MAYO CLINIC

# I'VE GOT FRIENDS WITH LOW PLATELETS

## HOSPITAL CASES OF THROMBOCYTOPENIA

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Minivan Driver

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MAYO CLINIC

# *NO DISCLOSURES*

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# LEARNING OBJECTIVES

| Recognize | Understand | Review | Ensure |
| --- | --- | --- | --- |
| Recognize causes of thrombocytopenia in hospitalized patients | Understand workup of thrombocytopenia in hospitalized patients | Review management of thrombocytopenia | Ensure Garth Brooks is stuck in your head for rest of day |

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***The basics…***

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**Causes of thrombocytopenia in adults**

| |
|---|
| **Falsely low platelet counts (pseudothrombocytopenia)** |
| In vitro platelet clumping caused by ethylenediaminetetraacetic acid (EDTA)-dependent agglutinins (naturally occurring antibodies) |
| In vitro platelet clumping caused by an insufficiently anticoagulated specimen |
| In vitro platelet clumping caused by glycoprotein IIb/IIIa inhibitors (eg, abciximab) (NOTE: these can also cause true thrombocytopenia) |
| Giant platelets counted by automated counter as white blood cells rather than platelets |
| **Common causes of thrombocytopenia** |
| **Primary immune thrombocytopenia (ITP)** |
| **Drug-induced immune thrombocytopenia (DITP)** |
| Heparin (NOTE: special case, also can cause thrombosis) |
| Quinine (as in over-the-counter tablets for leg cramps; also in beverages) |
| Sulfonamides (eg, trimethoprim-sulfamethoxazole [Bactrim; Septra]) |
| Acetaminophen (Tylenol, Panadol) |
| Cimetidine (Tagamet) |
| Ibuprofen (Advil, Motrin) |
| Naproxen (Aleve, Midol) |
| Ampicillin (Omnipen, Apo-Ampi) |
| Piperacillin (Pipracil, Zosyn) |
| Vancomycin (Vancocin) |
| Glycoprotein IIb/IIIa inhibitors (abciximab [ReoPro], tirofiban [Aggrastat], eptifibatide [Integrilin]) |
| **Food and beverages** |
| Quinine-containing beverages (tonic water, Schweppes bitter lemon) |
| Walnuts |
| Certain herbal teas |
| **Infections** |
| HIV |
| Hepatitis C |
| Epstein-Barr virus (EBV; can be associated with infectious mononucleosis) |
| *Helicobacter pylori* (suspected in patients with symptoms of dyspepsia or peptic ulcer disease) |
| Sepsis with disseminated intravascular coagulation (DIC) |
| Intracellular parasites (eg, malaria, babesia) |
| **Hypersplenism due to chronic liver disease** |
| **Alcohol** |
| **Nutrient deficiencies (eg, vitamin B12, folate, copper)** |
| **Rheumatologic/autoimmune disorders (eg, systemic lupus erythematosus, rheumatoid arthritis)** |
| **Pregnancy** |
| Gestational thrombocytopenia |
| Preeclampsia |
| HELLP syndrome (hemolysis, elevated liver function tests, low platelets) |
| **Other causes of thrombocytopenia** |
| **Myelodysplasia** |
| Suspected in older patients, in whom a bone marrow biopsy may be appropriate |
| **Cancer with disseminated intravascular coagulation** |
| **Cancer with bone marrow infiltration or suppression (eg, lymphoma, leukemia, some solid tumors)** |
| **Paroxysmal nocturnal hemoglobinuria (PNH)** |
| **Thrombotic microangiopathy (TMA)** |
| Thrombotic thrombocytopenic purpura (TTP) is manifested by thrombocytopenia and microangiopathic hemolytic anemia; fever, renal failure, and/or neurologic symptoms may or may not be present |
| Hemolytic uremic syndrome (HUS) is typically seen in children following infection with a Shiga-toxin producing organism (*Escherichia coli* or *Shigella*) |
| Drug-induced TMA may occur with quinine, certain cancer therapies, calcineurin inhibitors, and others |
| **Antiphospholipid syndrome (APS)** |
| **Aplastic anemia** |
| **Hereditary thrombocytopenias** |
| An important consideration, especially in young patients who do not respond to treatment. Some specific syndromes are listed. However, many patients appear to have autosomal dominant thrombocytopenia with no other clinical features. |
| Von Willebrand disease type 2B |
| Wiskott-Aldrich syndrome |
| Alport syndrome |
| May-Hegglin anomaly |
| Fanconi syndrome |
| Bernard-Soulier syndrome |
| Thrombocytopenia absent radius syndrome |

The table lists possible causes of isolated thrombocytopenia. Refer to the UpToDate topics on thrombocytopenia, immune thrombocytopenia, heparin-induced thrombocytopenia, and drug-induced thrombocytopenia for further details and a more complete list of drugs that can cause drug-induced thrombocytopenia.

UpToDate®

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# THROMBOCYTOPENIA

**<150,000**

Decreased production (Cancers, Viral Infections, Chemo, ETOH) *

Increased destruction(ITP, DIC,TTP, HUS,HIT) *

Increased consumption

Dilutional

Sequestration

Drugs

Spurious

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***Work up?***

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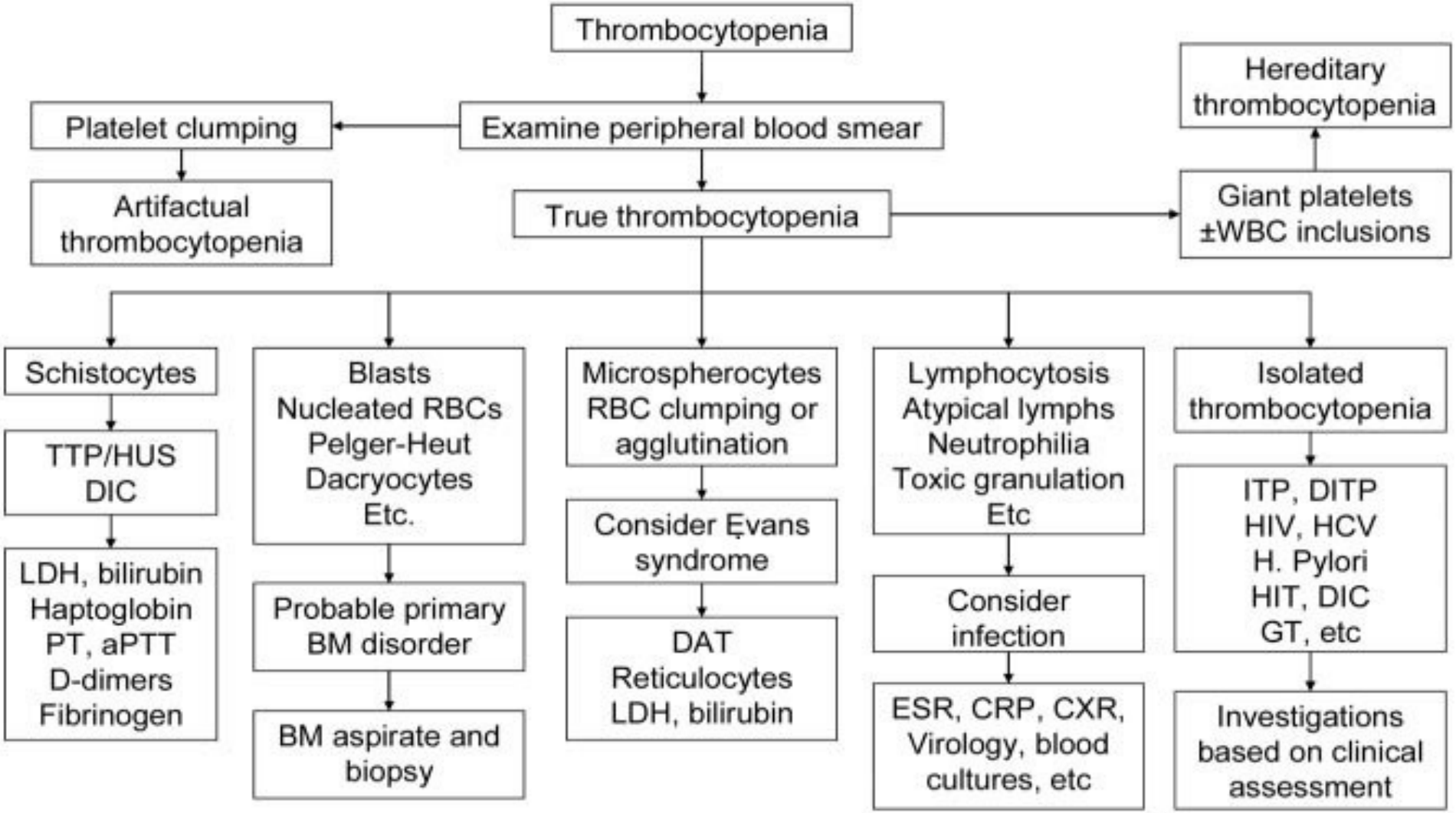


***Blood 2012***

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# CENSUS

Mr. Spots

Mrs. Spots

Mrs. Popcorn

Mrs. Chemo

Mr. Etoh

Mrs. Sofa

Mrs. College

Mr. Seymour

Mrs. Heparin

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# MR. SPOTS

## Past Medical History

None

## Past Surgical History

Tonsillectomy

## Meds:

Ibuprofen 800mg

## Review of Systems:

Epistaxis

“Tiny spots on both my ankles”

Specifically denies fevers or new medications.

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# LABS

| HGB | WBC | Plts | Na | K | Cr | AST | ALT | Bili | UA |
|---|---|---|---|---|---|---|---|---|---|
| 14 | 8 | 22 | 138 | 4.8 | 0.8 | 57 | 63 | 0.2 | Neg |

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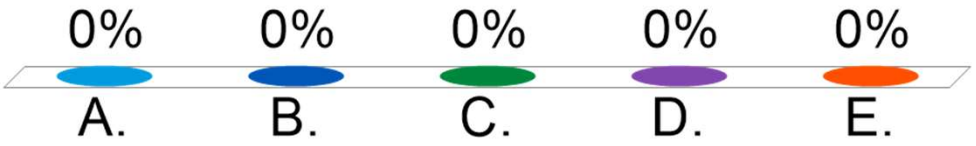
# NEXT BEST STEP?

A. Peripheral Smear
B. Bone Marrow Biopsy
C. Platelet Transfusion
D. Plasmapheresis
E. Friend Request the phlebotomist

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# LABS

| HGB | WBC | Plts | Na | K | Cr | AST | ALT | Bili | UA |
|---|---|---|---|---|---|---|---|---|---|
| 14 | 8 | 22 | 138 | 4.8 | 0.8 | 57 | 63 | 0.2 | Neg |

| Peripheral Smear |
|---|
| No abnormalities seen. |

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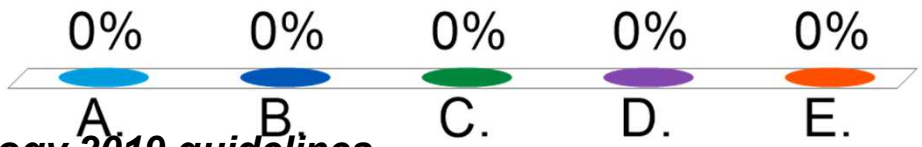
# NOW WHAT?

A. Observe
B. Dexamethasone
C. IVIG
D. Plasmapheresis
E. Splenectomy




***American Society of Hematology 2019 guidelines***

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# WHERE SHOULD WE TREAT THIS GUY?

A. Treat and Street
B. Admit to Hospital


***American Society of Hematology 2019 guidelines***

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# ITP

Most common cause of isolated thrombocytopenia.

5 cases per 100,000 people in US.

Drug induced thrombocytopenia (2-3 days after exposure)

Eltrombogpag? Romiplostim? Rituxan? Splenectomy?

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# MRS. SPOTS

## Past Medical History

None.

## Past Surgical History:

None.

## Meds:

Melatonin

## Review of Systems:

Worried she picked up ITP from her husband.

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# LABS

| HGB | WBC | Plts | Na | K | Cr | AST | ALT | Bili | UA |
|---|---|---|---|---|---|---|---|---|---|
| 14 | 8 | 22 | 138 | 4.8 | 0.8 | 57 | 63 | 0.2 | Neg |

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# PERIPHERAL SMEAR

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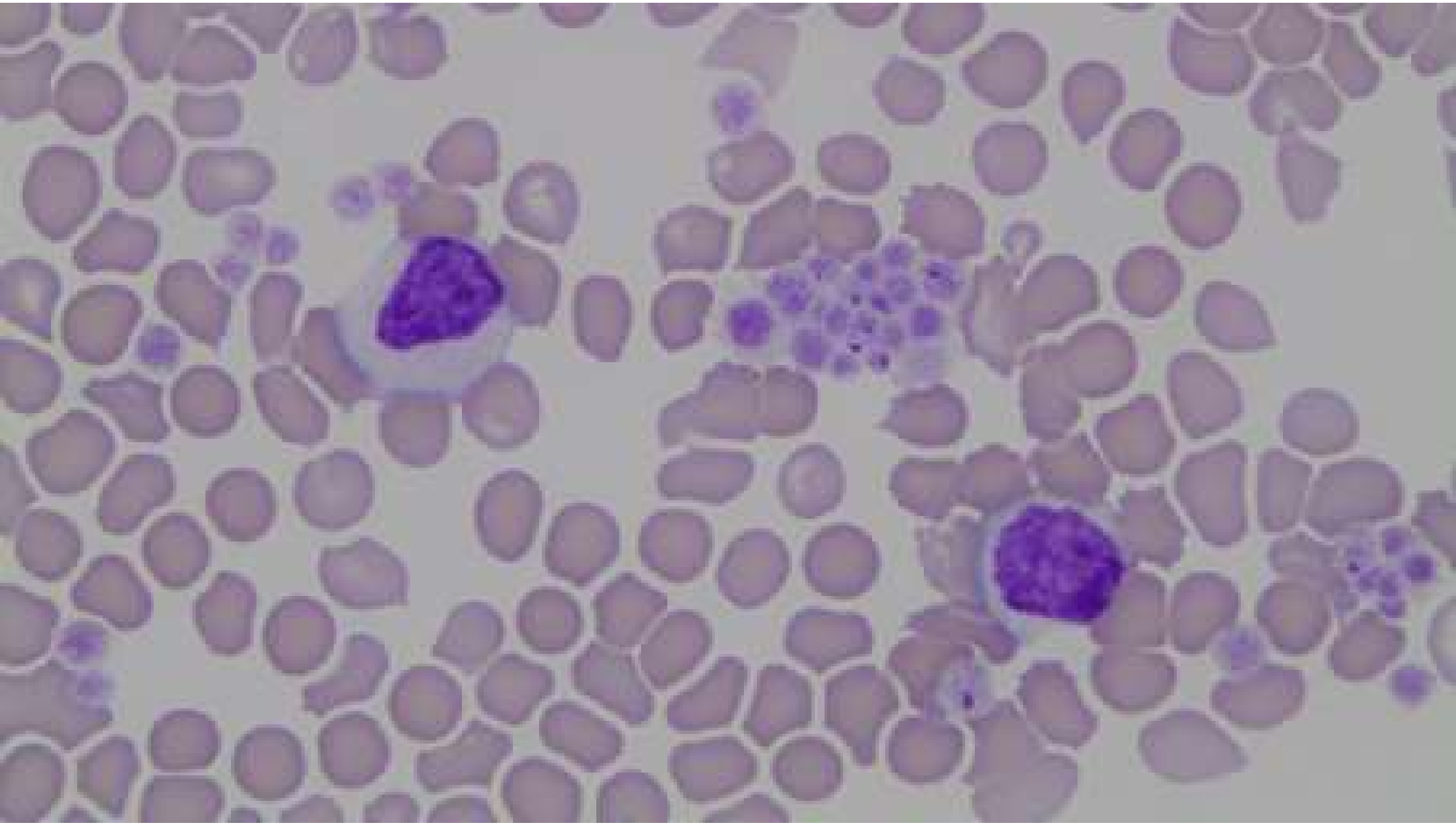
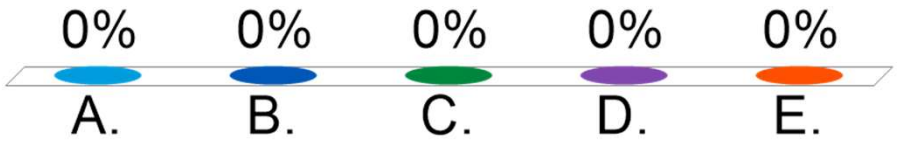


# NOW WHAT?

A. Dexamethasone
B. IVIG
C. Plasmapheresis
D. Splenectomy
E. Friend Request the Phlebotomist

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# PLATELET CLUMPING

Traumatic Venipuncture

EDTA dependent antibodies that react with platelet glycoproteins

Sodium Citrate or Heparin

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# MRS. POPCORN

## Past Medical History:

Diverticulosis

Hemorrhoids

Coronary Artery Disease with DES

Recent Klebsiella UTI with Bloodstream infection with PICC

## Past Surgical History:

Right Total Knee Replacement

## Meds:

Aspirin, Metoprolol, Atorvastatin, Ceftriaxone, PICC site care heparin and saline flushes

## Review of Systems:

Painless rectal bleeding x4 days.  PICC site cares at home.  Didn't want to "catch the covid"

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# LABS

| HGB | WBC | Plts | Na | K | Cr | AST | ALT | Bili | UA |
|---|---|---|---|---|---|---|---|---|---|
| 5.8 | 8 | 179 | 138 | 4.8 | 1.5 | 57 | 63 | 0.2 | Neg |

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# TRANSFUSE?

**Impact of More Restrictive Blood Transfusion Strategies on Clinical Outcomes: A Meta-analysis of Systematic Review**

*Salpeter, MD et al*

*The American Journal of Medicine*

**Restrictive versus liberal transfusion strategy for red blood cell transfusions: systematic review of randomized trials with meta-analysis and trial sequence analysis**

*Holst, et al*

*BMJ 2015*

**Outcomes Using Lower vs Higher Hemoglobin Thresholds for Red Blood Cell Transfusion**

*Carson, MD et al*

*Journal of American Medical Association 2013*

**Red Blood Cell Transfusion: A Clinical Practice Guideline From the AABB**

*Carson, MD et al*

*Annuals of Internal Medicine, 2012*

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# LABS

| HGB | WBC | Plts | Na | K | Cr | AST | ALT | Bili | UA |
|---|---|---|---|---|---|---|---|---|---|
| 8.5 | 8 | 94 | 138 | 4.8 | 1.3 | 57 | 63 | 0.2 | Neg |

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# WHAT'S NEXT?

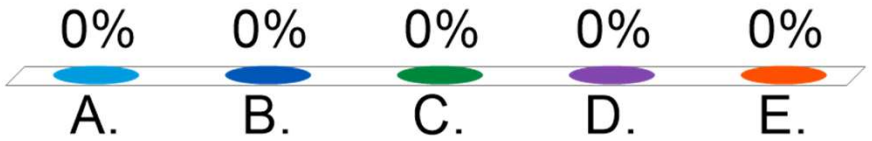
A. Obtain Peripheral Smear

B. Stop heparin flushes to PICC and draw PF4 Ab, and start agatroban

C. Repeat draw in sodium citrate

D. Transfuse platelets

E. Steal 3 day old pizza from nursing breakroom

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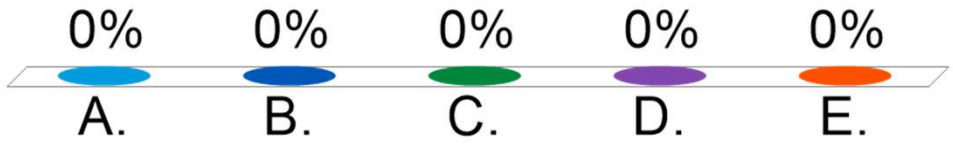
# EXTRA CREDIT: WHICH OF THE FOLLOWING LABS WOULD DECREASE WITH A FEW UNITS OF BLOOD?

A. Potassium
B. Bilirubin
C. White Blood Cells
D. Calcium
E. AST

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# MRS. CHEMO

**Past Medical History**

Large B Cell Lymphoma

**Past Surgical History:**

Port-A-Cath Placement

**Meds:**

R-CHOP

**Review of Systems:**

Epistaxis

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# LABS

| HGB | WBC | Plts | Na | K | Cr |
|---|---|---|---|---|---|
| 7.1 | 1.1 | 8 | 138 | 4.8 | 0.9 |

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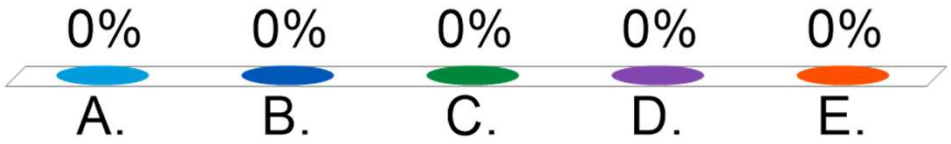
# WHAT IS THE NEXT STEP?

A. Peripheral Smear
B. Transfuse Platelets
C. Prednisone 60mg x 5 days
D. IVIG
E. GCSF

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# TRANSFUSING PLATELETS

- 1 apheresis platelets equal 4-6 units of whole blood
- AABB recommends transfusing to maintain platelets above 10K.
- Central line 20K
- LP 50K
- Major elective surgery 50K
- Stored at room temp (Shelf life 5days)
- Highest risk blood product
- Fever 1/14  Allergic Rx 1/50

***Platelet Transfusion: A Clinical Practice Guideline From the AABB***

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***Enough with the fastballs… Try this one***

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# MR. ETOH

## Past Medical History

Alcohol

Nicotine

## Past Surgical History:

Unknown

## Meds:

??????????????

## Review of Systems:

Found cutting lawn in winter apparel.  Well check called in to local PD.

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# LABS

| Lab | Admission |
|---|---|
| Hemoglobin | 10.2 |
| MCV | 101 |
| Platelets | 14,000 |
| Sodium | 131 |
| Potassium | 3.6 |
| Magnesium | 0.7 |
| Creatinine | 1.4 |
| BUN | 28 |
| AST | 252 |
| ALT | 112 |
| Lactate | 4.6 |
| INR | 2.1 |

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***“Banana bag, CIWA, Admit to Medicine”***

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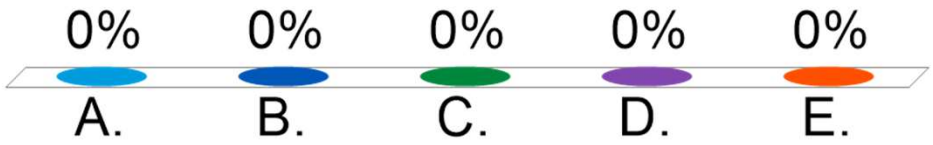
# RN CALLING…AGITATION, TREMORS, AND CONFUSION?

A. Extra dose of Ativan
B. Stat Head CT
C. Lactulose and Rifaximin
D. Empiric Vancomycin, Ceftriaxone, Acyclovir
E. Abdominal CT scan

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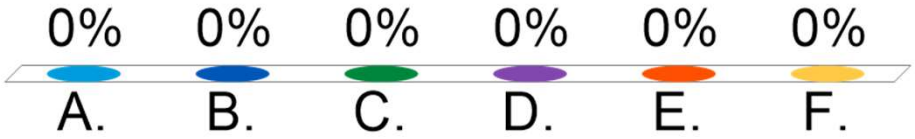
# STILL AGITATED…RN CALLS AGAIN???

A. Ativan 4mg IV
B. Lumbar Puncture
C. Repeat Lactate
D. Abdominal CT
E. Stat Head CT
F. 4mg IV Ativan for RN

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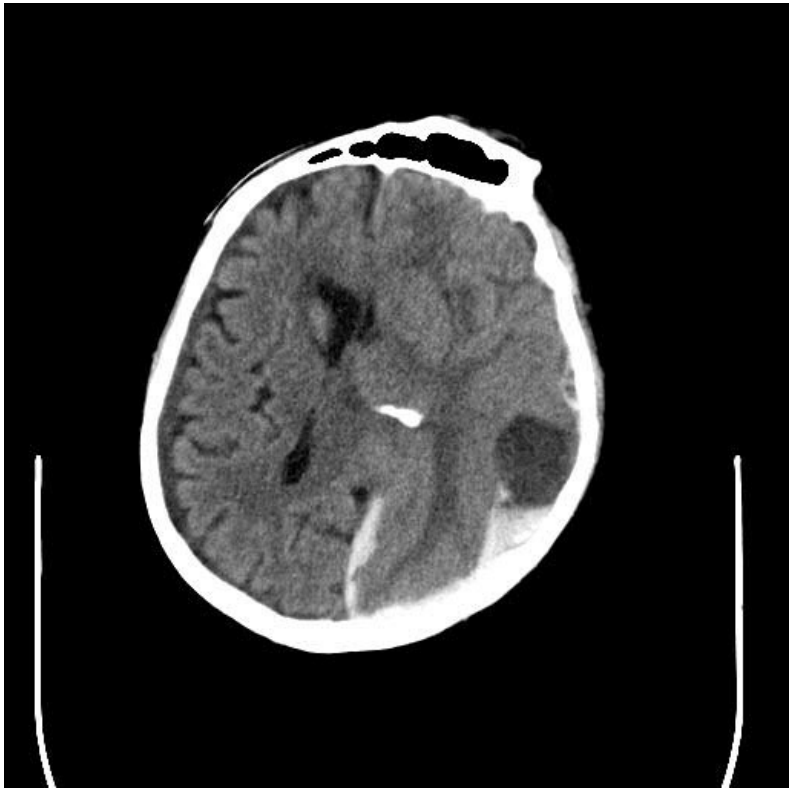
# #OHCRAP



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# AUTOPSY

Cirrhosis

Lung Cancer

Head Trauma/Subdural

Liver Disease + ETOH + Malignancy + Trauma

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# ETOH

Decreases platelet aggregation 20 minutes after ingestion

Toxic to megakaryocytes

Causes liver disease and splenomegaly

Accelerates platelet apoptosis

Decreased TPO

## Extra Credit:

MCV goes Up (Folate)

AST/ALT ratio 2:1 and typically less than 300

Magnesium down

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# DIC

**Sepsis**

**Malignancy** (leukemia, mucinous tumors (eg, pancreatic, gastric, ovarian), and brain tumors).

**Trauma** (central nervous system)

**Infection** (Bacterial, COVID)

**Obstetrical complications**

**Intravascular hemolysis**

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# WHAT IS THIS DIC YOU SPEAK OF?

**Disseminated Intravascular Coagulation**

Coagulation and Fibrinolysis at same time

Blood exposed to procoagulant (TF, LPS)

Acute vs Chronic

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# DIC MANAGEMENT

Treat underlying disorder

Are they Clotting?

- Clinically overt Art/Ven TE or extensive deposition of fibrin (ischemia/skin infarcts)
- low dose heparin 500-1000u/hr (10u/kg/hr)
- Consider antithrombin replacement

Are they Bleeding?

- FFP replace clotting factors (16cc/kg)
- Cryoprecipitate for fibrinogen (>100)
- Platelets (keep >50K)

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***How about this one…***

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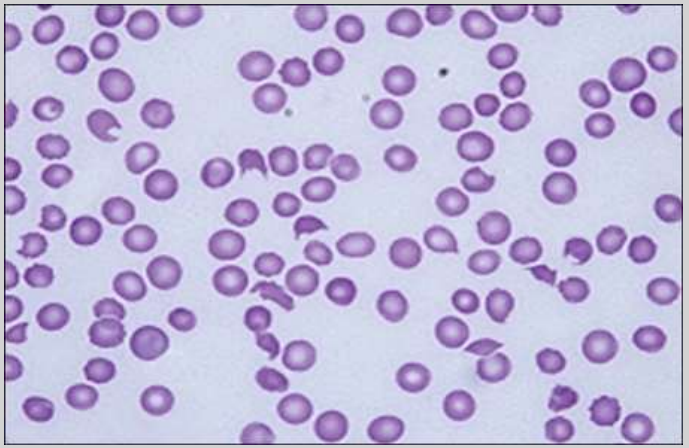
Mrs. Sofa is a 45F with history of diabetes is admitted with fever, back pain and dysuria.

- Vitals normal other than fever
- Was mildly confused on exam
- Labs: PLT 20K, Hb 7.8, WBC 17
- AST, ALT, creatinine - normal
- Peripheral smear = Schistocytes



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# WHAT IS THE MOST LIKELY DIAGNOSIS?

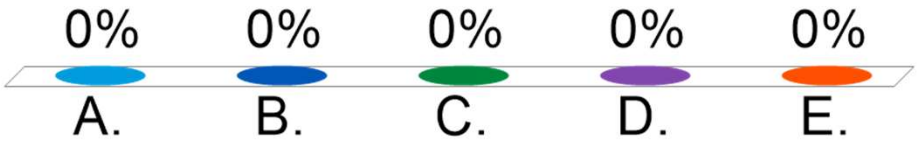
A. Thrombotic thrombocytopenia purpura

B. Hemolytic uremic syndrome

C. DIC from sepsis

D. Immune thrombocytopenic purpura

E. I have no idea, need more laboratory data

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| INR | LDH | Coombs | D Dimer | Fibrinogen |
|---|---|---|---|---|
| 1.8 | 350 | Negative | 900 | 100 |

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# NOW, WHAT IS THE MOST LIKELY DIAGNOSIS?

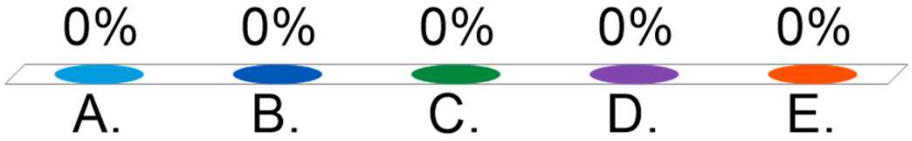
A. Thrombotic thrombocytopenia purpura

B. Hemolytic uremic syndrome

C. DIC from sepsis

D. Immune thrombocytopenic purpura

E. Wait… What were we talking about again?

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| INR | LDH | Coombs | D Dimer | Fibrinogen |
|---|---|---|---|---|
| 1.8 | 350 | Negative | 900 | 100 |

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***Moving right along…***

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# MRS. COLLEGE

## Past Medical History

Exercise Induced Asthma

GERD

## Past Surgical History:

Ankle Fracture Repair

## Meds:

Prilosec 20mg daily (noncompliant)

Albuterol (Non Compliant)

Birth Control

## Review of Systems:

Binge drinking last night at an “80s” party.  Sore throat, fevers, body aches, and abdominal pain.

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# LABS

| HGB | WBC | Plts | Na | K | Cr | AST | ALT | Bili | UA |
|---|---|---|---|---|---|---|---|---|---|
| 14 | 14.8 | 68 | 138 | 4.8 | 0.8 | 257 | 157 | 0.2 | Neg<br>- pregnancy |

| Peripheral Smear |
|---|
| Reactive lymphocytes. Thrombocytopenia. |

| "FluRona Swab" and Strep Swab |
|---|
| Negative |

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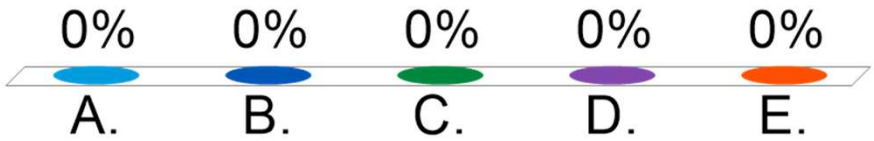
# NEXT STEP?

A. Blood cultures, Saline bolus, empiric vancomycin and cefepime
B. CIWA protocol
C. Woods Lamp + Iphone
D. Check INR and Fibrinogen
E. Call her mom

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Totally
Awesome
80's

**Brinker AD, Beitz J.**
**Spontaneous reports of thrombocytopenia in association with quinine: clinical attributes and timing related to regulatory action.**
**Am J Hematol. 2002 Aug;70(4):313-7.**

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# SPLENOMEGALY

- Viral infections, such as mononucleosis
- Bacterial infections, such as syphilis or endocarditis
- Parasitic infections, such as malaria
- Cirrhosis and other diseases affecting the liver
- Hemolytic anemia
- Blood cancers, such as leukemia and myeloproliferative neoplasms, and lymphomas, such as Hodgkin's disease
- Metabolic disorders, such as Gaucher's disease and Niemann-Pick disease
- Pressure on the veins in the spleen or liver or a blood clot in these veins

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***Next…***

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# MR. SEYMOUR

**Past Medical History**

Hyperlipidemia

BPH

**Meds:**

Simvastatin

Flomax

**Review of Systems:**

Fevers, confused, hematochezia.

**Past Surgical History:**

Left TKA

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# LABS

| HGB | WBC | Plts | Na | K | Cr | AST | ALT | Bili | INR |
|---|---|---|---|---|---|---|---|---|---|
| 8.4 | 11.8 | 18 | 138 | 5.3 | 1.8 | 257 | 57 | 3.8 | 0.9 |

| Fibrinogen | Coombs |
|---|---|
| 358 | Negative |

| Peripheral Smear |
|---|
| Schistocytes. Thrombocytopenia. |

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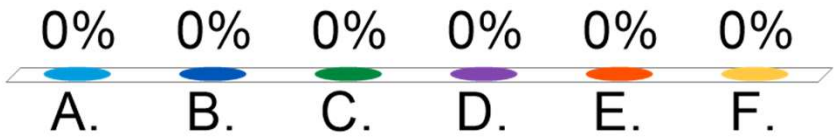
# WHAT THREE LETTER ACRONYM IS THIS?

A. HUS
B. DIC
C. TTP
D. HIT
E. LOL
F. IDK

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# LABS

| HGB | WBC | Plts | Na | K | Cr | AST | ALT | Bili | INR |
|---|---|---|---|---|---|---|---|---|---|
| 8.4 | 11.8 | 18 | 138 | 5.3 | 1.8 | 257 | 57 | 3.8 | 0.9 |

| Fibrinogen | Coombs |
|---|---|
| 358 | Negative |

| Peripheral Smear |
|---|
| Schistocytes. Thrombocytopenia. |

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| Test | DIC | TTP/HUS | Liver Disease |
|---|---|---|---|
| Peripheral blood smear | **Schistocytes**<br>**Thrombocytopenia** | **Schistocytes**<br>**Thrombocytopenia** | **Thrombocytopenia** |
| D-DIMERS<br>Soluble fibrin monomer | **Positive**<br>**Positive** | **Negative**<br>**Negative** | **Positive**<br>**Negative** |
| PT/PTT<br>Fibrinogen | **Prolonged**<br>**Decreased** | **Normal**<br>**Normal** | **Prolonged**<br>**Decreased** |
| Factor Assays | **All factors decreased** | **Normal** | **All decreased except FVIII** |

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# WHAT'S NEXT?

A. Check ADAMS13 activity
B. Initiate Plasma Exchange
C. Give 40mg of Dexamethasone
D. Transfuse Platelets
E. Watch Addams Family
F. Draft Davante Adams on your FF team
G. Watch Amy Adams movies
H. Enough with the ADAMS already


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# STANDARD MANAGEMENT OF TTP

- Plasma Exchange  (90% effect-daily till recovery for 48hrs)
- Glucocorticoids (1g daily x3 or 1-2mg/kg daily till CR then taper)
- Rituximab 375mg weekly x4 weeks
- Red Cell Transfusions
- Folic Acid
- Caplacizumab (high risk only)
- Avoid Platelet Transfusion (only for Life threat bleed or procedure)

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# CAUSES OF TTP

- Drug (Plavix, ticlopidine, cyclosporine)
- Infection
- Pregnancy/ Postpartum
- Autoimmune disorders
- Malignancy
- Stem Cell or Organ Transplantation

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# TTP

## Classic Pentad

- Microangiopathic Hemolytic Anemia
- Thrombocytopenia
- Fever
- Mental Status Changes
- Renal Insufficiency

## Clinical "Triad"

- Microangiopathic Hemolytic Anemia
- Thrombocytopenia
- Absence of an alternative explanation (DIC, sepsis…)

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## TABLE 5

### PLASMIC Score for Predicting ADAMTS13 Enzyme Activity

Platelet count < $30 \times 10^3$ per µL ($30 \times 10^9$ per L)

Hemolysis

No cancer history

No transplantation history

Mean corpuscular volume < 90 $\mu m^3$ (90 fL)

Creatinine < 2.0 mg per dL (177 µmol per L)

International normalized ratio < 1.5

**PLASMIC score (one point per item present)**

0 to 4: low risk (4.3%)

5 to 6: intermediate risk (56.8%)

7: high risk (96.2%)

**Note:** Low ADAMTS13 enzyme activity is defined as ≤ 10%.

*Information from reference 10.*

*Am Fam Physician.* 2018 Sep 15;98(6):354-361.

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Mrs. Heparin is a 75 year old female was recently diagnosed with right leg DVT after Ortho surgery for femur fracture.

- Hb 14, WBC 6, PLT 360
- She was started on UFH and transitioned to enoxaparin and discharged to SNF.
- She returns one week later with new onset left arm swelling. An ultrasound shows new DVT. Hb 13, WBC 8, PLT 130

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# WHAT IS THIS?

A. HIT Type 1
B. HIT Type 2
C. DIC
D. TTP
E. Reaction to COVID Vaccine

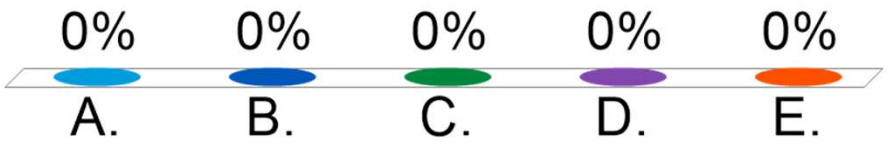


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**Table 1. 4T Scoring System for Evaluating the Pretest Probability of Heparin-Induced Thrombocytopenia.***

| Variable | Score | | |
|---|---|---|---|
| | 2 | 1 | 0 |
| Acute thrombocytopenia | Platelet count decrease of >50% and nadir ≥20,000/mm$^3$ | Platelet count decrease of 30–50% or nadir 10,000–19,000/mm$^3$ | Platelet count decrease of <30% or nadir ≤10,000/mm$^3$ |
| Timing of onset | Day 5–10, or day 1 if recent heparin exposure | >Day 10 or unclear exposure | ≤Day 4 with no recent heparin exposure |
| Thrombosis | New thrombosis or anaphylactoid reaction after heparin bolus | Progressive or recurrent thrombosis | None |
| Other cause of thrombocytopenia | None | Possible | Definite |
| **Total score** | 6–8, indicating high score | 4 or 5, indicating intermediate score | 0–3, indicating low score |

Lo GK, Juhl D, Warkentin TE, Sigouin CS, Eichler P, Greinacher A. Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. J Thromb Haemost 2006; 4: 759–65

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# MANAGEMENT

- Stop heparin
- PF4Ab and Serotonin Release Assay?
- Agatroban and Bivalirudin
- Renal➔ argatroban to warfarin
- Hepatic ➔ Bivalirudin to Eliquis/Arixtra
- Doacs ok at treatment dosing

Treat 4wks to 3months

*****20% mortality rate if untreated*****
**UFH>LMWH**
**Treatment dose> Prophylactic dose**
**Female>Male**

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# “LETS RUN THE LIST”

Mr. Spots

Mrs. Spots

Mrs. Popcorn

Mrs. Chemo

Mr. Etoh

Mrs. Sofa

Mrs. College

Mr. Seymour

Mrs. Heparin

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# QUESTIONS?

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