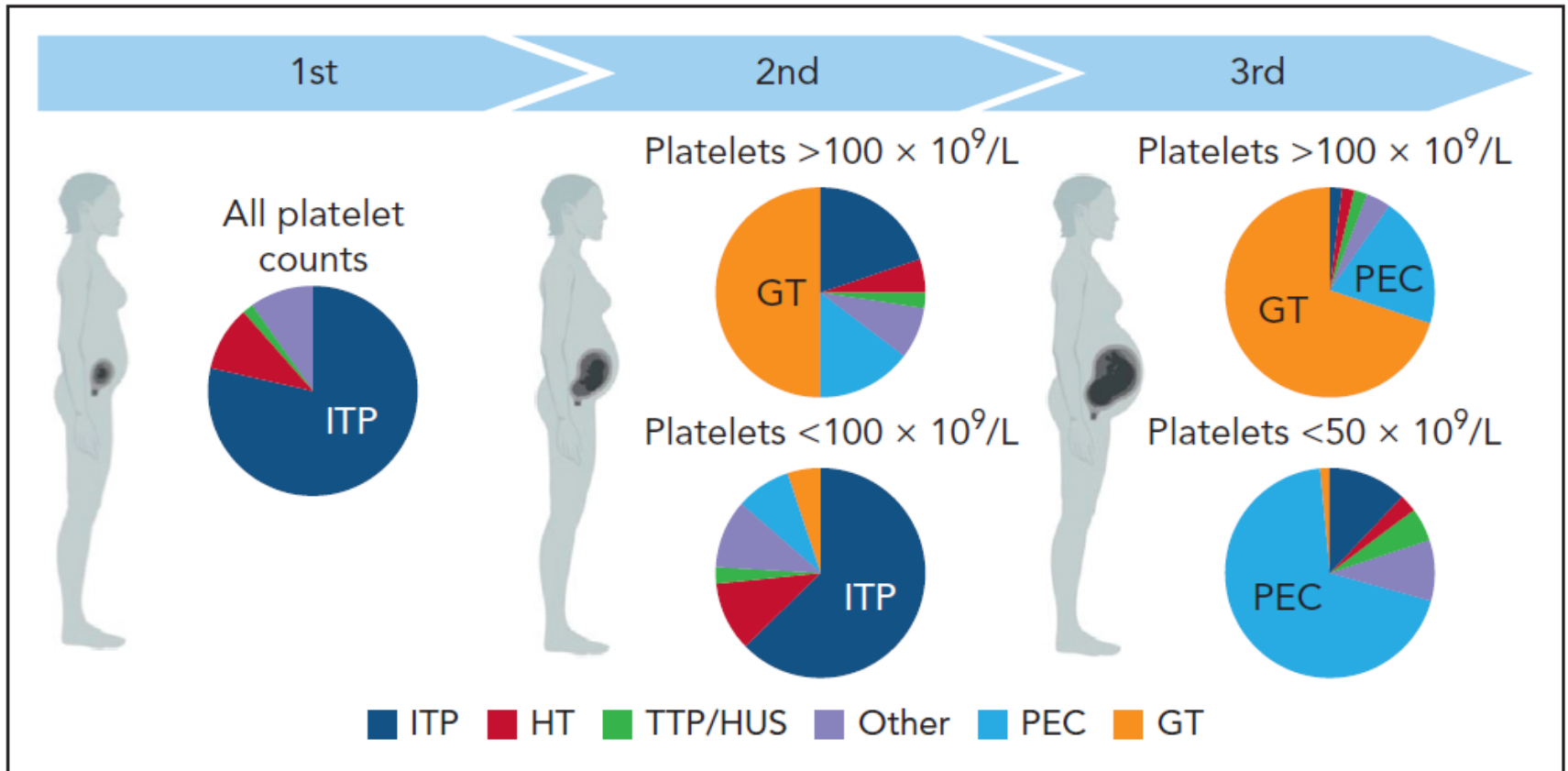
- Thrombocytopenia: platelet count  $<150 \times 10^9/L$
- 10% of all pregnancies
- Third trimester



# GT/ITP/PEC

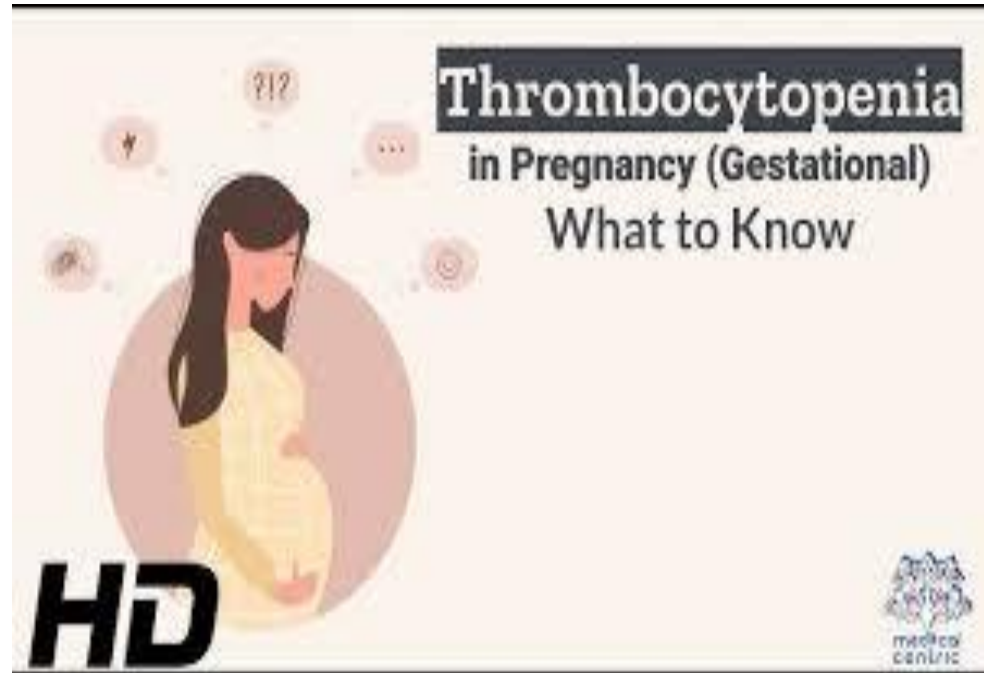


# Trimester of onset and severity



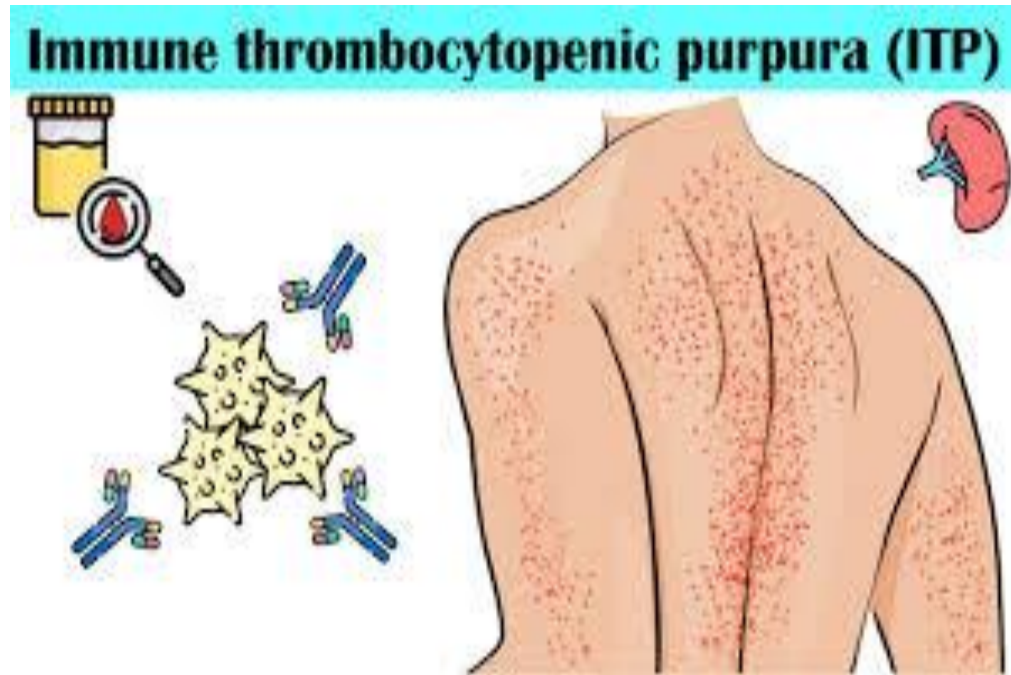
# Gestational thrombocytopenia

- 70% to 75% of thrombocytopenia:~10 %
- Diagnosis of exclusion
- postpartum complete Recovery
- platelets  $>70 \times 10^9/L$  (safe for Epidural)



# ITP

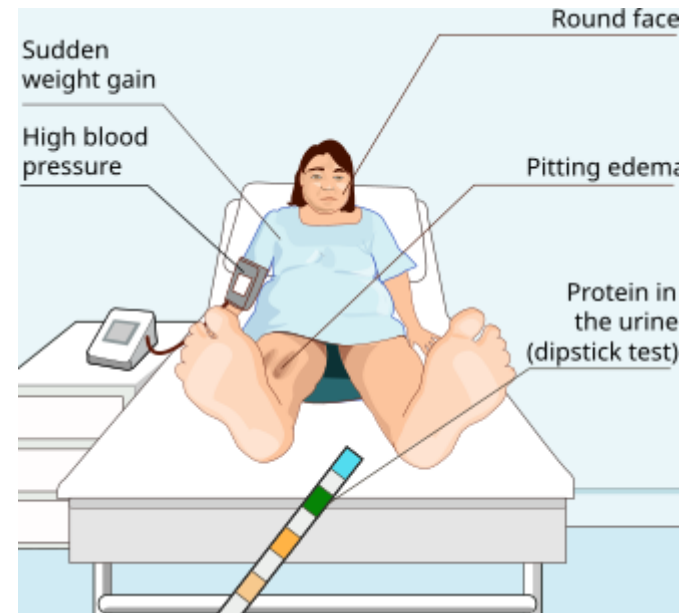
- First and early second trimesters
- 30% : First diagnosis of ITP
- Few resolve fully after delivery
- Antiplatelet antibodies
- Increase platelet destruction
- Inhibit the production









- First 8 months of pregnancy: platelet count falls below  $20 \times 10^9/L$  / Bleeding
- Platelet count  $>70 \times 10^9/L$  to allow for epidural anesthesia
- Platelet count  **$>50 \times 10^9/L$**  (NVD)
- First-line therapy : prednisone / IVIG
- Deferred until about week 35 or 36
- IVIG :0.4 g/kg every 1 to 5 days (Every 2 to 3 W)
- Intermittent pulses of corticosteroids/IVIG
- 2<sup>nd</sup> line: azathioprine, cyclosporine, and rituximab
- Platelet transfusion : Acute bleeding
- TPO-RAs :***Romiplostim*** / Eltrombopag

# Preeclampsia

- **HTN** (BP:140/90 mm Hg) with **proteinuria** and/or **end-organ dysfunction** after 20 weeks
- Early postpartum
- (TMA) :Schistocytes on the PBS
- Cerebral hemorrhage, hepatic rupture, renal failure, pulmonary edema, MI, ARDS, seizure
- (TTP) :ADAMTS13 <10%
- **Pregnancy-specific TMAs**:Treatment of preeclampsia, HELLP and acute fatty liver disease of pregnancy is **fetal delivery**
- TTP, complement mediated HUS, and CAPS in pregnancy are treated the same as in nonpregnant patients and do not mandate fetal delivery





1. History	Bleeding symptoms Infectious symptoms Prior platelet counts: pregnant and nonpregnant Family history of thrombocytopenia Autoimmune disorders Medications Headache		
2. Physical examination	Bleeding: bruising, petechiae, purpura, oral mucosal blood blisters, conjunctival hemorrhages Blood pressure Lymphadenopathy, hepatomegaly, splenomegaly Abdominal tenderness Lower extremity edema Rashes or synovitis		
3. Timing	Categorize by onset and severity of thrombocytopenia (Figure 2)		
4. Peripheral smear examination	Platelet clumping (Pseudothrombocytopenia) 	Normal morphology of all 3 cell lines 	Schistocytes (TMA) 
Laboratory assessment	None indicated 	Investigate potential contributors Infection Screen for HIV, HBV, HCV, <i>H pylori</i> Thorough assessment of any current infectious symptoms Liver injury LFTs Coagulation profile Autoimmune processes APLA panel ANA 	Hemolytic panel LDH Reticulocyte count Haptoglobin LFTs (bilirubin) Urinalysis Renal function ADAMTS13 activity Coagulation profile 
Management	Standard obstetric care	Trend platelet count Reserve treatment for clinically significant processes/bleeding or as needed to prepare for delivery	Initiate therapy for the most likely TMA Revisit the diagnosis and escalate or redirect therapies pending clinical course

# Patient 1

- A 27-year-old female (G3P2) at 34 weeks is referred for a platelet count of  $108 \times 10^9/L$ .
- On physical examination, she is well appearing, afebrile, and normotensive. There is no leg edema, rash, purpura, petechiae, or joint inflammation.
- Other laboratory tests include a white blood cell (WBC) count of  $7.6 \mu L$  and an Hb level of 11.4 g/dL; negative HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV) tests; and normal liver function tests (LFTs), basic metabolic panel, prothrombin time (PT), and partial thromboplastin time (PTT)

# Discussion

- The most likely diagnosis is **GT** based on presentation in the third trimester and platelets  $>100 \times 10^9/\text{L}$ .
- Smear review confirms no schistocytes, and she is normotensive, arguing against TMAs and preeclampsia.
- ITP is the leading alternative diagnosis, but with no confirmatory test for either GT or ITP, the diagnosis will be chiefly informed by platelet trend over time.
- We plan to repeat the CBC in 2 weeks.

- At 36 weeks, the platelet count is  $96 \times 10^9/\text{L}$ . She remains asymptomatic and normotensive without bleeding, bruising, or headache
- In discussion with anesthesia and obstetrics, a threshold platelet count of  $70 \times 10^9/\text{L}$  is agreed to for delivery
- We follow weekly CBCs, and she presents in labor at 39 weeks with a platelet count of  $78 \times 10^9/\text{L}$
- She delivers vaginally with epidural anesthesia with no bleeding complications
- The neonate has a normal platelet count

- Her platelet count starts to rebound on postpartum day 1, and she is discharged
- At her 6-week postpartum visit, her platelet count is  $187 \times 10^9/L$
- A diagnosis of **GT** is now confirmed
- We expect a similar pattern of thrombocytopenia in future pregnancies CBC monitoring between pregnancies is not indicated

# Patient 2

- A 29-year-old female (G1P0) at 16 weeks is referred for a platelet count of  $58 \times 10^9/L$
- She denies any bleeding or bruising. She had a viral respiratory process 4 weeks ago, now fully resolved
- Her only medication is a prenatal vitamin. She has no known history of thrombocytopenia and a prior CBC from college was normal (platelets,  $216 \times 10^9/L$ )
- There is no family history of thrombocytopenia or bleeding disorders. She is well appearing, afebrile, and normotensive
- There is no palpable hepatosplenomegaly or lymphadenopathy, leg edema, rash, purpura, petechiae or bruising
- Other laboratory results included: WBC  $4.6 \times 10^9/L$ , Hb 12.8 g/dL; negative HIV, HBV, and HCV tests; and normal LFTs, basic metabolic panel, PT, and PTT

# Discussion

- At 16 weeks with a platelet count  $<100 \times 10^9/\text{L}$ , her most likely diagnosis is *ITP*
- Her recent viral illness is of note because infections can decrease platelet counts
- She has no prior history of autoimmune conditions and tests negative for antinuclear antibodies, antiphospholipid antibodies
- Peripheral blood smear shows only thrombocytopenia, large platelets, and *no schistocytes*
- Her prior documented normal platelet count argues against inherited thrombocytopenia.

- Many pregnant patients with ITP, such as this one, do not require treatment and tolerate platelet counts **as low as  $15 \times 10^9/L$  to  $20 \times 10^9/L$**  during pregnancy with minimal bleeding
- We discuss with her the potential use of **steroids or IVIG** if her platelet count falls **below  $20 \times 10^9/L$**  or to manage bleeding and the likely need for therapy closer to delivery if thrombocytopenia persists
- We monitor her CBC every 4 weeks during the first 2 trimesters and increase the frequency to every 1 to 2 weeks in the third trimester or more frequently for any clinically significant bleeding or a substantial decline in platelet count



- Her platelet counts were  $55 \times 10^9/\text{L}$  to  $69 \times 10^9/\text{L}$  between weeks 20 and 30 and are now  $48 \times 10^9/\text{L}$  at week 33
- She has no bleeding or hypertension
- No schistocytes are evident on serial review of her blood smears

- She desires epidural anesthesia, and multidisciplinary discussion sets a threshold platelet count of  $70 \times 10^9/\text{L}$ . In preparation, she starts prednisone 60 mg daily at week 36
- Her platelet count is  $103 \times 10^9/\text{L}$  after 7 days of treatment, and prednisone is continued
- At 39 weeks, she presents in spontaneous labor, epidural is placed uneventfully, and she delivers vaginally without complications
- Her neonate has a normal platelet count
- Corticosteroids are tapered off over 10 days post partum. Her platelets decrease to  $\sim 80 \times 10^9/\text{L}$  and persist in this range for the next 12 months
- She continues without any bleeding complications or need for active therapy
- She is diagnosed with *chronic ITP*

# Patient 3

- A 36-year-old female (G2P0010) at **33 weeks** is referred for a platelet count of  $113 \times 10^9/\text{L}$ . Her WBC count is  $12.3 \times 10^9/\text{L}$  and **Hb is 9.8 g/dL**. Prior platelet counts in this pregnancy were normal
- She reports no bleeding or bruising but has pedal edema, which worsens by the end of the day
- She had 2 episodes of dull **headache** in the last week
- She is afebrile without infectious symptoms
- Her heart rate and blood pressure are 98 beats per minute and **136/82** mm Hg, respectively
- She has trace **nonpitting pedal edema bilaterally**, without calf tenderness or palpable cord
- Her abdomen is gravid without tenderness or palpable hepatosplenomegaly
- There are no rashes, bruising, petechiae, or purpura
- Other laboratory tests include normal aspartate transferase, alanine transaminase, PT, and PTT; alkaline phosphatase 121 U/L; **creatinine 1.21** mg/dL; and negative HIV, HBV, and HCV test
- Her peripheral smear demonstrates **schistocytes**

- Although GT is the most common diagnosis for thrombocytopenia initially presenting in the third trimester with a platelet count  $>100 \times 10^9/\text{L}$ , this patient also has ***anemia, mild hypertension, headaches, and a relative increase in creatinine***
- Her peripheral smear demonstrates ***schistocytes***, suggesting a ***TMA***
- We send a hemolytic panel, including ADAMTS13 level. Her lactate dehydrogenase is elevated at 647 U/L, total bilirubin is 3.2 mg/dL (direct bilirubin 0.7 mg/dL), reticulocyte count is 5.9%, and haptoglobin is  $<10$  mg/dL
- Of the TMAs, ***preeclampsia*** is the prime suspect
- ***TTP is less likely given that thrombocytopenia is mild***, so, we do not recommend plasma exchange
- Normal LFTs make HELLP and acute fatty liver disease of pregnancy unlikely

- Her repeat blood pressure 2 days later is 146/92 mm Hg, and urinalysis shows **proteinuria**
- She is diagnosed with **preeclampsia**, admitted to obstetrics, and started on aspirin, hydralazine for blood pressure management, and magnesium therapy per protocol
- Her neurologic examination remains nonfocal, but creatinine increases to 1.84 mg/dL, repeat platelet count is  $83 \times 10^9/\text{L}$ , and hypertension persists despite hydralazine
- With a platelet count  $<100 \times 10^9/\text{L}$ , she is classified as having preeclampsia with severe features
- Now at 34 weeks, obstetrics prepares for delivery
- She responds to induction of labor, receives an epidural with no bleeding complications, and **delivers vaginally**

- Her *platelets continue to decline* steadily, however, down to  $44 \times 10^9/\text{L}$  at 48 hours post partum
- Her *creatinine* continues to rise, now **2.23** mg/dL
- The previously sent ADAMTS13 activity is 49%

- **Placental delivery** is the cornerstone of management for preeclampsia
- Although hypertension and laboratory abnormalities may not resolve immediately after delivery, **progression** of abnormalities is unusual
- We now favor an alternative TMA diagnosis to preeclampsia
- TTP is ruled out with an ADAMTS13 of 49%
- In addition to progressive thrombocytopenia, her renal function is the predominant laboratory abnormality, making **complement-mediated hemolytic uremic syndrome** the most likely diagnosis
- We treat her with **eculizumab** with excellent hematologic response.
- She does not require renal replacement therapy, and her creatinine and blood pressure normalize over the ensuing weeks

# با تشکر

