Not all thrombocytopenia is ITP…

(… nor is it TTP, HUS, gestational thrombocytopenia, nor HIT)

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Disclosures

None

Classical approach to thrombocytopenia

↓ Production

- Medications
- Alcohol
- Toxins
- Infections
- Nutritional deficiencies
- Liver disease
- Bone marrow/hematologic disorders
- Inherited thrombocytopenias

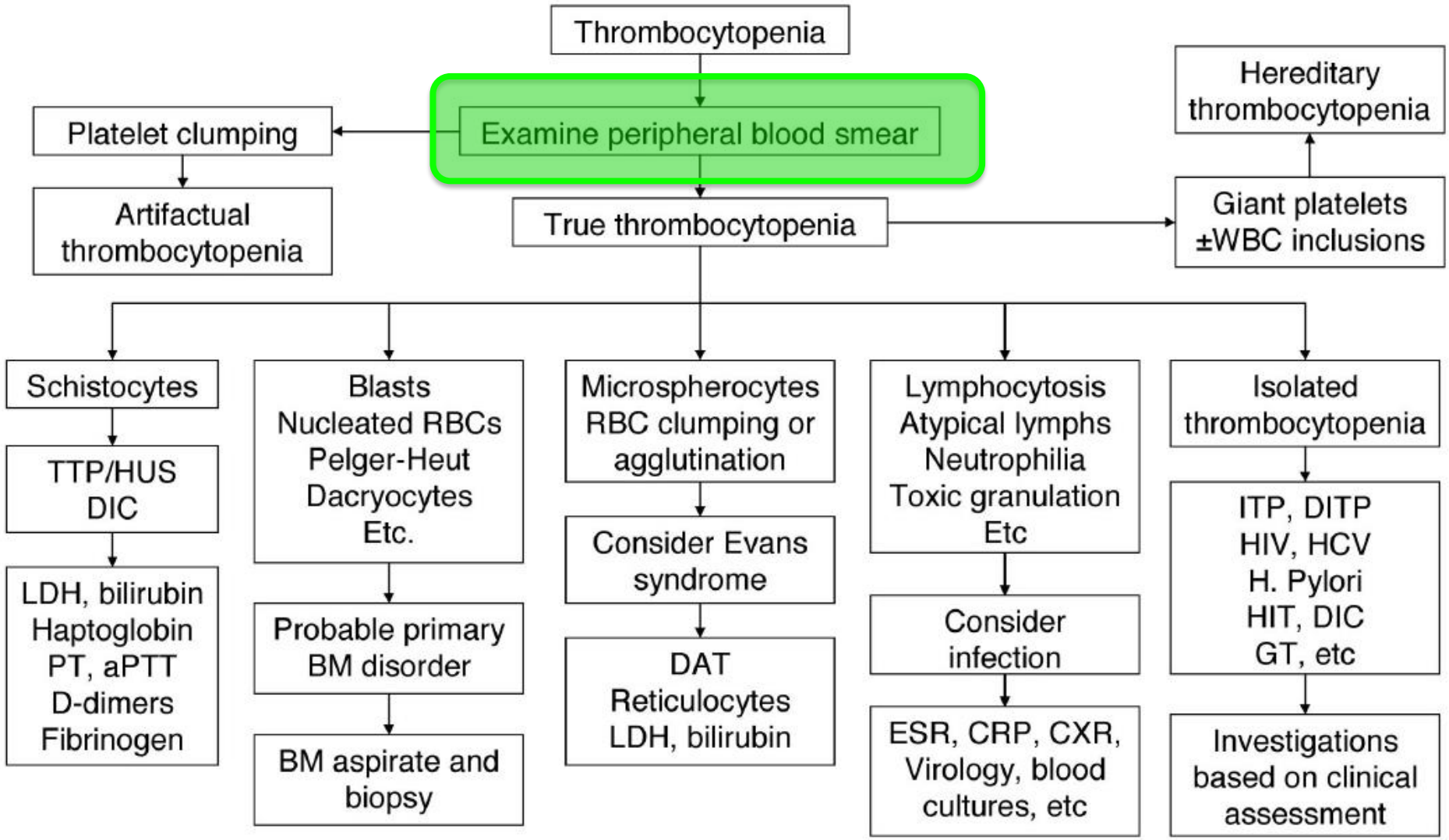
↑ Destruction

- Immune thrombocytopenia (ITP)
- Drug-induced ITP
- Thrombotic microangiopathy
- Disseminated intravascular coagulation
- Post-transfusion purpura
- Neonatal alloimmune thrombocytopenia

↑ Sequestration

- Splenomegaly

Smear-based approach to thrombocytopenia



(Stasi R, *Hematology Am Soc Hematol Educ Prog* 2012;2012:191)

Case 1: L.S.

L.S. is a 68-year-old woman who is hospitalized for vertigo. She is clinically stable. The hematology service is consulted as her blood counts show isolated thrombocytopenia.

Labs

WBC 11,000/mL (normal 5-11,000)
Hemoglobin 12.5 g/dL (normal 10-13)
Platelets 84,000/mL (normal 150-350,000)
- Repeat platelets 78,000/mcL

PT 12.0 sec (normal 11-13)
INR 1.0 (normal 0.9-1.1)
PTT 29 sec (normal 23-32)

What's the next step in evaluating this patient's thrombocytopenia?

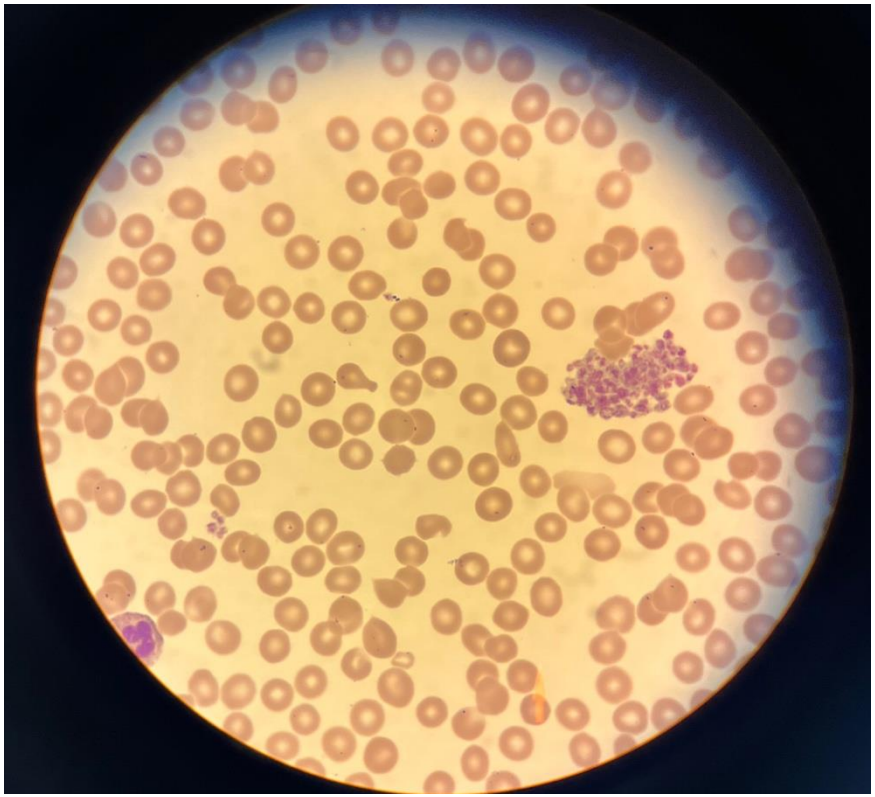
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Peripheral blood smear



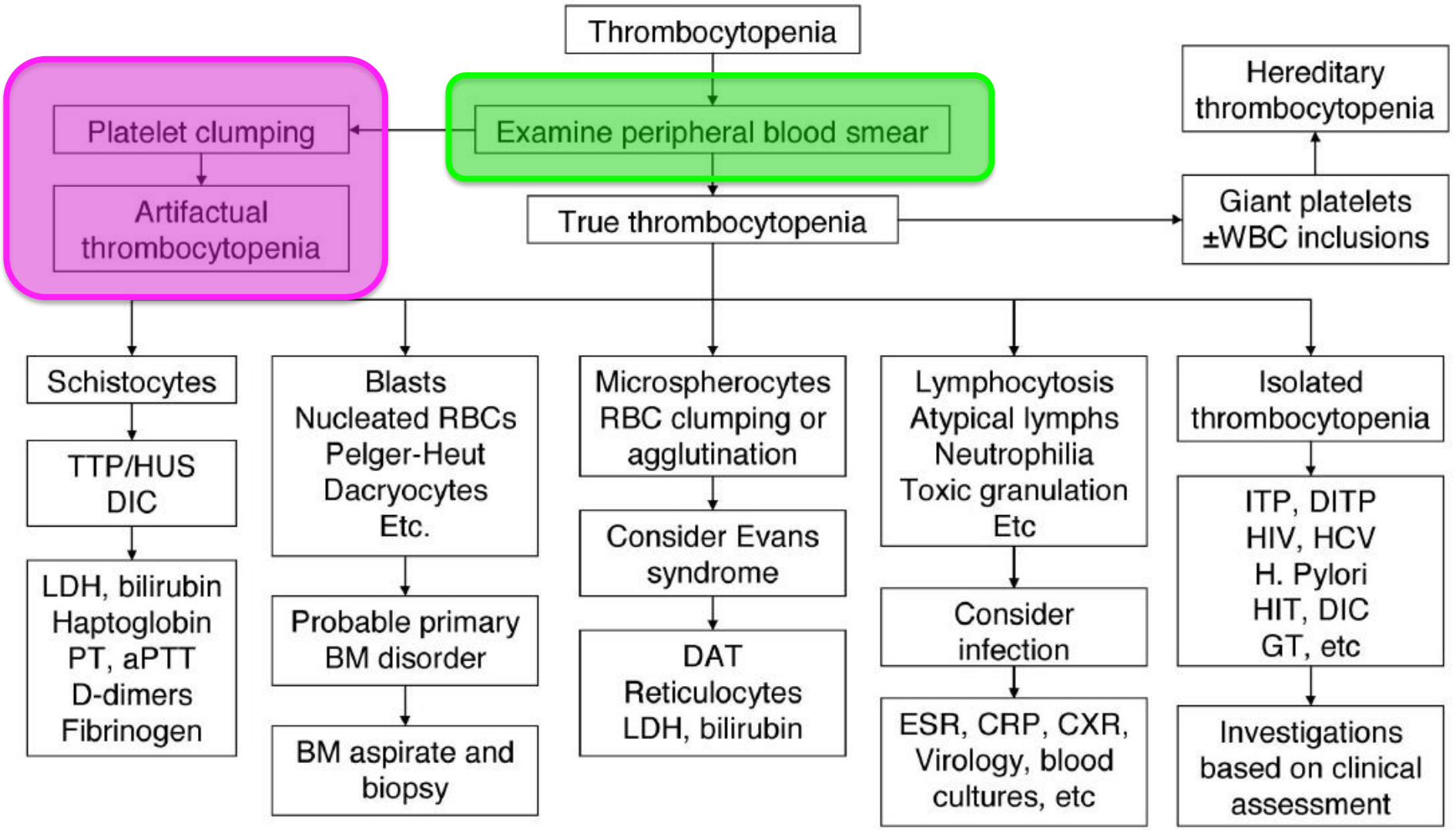
What's the diagnosis?

Clinical pearl

The peripheral blood smear is very useful in evaluating thrombocytopenia

- Assess for pseudothrombocytopenia
- Assess for other abnormal cell morphologies

Smear-based approach to thrombocytopenia

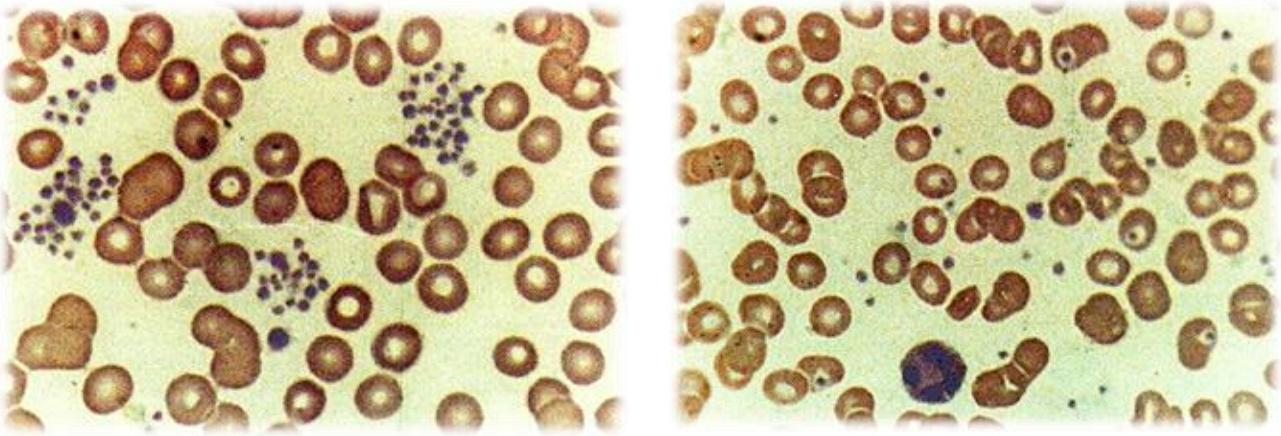


(Stasi R, *Hematology Am Soc Hematol Educ Prog* 2012;2012:191)

Pseudothrombocytopenia

- In-vitro phenomenon of no clinical significance
- Occurs in presence of EDTA
  - Mechanism: EDTA alters GPIIb conformation on platelet surface, allowing for binding of anti-GPIIb antibodies, leading to platelet clumping

EDTA



Heparin or citrate

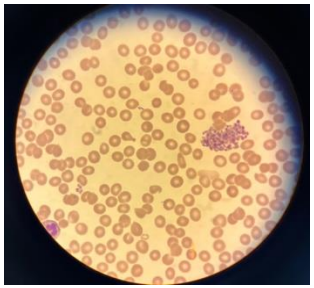
(Shalev O and Lotman A, *N Engl J Med* 1993;329:1467)

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Labs

WBC 11,000/mL (normal 5-11,000)
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Platelets 84,000/mL (normal 150-350,000)
PT 12.0 sec (normal 11-13)
INR 1.0 (normal 0.9-1.1)
PTT 29 sec (normal 23-32)

Smear



What's the diagnosis?

The patient is diagnosed with pseudothrombocytopenia based on the presence of copious platelet clumping on her blood smear. A repeat platelet count measured in citrate is in the normal range.

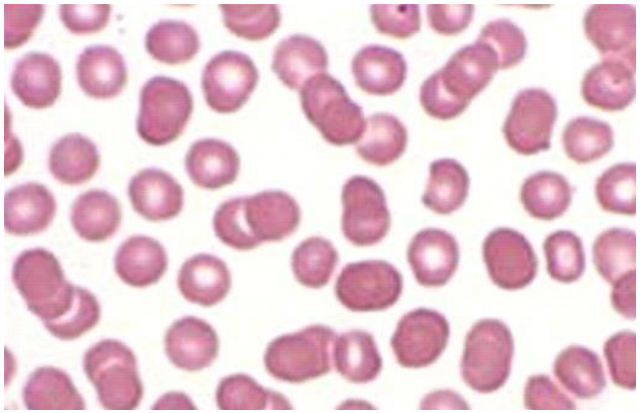
Case 2: E.F.

E.F. is a 73-year-old woman who is hospitalized for pneumonia. She is treated with vancomycin and piperacillin/tazobactam. One week later, she develops copious petechiae on her shins, with blood counts showing new-onset, severe isolated thrombocytopenia.

Labs

WBC	14,500/μL (normal 4-10,000)
Hemoglobin	12 g/dL (normal 12-15)
Platelets	12,000/μL (normal 150-350,000)
PT	13.1 sec (normal 11-15)
INR	1.1 (normal 0.9-1.1)
PTT	28 sec (normal 23-32)

Smear



What's the diagnosis?

Clinical pearl

Severe, isolated thrombocytopenia should raise suspicion for an immunologic cause

In the setting of drugs or medications, consider drug-induced immune thrombocytopenia (DITP)

DITP

- Antibodies against platelets in presence of drug lead to immune-mediated platelet destruction and severe thrombocytopenia

- Multiple drugs have been described in association with DITP

Abciximab (ReoPro™)	Loracarbef	Rifampin
Carbamazepine	Naproxen Glc	Sulfamethoxazole
Ceftazidime	Orbofiban	Sulfisoxazole
Ceftizoxime	Phenytoin	Suramin
Ceftriaxone	Propoxyphene	Tirofiban (Aggrastat™)
Eptifibatide (Integrelin™)	Quinidine	Trimethoprim
Fentanyl	Quinine	Vancomycin
Ibuprofen	Ranitidine	Xemilofiban

- Drug-dependent platelet antibodies to any drug may be checked at

versiti™

Platelet and Neutrophil Immunology Laboratory

(Reese JA et al, *Blood* 2010;116;2237)

Types of DITP

Hapten-dependent antibody

Hapten links covalently to platelet membrane protein
drug-specific immune response

Penicillin, cephalosporins

Quinine

Preexisting autoantibody in presence of drug binds to platelet GPIIb/IIIa or GPIb/IX/V

Quinine, sulfa drugs, vancomycin, NSAIDs

GPIIb/IIIa inhibitor

Drug binds GPIIb/IIIa
conformational change recognized by antibody

Eptifibatide, tirofiban

Drug is a murine monoclonal antibody that induces anti-murine antibody production → antiplatelet antibody

Abciximab

ITP

Drug-induced autoantibody against platelet antigen

Gold salts, procainamide

Immune complex

Drug-induced immune complex deposits onto platelets

Heparin (i.e., heparin-induced thrombocytopenia)

(Aster RH and Bougie DW, *N Engl J Med* 2007;357;580)

Types of DITP

Hapten-dependent antibody

Hapten links covalently to platelet membrane protein
drug-specific immune response

Penicillin, cephalosporins

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Severe thrombocytopenia, occurring several days after drug exposure

Preexisting autoantibody in presence of drug binds to platelet GPIIb/IIIa or GPIb/IX/V

Quinine, sulfa drugs, vancomycin, NSAIDs

GPIIb/IIIa inhibitor

Drug binds GPIIb/IIIa
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Abciximab

ITP

Drug-induced autoantibody against platelet antigen

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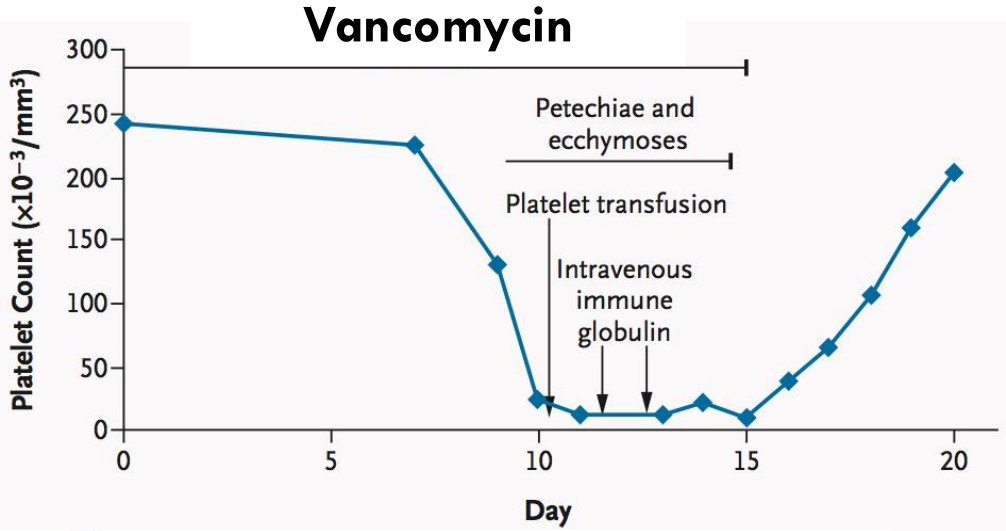
Immune complex

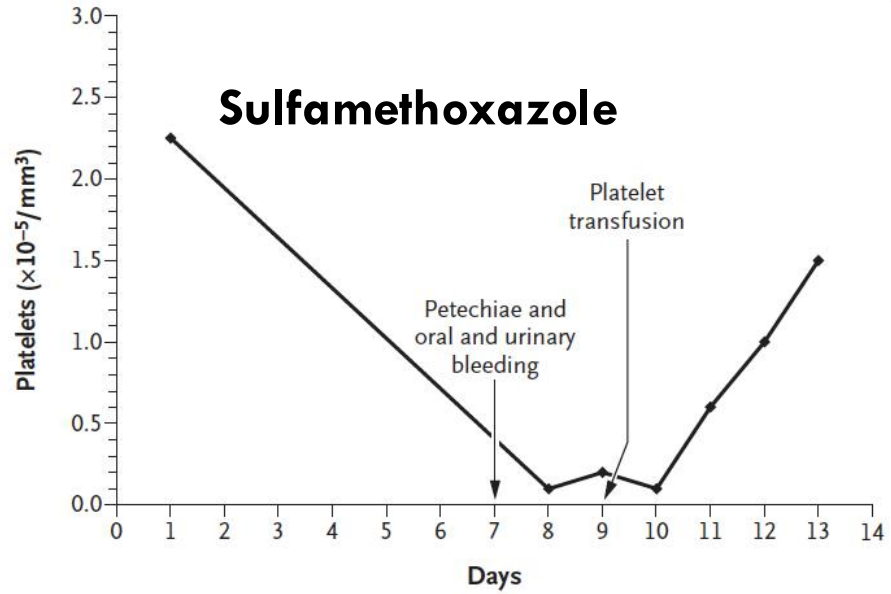
Drug-induced immune complex deposits onto platelets

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Quinine model of DITP





- Severe thrombocytopenia 5-10 days after drug exposure
- Treatment: stop offending drug

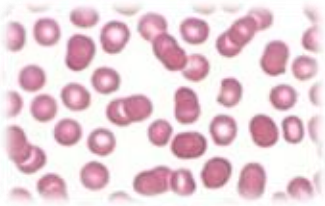
(Von Drygalski A et al , *N Engl J Med* 2007;356;904; Aster RH and Bougie DW, *N Engl J Med* 2007;357;580)

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Labs

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PT	13.1 sec (normal 11-15)
INR	1.1 (normal 0.9-1.1)
PTT	28 sec (normal 23-32)

Smear



What's the diagnosis?

The patient is suspected of having DITP based on the development of severe isolated thrombocytopenia a week after initiation of antibiotics known to be associated with DITP. Vancomycin and piperacillin/tazobactam are stopped, and she is instead treated with levofloxacin. Four days after changing antibiotics, her platelet count begins to rise. Drug-dependent platelet antibody testing returns a few weeks later showing antibodies against vancomycin.

Case 3: E.S.

E.S. is a 52-year-old man with nonischemic cardiomyopathy due to viral myocarditis. He undergoes an orthotopic heart transplant. His immune suppression is with tacrolimus, mycophenolate, and prednisone. Over the span of 4 weeks following his cardiac transplant, he suffers from cellulitis, deep venous thrombosis, renal insufficiency, and ARDS requiring intubation. He develops ventilator-associated pneumonia and shock and is treated with broad-spectrum antibiotics and on vasopressor support. In this setting, his blood counts show progressive anemia and thrombocytopenia.

Labs

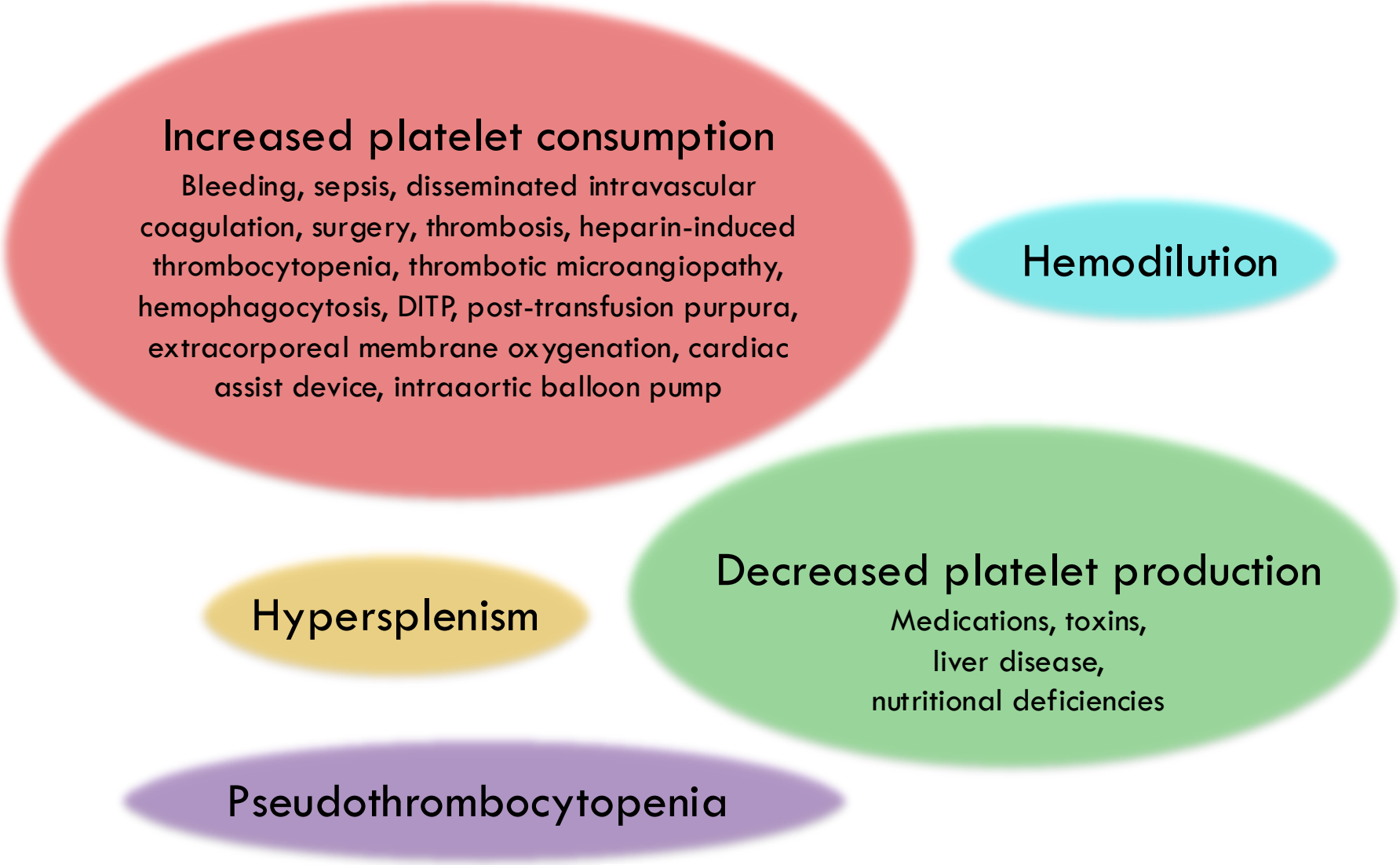
WBC	15,200/μL (normal 4-10,000)
Hemoglobin	8.5 g/dL (normal 12-15)
Platelets	16,000/μL (normal 150-350,000)
PT	12.7 sec (normal 11-15)
INR	1.1 (normal 0.9-1.1)
PTT	30 sec (normal 23-32)

What's the etiology of his thrombocytopenia?

Clinical pearl

Thrombocytopenia in the setting of critical illness usually reflects "critical illness thrombocytopenia"

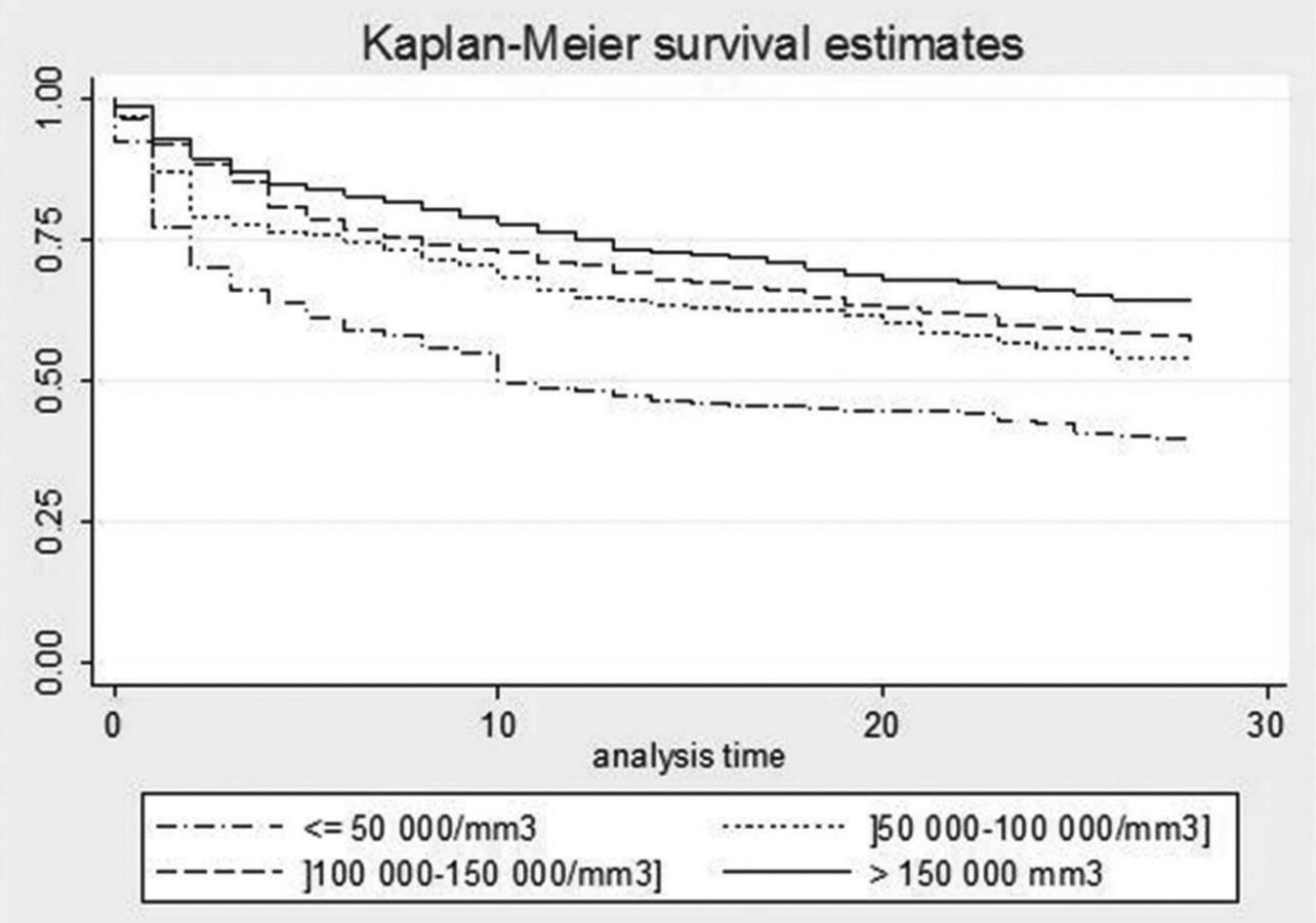
Critical illness thrombocytopenia



(Greinacher A and Selleng K, *Hematology Am Soc Hematol Educ Prog* 2010;2010:135; Zarychanski R and Houston DS, *Hematology Am Soc Hematol Educ Prog* 2017;2017:660)

Thrombocytopenia is a poor prognostic marker in critically ill patients

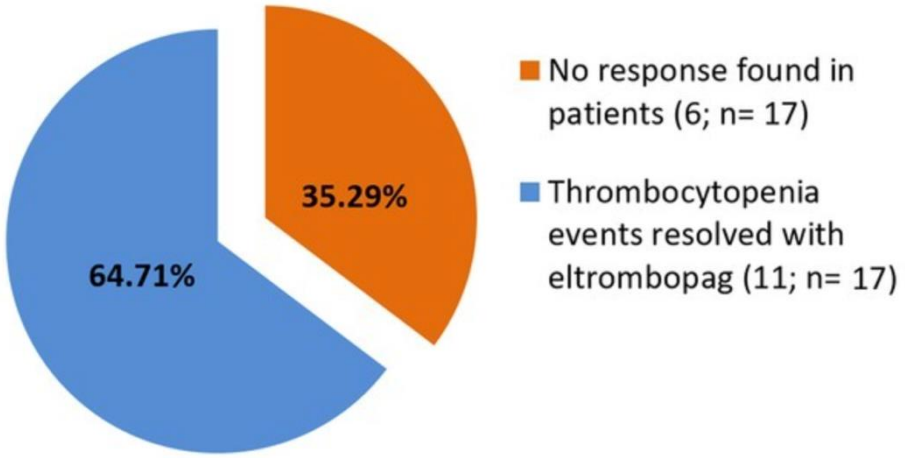
Septic Shock Study, 2009-2011



(Thieri-Antier N et al, *Crit Care Med* 2016;44:746)

Treatment of critical illness thrombocytopenia is directed at the underlying diseases

Thrombopoietin receptor agonists (TPO-RAs) may have a role



(Jhadul Hasan Md et al, *J Crit Care Med (Targu Mures)* 2015;5:123; Northam K and Rana R, *Crit Care Med* 2025;53:abstract 492; Shi N et al, Clin Appl Thromb Hemost 2026;32:10760296261431920)

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What's the etiology of his thrombocytopenia?

His thrombocytopenia is attributed to critical illness. Ongoing optimization of medical supportive care is advised.

Case 4: J.D.

J.D. is a 57-year-old woman with cirrhosis due to hepatitis C. In the past, she was treated with sofosbuvir/ledipasvir (Harvoni) and achieved a sustained virologic response. As a result of cirrhosis, she has chronic pancytopenia. She has now been admitted for cough and found on imaging to have a lung mass.

Labs

WBC	3,800/μL (normal 4-10,000)
Hemoglobin	10.8 g/dL (normal 12-15)
Platelets	26,000/μL (normal 150-350,000)
PT	11.8 sec (normal 11-15)
INR	1.1 (normal 0.9-1.1)
PTT	30.2 sec (normal 23-32)
Fibrinogen	166 mg/dL (normal 150-400)

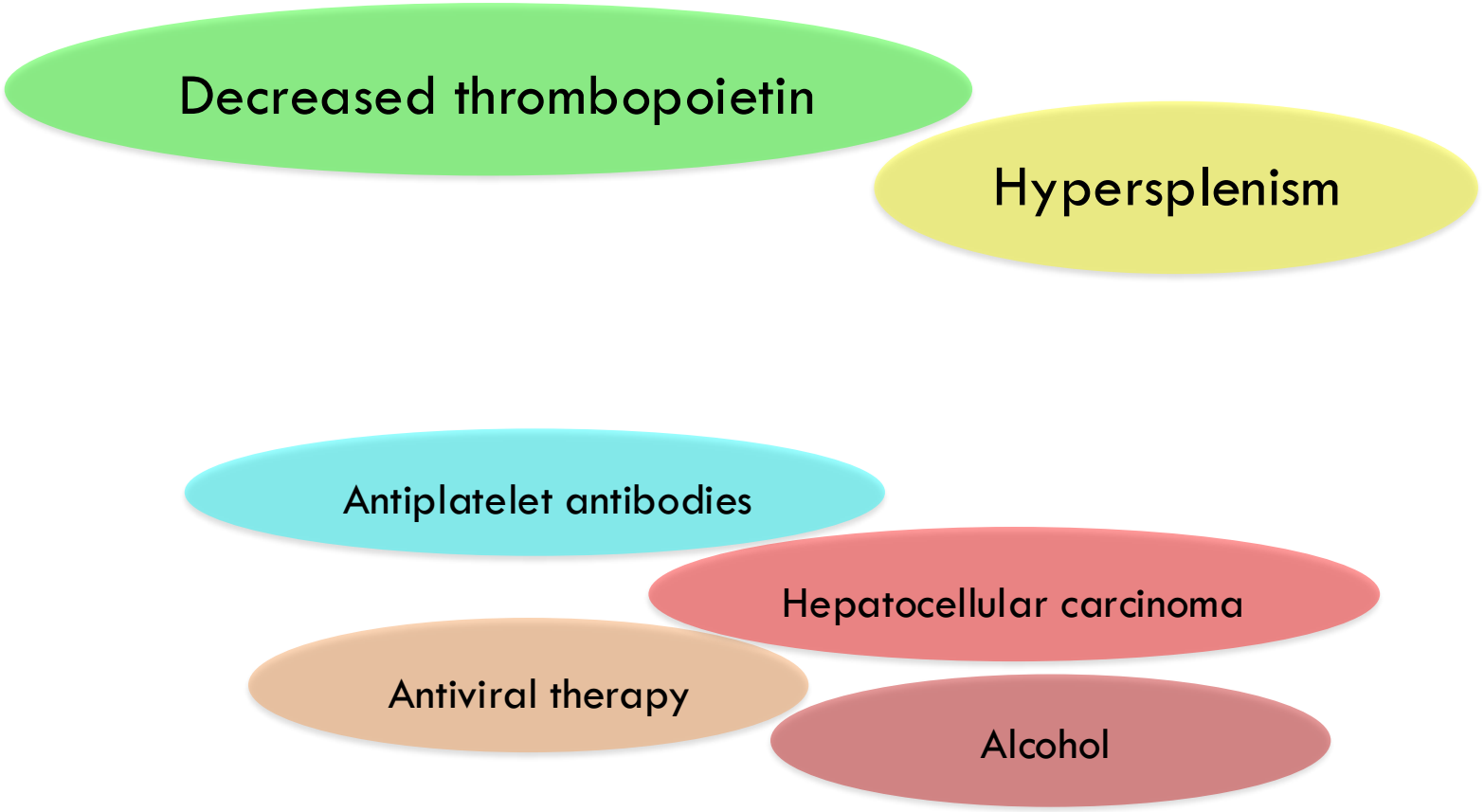
The interventional radiology service would like her platelet count to be at least 50,000/μL before moving forward with a biopsy of the lung mass.

Other than platelet transfusions, how can this patient's platelet count be increased for her procedure?

Clinical pearl

TPO-RAs are effective and generally safe when used periprocedurally for a limited duration to treat thrombocytopenia due to cirrhosis

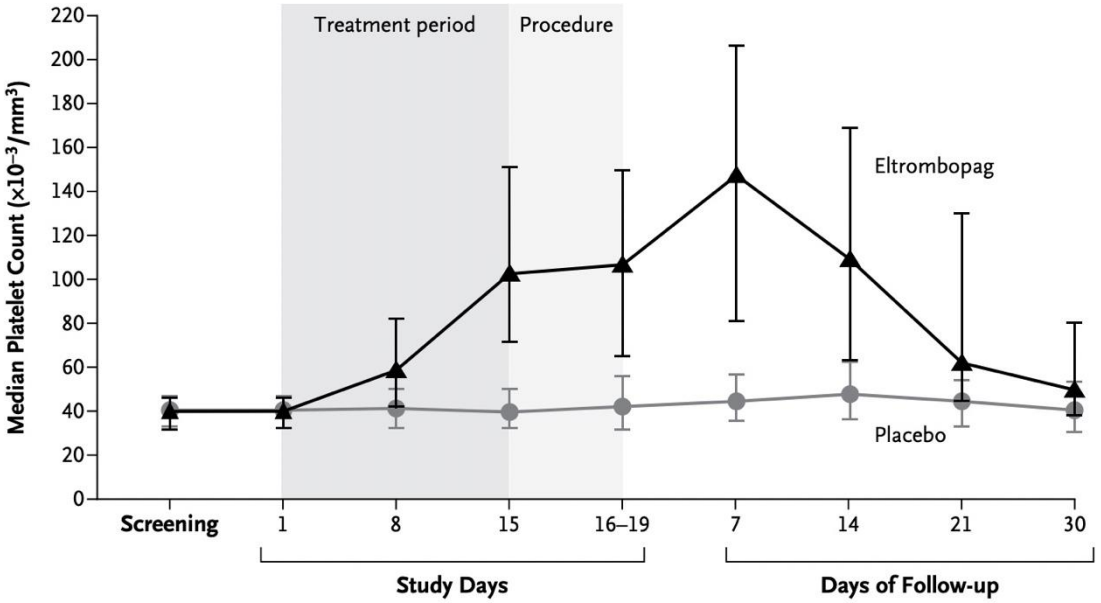
Thrombocytopenia in cirrhosis



(Peck-Radosavljevic M, *Liver Int* 2017;37:778)

TPO-RAs in cirrhosis

Eltrombopag for 14 days is effective but may lead to splanchnic vein thrombosis



No. with Available Data									
Placebo	147	145	139	132	50	128	116	120	125
Eltrombopag	144	141	134	131	49	125	125	117	127

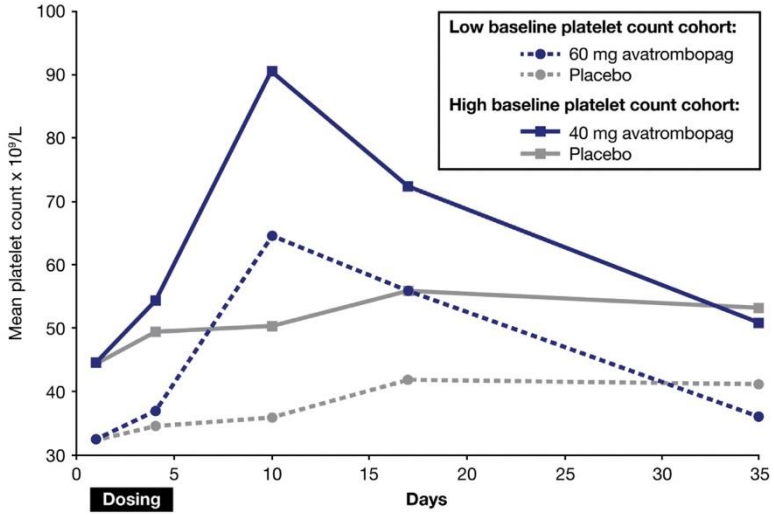
Eltrombopag
Portal-vein and superior-mesenteric-vein thrombosis†
Portal-vein thrombosis
Superior-mesenteric-vein thrombosis
Superior-mesenteric-vein and mesenteric-vein thrombosis
Splenoportal venous thrombosis
Portal-vein thrombosis
Placebo
Acute myocardial infarction
Nonocclusive portal-vein and mesenteric-vein thrombosis

(Afdhal NH et al, *N Engl J Med* 2012;367:716)

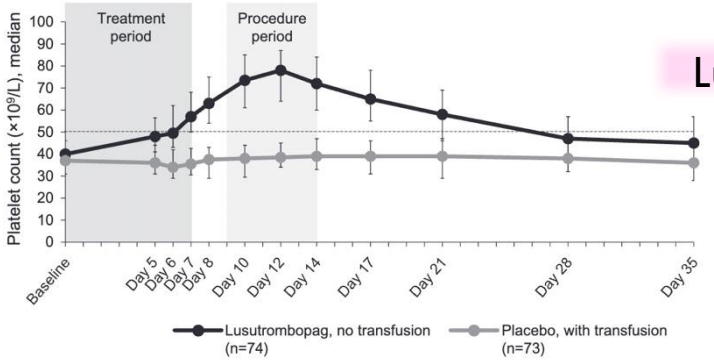
TPO-RAs in cirrhosis

Avatrombopag for 5 days, lusutrombopag for 4-7 days, and romiplostim for ≤ 4 weeks are all effective and have no major increase in thrombosis risk

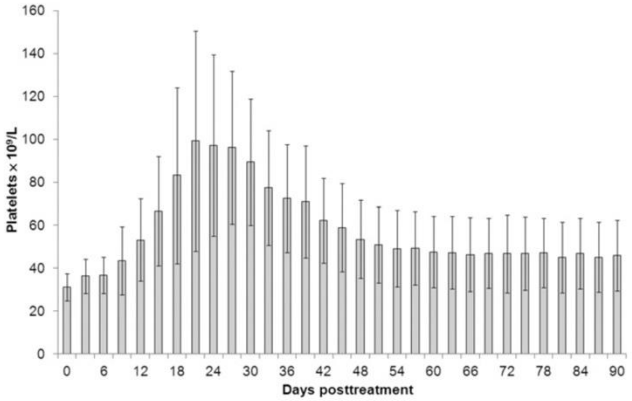
Avatrombopag



Lusutrombopag



Romiplostim



(Moussa MM and Mowafy N, *J Gastroenterol Hepatol* 2013;28:335; Terrault N et al, *Gastroenterology* 2018;155:705; Peck-Radosavljevic M et al, *Hepatology* 2019;70:1336)

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PT	11.8 sec (normal 11-15)
INR	1.1 (normal 0.9-1.1)
PTT	30.2 sec (normal 23-32)
Fibrinogen	166 mg/dL (normal 150-400)

The interventional radiology service would like her platelet count to be at least 50,000/μL before moving forward with a biopsy of the lung mass.

Other than platelet transfusions, how can this patient's platelet count be increased for her procedure?

She is treated with avatrombopag for 5 days. Within several days, her platelet count rises above 50,000/μL, and she is able to proceed with biopsy of her lung mass.

Case 5: G.T. – part 1

G.T. is a 68-year-old man with mesothelioma who is undergoing treatment with carboplatin and pemetrexed, for a planned 6 cycles of chemotherapy administered every 21 days. As a result of chemotherapy, he has developed dose-limiting thrombocytopenia that caused a 1-week delay in starting cycle 2. Presently, he is 2 weeks overdue for cycle 3, with chemotherapy on hold due to thrombocytopenia.

Labs

WBC	5,600/μL (normal 4-10,000)
Hemoglobin	11.8 g/dL (normal 12-15)
Platelets	36,000/μL (normal 150-350,000)
PT	12.8 sec (normal 11-15)
INR	1.1 (normal 0.9-1.1)
PTT	27.5 sec (normal 23-32)

What's a feasible strategy to improve his platelet counts and reduce further chemotherapy treatment delays?

Clinical pearl

TPO-RAs, specifically romiplostim and avatrombopag, are effective in treating and preventing chemotherapy-induced thrombocytopenia

Thrombocytopenia in cancer

Antineoplastic therapy

Direct cancer effects

Myelophthisis of bone marrow, splenic infiltration leading to hypersplenism

Thrombotic microangiopathy

Systemic effects

Infection, sepsis, liver disease, thrombosis, critical illness

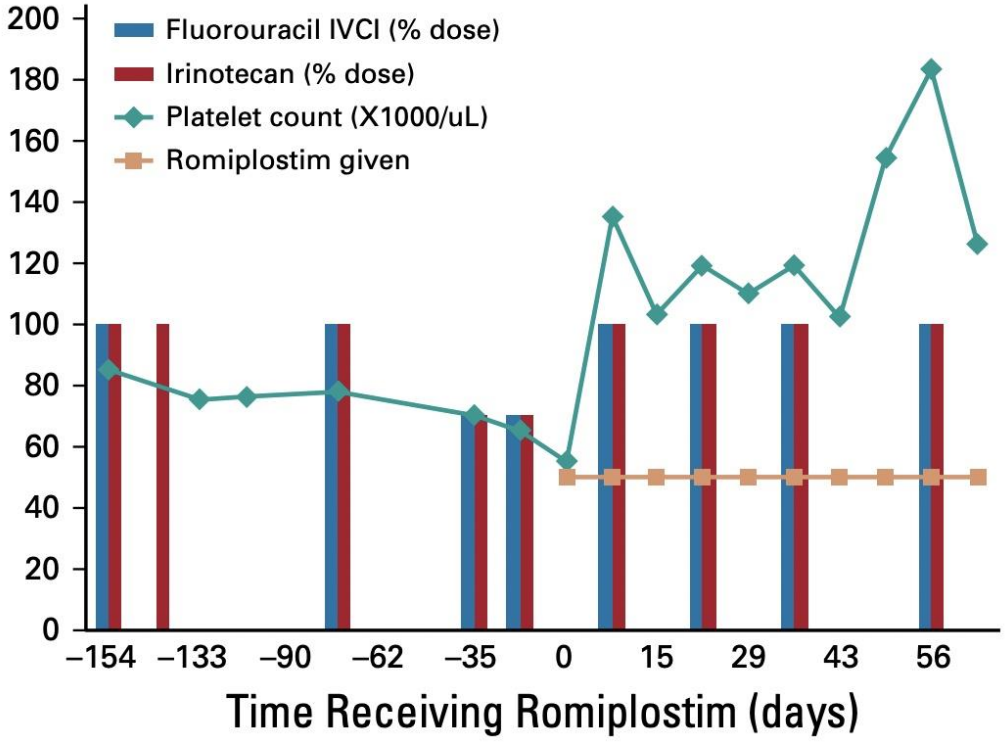
Immune disorders

ITP, heparin-induced thrombocytopenia

(Lliebman HA, *Thromb Res* 2014;133 Suppl 2:S63)

Romiplostim

When administered to patients with persistent chemotherapy-induced thrombocytopenia (platelet counts < 100,000/μL), romiplostim leads to improved platelet counts, reducing chemotherapy delays



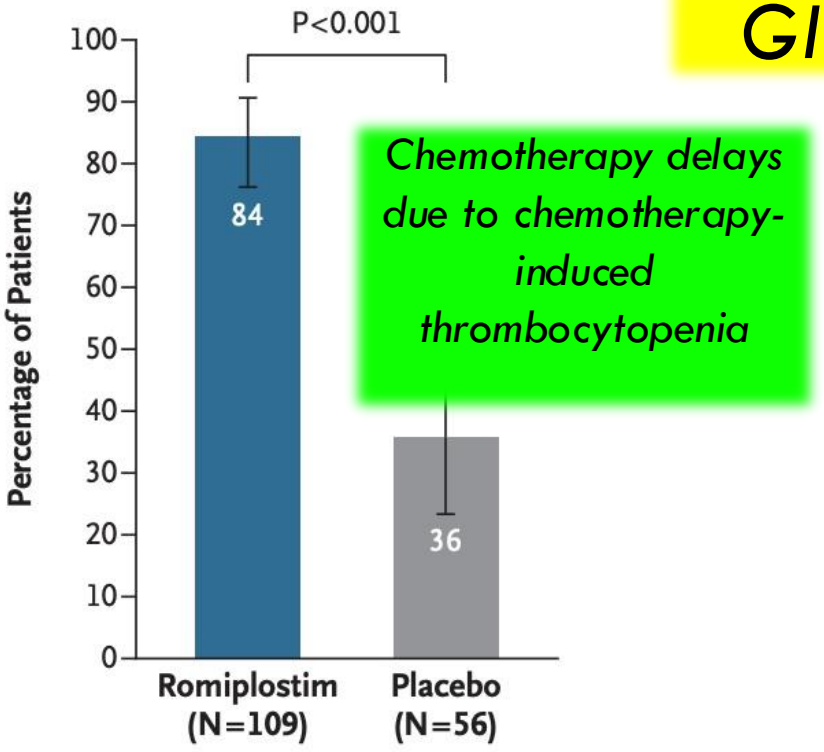
Less effective if myelophthisis of bone marrow is present

(Soff GA et al, *J Clin Oncol* 2019;37:2893; Al-Samkari H et al, *Haematologica* 2021;106:1148)

Romiplostim

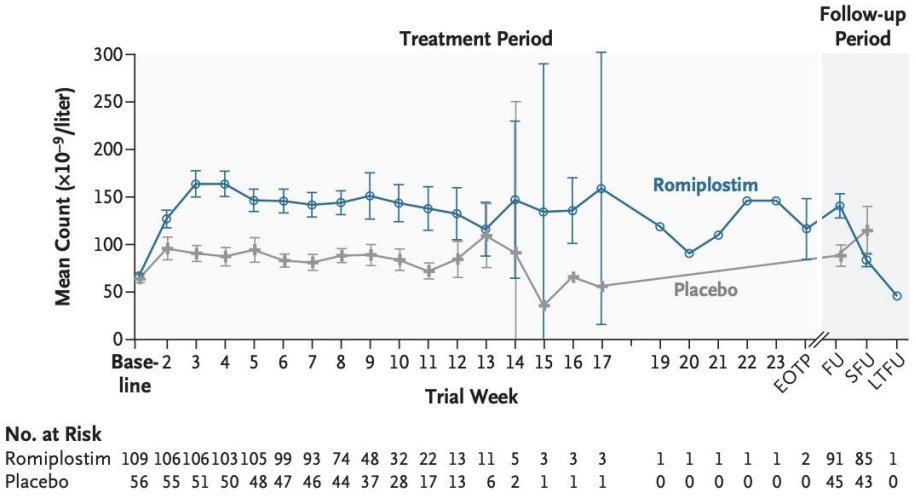
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GI cancer



Chemotherapy delays due to chemotherapy-induced thrombocytopenia

Platelet counts



(Al-Samkari H et al, *N Engl J Med* 2026;394:1061)

Avatrombopag

One RCT of avatrombopag administered to patients with persistent chemotherapy-induced thrombocytopenia (platelet counts < 50,000/μL) showed no difference in platelet counts or chemotherapy delays vs. placebo, but the placebo group had unexpectedly good platelet counts

Another RCT of avatrombopag in patients with GI cancers and persistent chemotherapy-induced thrombocytopenia (platelet counts < 85,000/μL) showed overwhelming efficacy with correction and prevention of recurrence of chemotherapy-induced thrombocytopenia

(Al-Samkari H et al, *Lancet Haematol* 2022;9:e179; Soff GA et al, *J Clin Oncol* 2026;44:3580 abstract)

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What's a feasible strategy to improve his platelet counts and reduce further chemotherapy treatment delays?

He is started on romiplostim 2 mcg/kg weekly. The dose is adjusted weekly based on his platelet counts. He eventually attains a romiplostim dose of 4 mcg/kg weekly, with platelet counts > 100,000/μL and no further chemotherapy delays.

Case 5: G.T. – part 2

G.T. is a 68-year-old man with mesothelioma who just completed his 6th cycle of chemotherapy with carboplatin and pemetrexed. As a result of these chemotherapy treatments, he has developed pancytopenia. He is now admitted for acute-onset dyspnea and has been diagnosed with bilateral pulmonary emboli involving the segmental vessels of the right and left upper lung lobes.

Labs

WBC	2,400/μL (normal 4-10,000)
Hemoglobin	10.8 g/dL (normal 12-15)
Platelets	32,000/μL (normal 150-350,000)
PT	13.2 sec (normal 11-15)
INR	1.1 (normal 0.9-1.1)
PTT	28.9 sec (normal 23-32)

What's the best anticoagulation strategy for this patient?

Clinical pearl

A dose-adjusted anticoagulation strategy is effective and safe in treating cancer-associated thrombosis (CAT) and thrombocytopenia

Two anticoagulation strategies for CAT and thrombocytopenia

With platelet transfusions

Platelet count ≥ 50,000/mcL	Full-dose anticoagulation • LMWH (e.g., enoxaparin 1 mg/kg twice-daily, or 1.5 mg/kg once-daily) • DOAC (e.g., apixaban 5 mg twice-daily; or rivaroxaban 20 mg once-daily)
Platelet count < 50,000/mcL	Full-dose anticoagulation • LMWH • DOAC Transfuse platelets to raise platelet count ≥ 50,000/mcL

No platelet transfusions

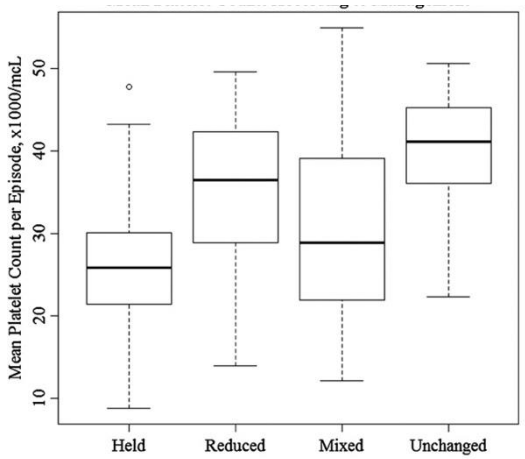
Platelet count ≥ 50,000/mcL	Full-dose anticoagulation • LMWH • DOAC
Platelet count 25,000-50,000/mcL	Half-dose anticoagulation • LMWH (e.g., enoxaparin 0.5 mg/kg twice-daily, or 0.75 mg/kg once-daily) • DOAC (e.g., apixaban 2.5 mg twice-daily; or rivaroxaban 10 mg once-daily)
Platelet count < 25,000/mcL	No anticoagulation

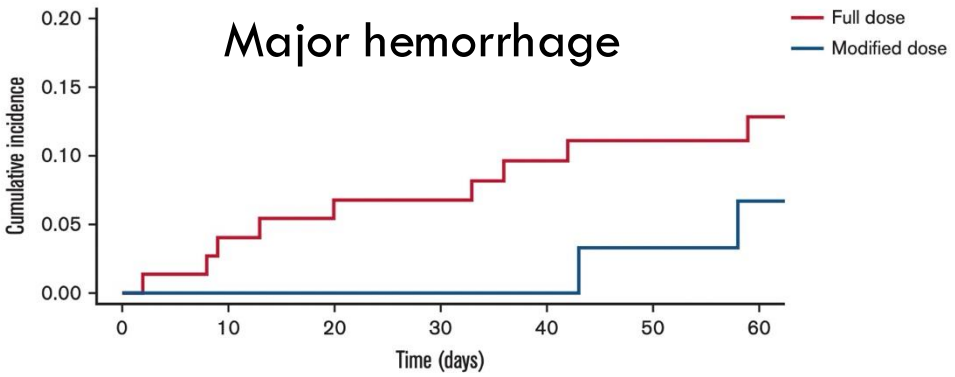
(Goshua G et al, *Hematology Am Soc Hematol Educ Prog* 2022)

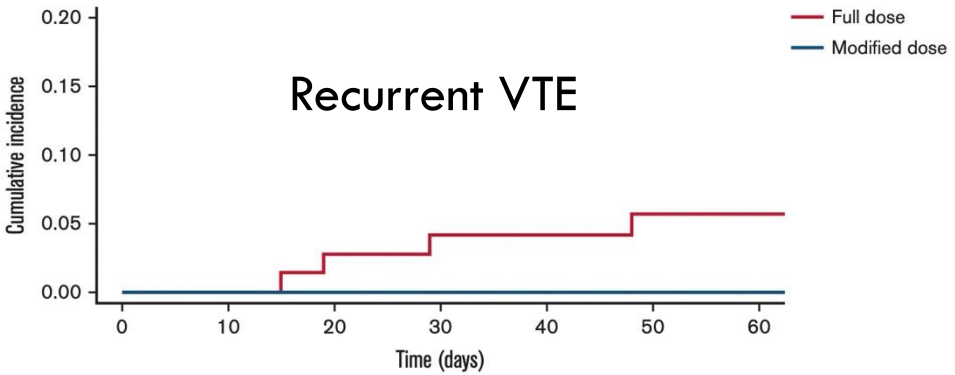
Dose-adjusted anticoagulation in CAT and thrombocytopenia

Enoxaparin, apixaban, or rivaroxaban

Enoxaparin







(Mantha S et al, *J Thromb Thrombolysis* 2017;43:514; Carney BJ et al, *Blood Adv* 2021;5:5546)

G.T. is a 68-year-old man with mesothelioma who just completed his 6th cycle of chemotherapy with carboplatin and pemetrexed. As a result of these chemotherapy treatments, he has developed pancytopenia. He is now admitted for acute-onset dyspnea and has been diagnosed with bilateral pulmonary emboli involving the segmental vessels of the right and left upper lung lobes.

Labs

WBC	2,400/μL (normal 4-10,000)
Hemoglobin	10.8 g/dL (normal 12-15)
Platelets	32,000/μL (normal 150-350,000)
PT	13.2 sec (normal 11-15)
INR	1.1 (normal 0.9-1.1)
PTT	28.9 sec (normal 23-32)

What's the best anticoagulation strategy for this patient?

He is started on anticoagulation with apixaban 2.5 mg twice-daily and tolerates this well without bleeding complications.

Case 6: R.K.

R.K. is a 40-year-old woman with a longstanding history of menorrhagia, who is discovered by her primary care physician to have severe and symptomatic iron deficiency anemia. She is started on oral iron supplementation and transfused 1 unit of RBC. One week later, she presents to the emergency department with diffuse petechiae and wet purpura and is found to have new-onset, severe thrombocytopenia.

Labs 1 week ago, prior to RBC transfusion		Labs now	
WBC	5,300/μL (normal 4-10,000)	WBC	4,200/μL (normal 4-10,000)
Hemoglobin	6.0 g/dL (normal 12-15)	Hemoglobin	9.5 g/dL (normal 12-15)
Platelets	420,000/μL (normal 150-350,000)	Platelets	14,000/μL (normal 150-350,000)

What's the diagnosis, and how should she be treated?

Clinical pearl

Severe, rapid-onset thrombocytopenia should raise suspicion for an immunologic cause

In the setting of transfusions, consider post-transfusion purpura (PTP)

PTP

- Most individuals have HPA-1a antigen on platelets
- In HPA-1a$^{(-/-)}$ individuals exposed to HPA-1a, anti-HPA-1a antibodies may develop
  - In such patients who are transfused blood products containing HPA-1a^{+} platelets, severe thrombocytopenia may develop 5-10 days after transfusion
  - Both an alloantibody response against HPA-1a^{+} platelets and an autologous response against native HPA-1a^{-} platelets are observed

Same pathophysiology as fetal/neonatal alloimmune thrombocytopenia

(Jawkins J et al, *J Blood Med* 2019;10;405)

PTP

- Diagnosis: HPA-1a genotyping and antibody testing



- Treatment:
  - IVIg 400-500 mg/kg/d for 1-10 days, or 1-2 g/kg/d for 1-2 days
  - If needed, HPA-1a$^-$ platelets may be transfused

(Jawkins J et al, *J Blood Med* 2019;10;405)

R.K. is a 40-year-old woman with a longstanding history of menorrhagia, who is discovered by her primary care physician to have severe and symptomatic iron deficiency anemia. She is started on oral iron supplementation and transfused 1 unit of packed RBC. One week later, she presents to the emergency department with diffuse petechiae and wet purpura and is found to have new-onset, severe thrombocytopenia.

Labs 1 week ago, prior to RBC transfusion	
WBC	5,300/μL (normal 4-10,000)
Hemoglobin	6.0 g/dL (normal 12-15)
Platelets	420,000/μL (normal 150-350,000)

Labs now	
WBC	4,200/μL (normal 4-10,000)
Hemoglobin	9.5 g/dL (normal 12-15)
Platelets	14,000/μL (normal 150-350,000)

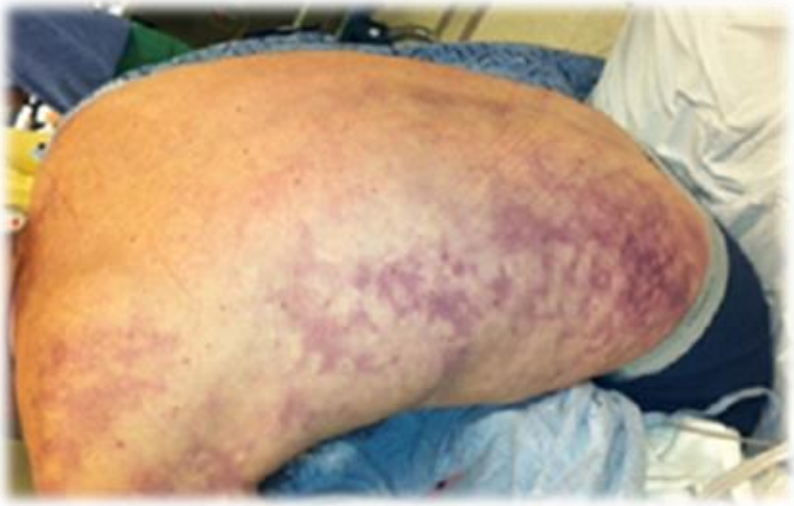
What's the diagnosis, and how should she be treated?

Based on severe thrombocytopenia occurring a week after RBC transfusion, she is suspected of having PTP. She is treated with IVIg. HPA-1a testing later returns showing an HPA-1a$^{(-/-)}$ genotype with anti-HPA-1a antibodies.

Case 7: B.H.

B.H. is a 37-year-old man who is admitted to the hospital for fever and fatigue. On initial presentation, he is in shock, requiring fluid resuscitation and vasopressor support. Blood cultures return positive for *Klebsiella pneumoniae*. He is treated with broad-spectrum intravenous antibiotics.

Exam





Labs

WBC	14,400/μL (normal 4-10,000)
Hemoglobin	11.8 g/dL (normal 12-15)
Platelets	45,000/μL (normal 150-350,000)
PT	27.2 sec (normal 11-15)
INR	2.4 (normal 0.9-1.1)
PTT	49 sec (normal 23-32)
Fibrinogen	65 mg/dL (normal 150-400)

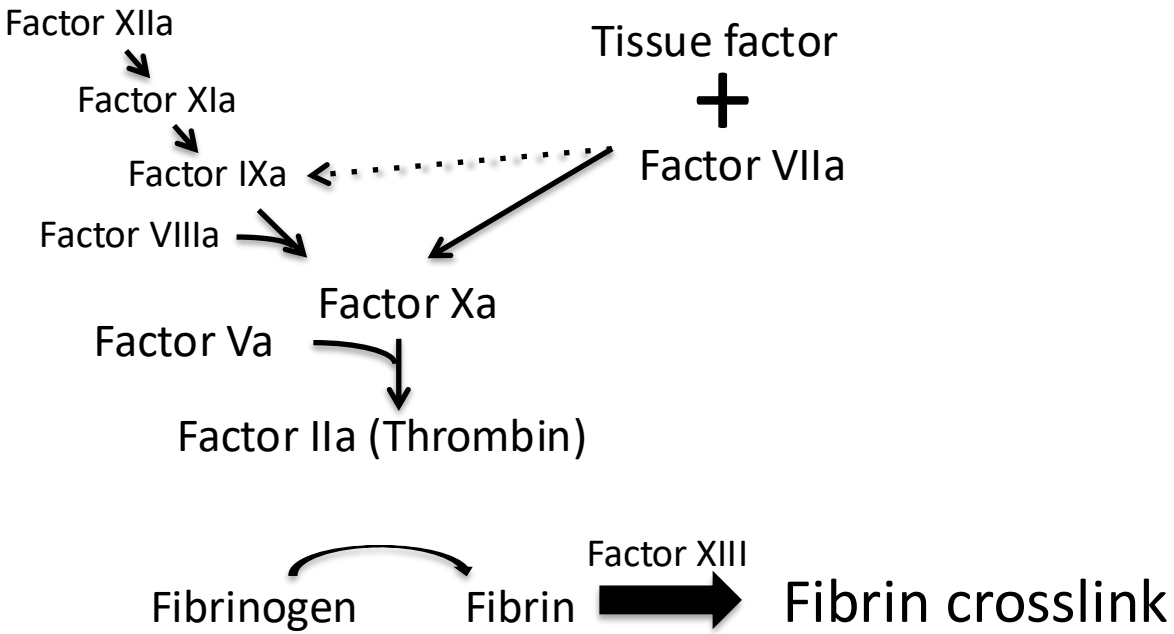
What's the diagnosis, and how should he be treated?

(Collling ME and Bendapudi PK, *Transfus Med Rev* 2018;32:69-76)

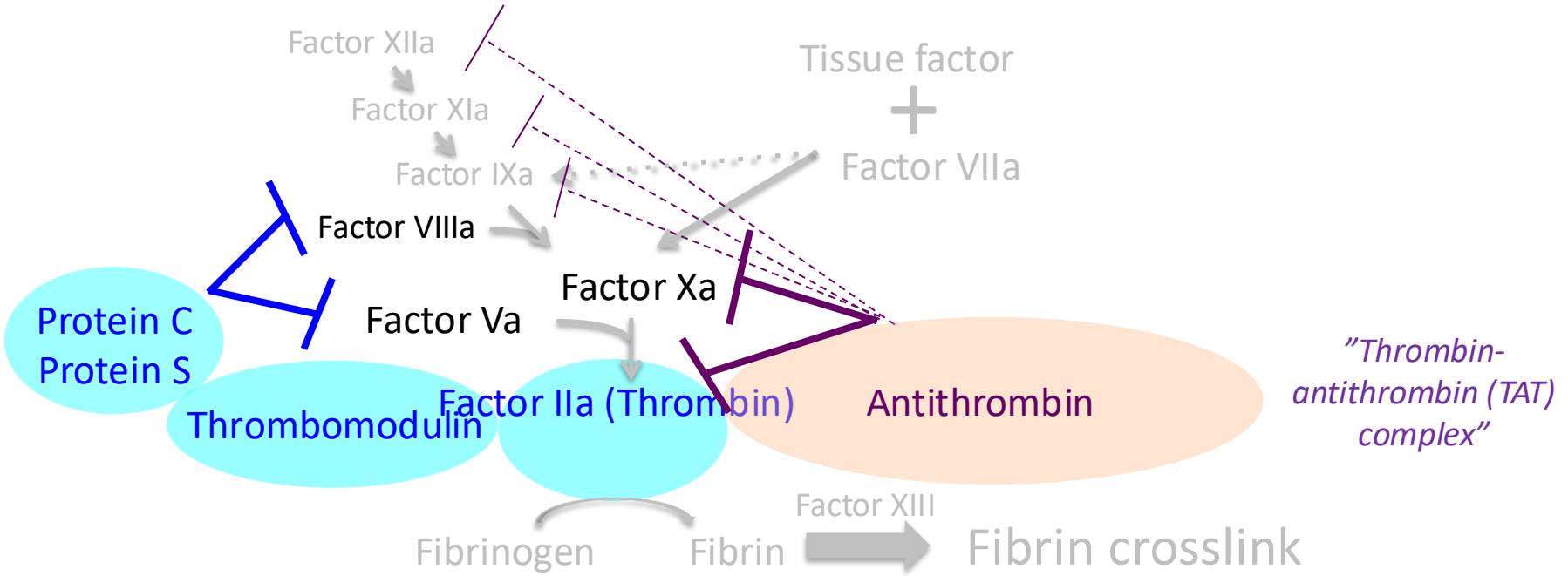
Clinical pearl

Purpura fulminans (PF) is an extreme thrombotic form of DIC and is optimally treated with anticoagulation, plasma transfusions, and protein C and antithrombin replacement

DIC is due to abnormal activation of the coagulation cascade …

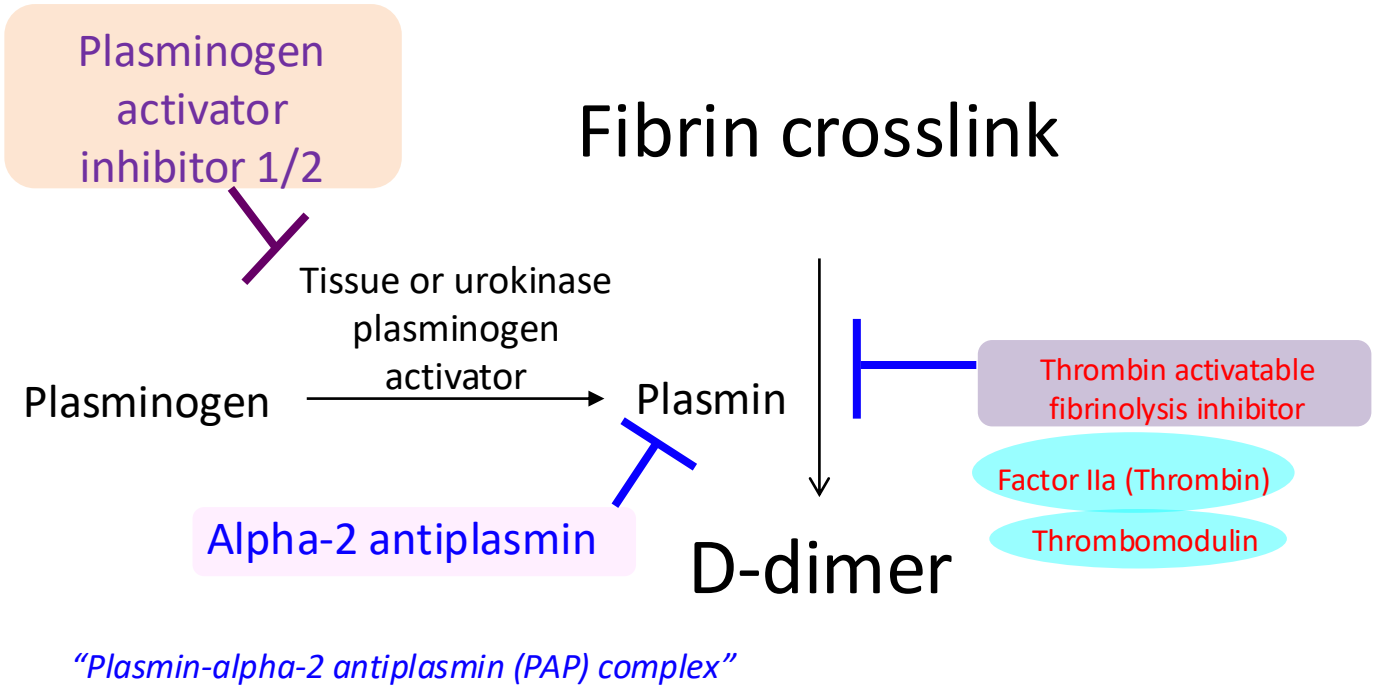


DIC is due to abnormal activation of the coagulation cascade …



… with consumption of endogenous anticoagulants

DIC is due to abnormal activation of the coagulation cascade …



"Plasmin-alpha-2 antiplasmin (PAP) complex"

… and with abnormalities of fibrinolysis

DIC is due to abnormal activation of the coagulation cascade, with consumption of endogenous anticoagulants and abnormalities of fibrinolysis leading to fibrin-rich thrombi

- ↑ D-dimer
- ↓ Fibrinogen
- ↑ Prothrombin time (PT)
- ↓ Platelet count
- ↑ TAT complexes
- ↓ Antithrombin
- ↓ Protein C (PC)
- ↓ Protein S (PC)
- ↑ PAP complexes

ISTH DIC score

Scoring system for overt DIC

Risk assessment: Does the patient have an underlying disorder known to be associated with overt DIC?

If yes: proceed

If no: do not use this algorithm

Order global coagulation tests (PT, platelet count, fibrinogen, fibrin related marker)

Score the test results

- Platelet count (>100 × 10^9/l = 0, <100 × 10^9/l = 1, <50 × 10^9/l = 2)
- Elevated fibrin marker (e.g. D-dimer, fibrin degradation products) (no increase = 0, moderate increase = 2, strong increase = 3)
- Prolonged PT (<3 s = 0, >3 but <6 s = 1, >6 s = 2)
- Fibrinogen level (>1 g/l = 0, <1 g/l = 1)

Calculate score:

≥5 compatible with overt DIC: repeat score daily

<5 suggestive for non-overt DIC: repeat next 1–2 d

(Levi M et al, *Br J Haematol* 2009;145:24)

Types of PF

	Inherited	Autoimmune or postinfectious ("idiopathic")	Acute infectious
Mechanism	Inherited PC or rarely PS deficiency	Neutralizing antibodies against PS or rarely PC	Aberrant tissue factor expression with concomitant failure of thrombomodulin-PC system
Associations		• Varicella zoster virus • Human herpesvirus-6	• *Neisseria meningitidis* • *Haemophilus influenza* • *Streptococcus pneumoniae* • Other encapsulated organisms • *Staphylococcus aureus* • *Capnocytophaga canimorsus* • Rickettsial infection • *Plasmodium falciparum*
Clinical setting	Neonatal	≤ 2 weeks after viral infection	Septic shock
Laboratory findings	• Thrombocytopenia • Elevated D-dimer or fibrin split products • Hypofibrinogenemia • Prolonged PT and/or aPTT • Low PC, PS, and antithrombin activities		

(Goshua G et al, *Hematology Am Soc Hematol Educ Prog* 2022; Bendapudi PK and Losman JA, *Blood* 2025;134:1358)

Treatment of PF

Days of presentation	Laboratory monitoring	Treatment				
		Intravenous unfractionated heparin	Fresh frozen plasma	Cryoprecipitate	PC replacement	Antithrombin concentrate
0-3	• Complete blood count • D-dimer or fibrin split products • Fibrinogen • PT and PTT • Anti-Xa (while on heparin) • Antithrombin, PC, and PS activities	80 units/kg bolus followed by 18 units/kg/hour, targeting anti-Xa 0.3-0.7 U/mL	2 units followed by 1 unit every 4 hours	10 units, targeting fibrinogen ≥ 100 mg/dL	PC concentrate 100 units/kg or prothrombin complex concentrate 25-50 U/kg, targeting PC activity > 80%	85 units/kg, targeting antithrombin activity > 80%
4-5			1 unit every 6 hours			
6-7			1 unit every 8 hours			

- **Consider intravenous vitamin K 5 mg at time of presentation**
- **In patients on anticoagulation, platelets may be transfused to maintain platelet count ≥ 30,000/mcL, but platelets should not be transfused in absence of anticoagulation or bleeding**

- **For acute infectious purpura fulminans: broad-spectrum antibiotics with coverage against Neisseria meningitidis and other encapsulated organisms as well as methicillin-resistant Staphylococcus aureus until a culprit microorganism is identified**

(Goshua G et al, *Hematology Am Soc Hematol Educ Prog* 2022; Bendapudi PK and Losman JA, *Blood* 2025;134:1358)

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Fibrinogen	65 mg/dL (normal 150-400)

What's the diagnosis, and how should he be treated?

He is diagnosed with PF. He is transfused fresh frozen plasma and cryoprecipitate, started on anticoagulation with intravenous heparin, and given intravenous vitamin K, prothrombin complex concentrate, and antithrombin concentrate.

Pseudothrombocytopenia

DITP

TPO-RAs in chemotherapy-induced thrombocytopenia

CAT and thrombocytopenia

Critical illness thrombocytopenia

PTP

TPO-RAs in cirrhosis

PF

(& a little DIC)

Questions?

CME questions

G.T. is a 54-year-old man with cryptogenic cirrhosis and symptomatic cholelithiasis, who has been recommended for an elective cholecystectomy. He has chronic pancytopenia due to cirrhosis and hypersplenism, with WBC counts in the range of 3,000-4,000/mcL, hemoglobin values in the range of 8-9 g/dL, and platelet counts in the range of 25-35,000/mcL. His baseline PT is prolonged in the range of 15-18 sec, presumably due to cirrhosis. His fibrinogen is 175 mg/dL and his thrombin time 12 sec. His creatinine is 1.3 mg/dL. His iron saturation is 49% and his ferritin 575 ng/mL. He is referred to a hematologist for preoperative evaluation.

Which of the following is (are) the most appropriate preoperative intervention(s) to optimize this patient's clinical status for cholecystectomy?

A. RBC transfusion
B. Platelet transfusion
C. Fresh frozen plasma transfusion
D. Cryoprecipitate transfusion
E. Intravenous iron
F. Darbepoetin
G. Epoetin-alfa.
H. Eltrombopag
I. Avatrombopag
J. Tranexamic acid
K. All of these are appropriate

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Teaching point

Preoperative TPO-RA therapy with avatrombopag, lusutrombopag, or romiplostim may be safely administered to patients with cirrhosis and chronic thrombocytopenia who are planned for invasive procedures

(Moussa MM and Mowafy N, *J Gastroenterol Hepatol* 2013;28:335; Terrault N et al, *Gastroenterology* 2018;155:705; Peck-Radosavljevic M et al, *Hepatology* 2019;70:1336)

Y.Z. is an 82-year-old woman with no past medical history, who is hospitalized for massive hematochezia. A colonoscopy shows extensive diverticulosis in the sigmoid colon. She is severely anemic on admission, with a hemoglobin of 6.3 g/dL. Her WBC is 9,400/mcL and her platelet count 325,000/mcL. She is transfused 1 unit of packed RBC and discharged home with plans for surgical follow-up for consideration of an elective hemicolectomy.

One week later, she notices extensive bruising on her legs. She presents to the emergency department for evaluation. Her blood counts at that time show a WBC of 7,800/mcL, hemoglobin 7.1 g/dL, and platelet count 12,000/mcL.

Which of the following best explains the mechanism for development of severe thrombocytopenia in this patient's case?

A. Alloantibody response
B. Autoantibody response
C. Both allo- and auto-antibody response

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A. Alloantibody response

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C. Both allo- and auto-antibody response

Teaching point

Post-transfusion purpura is due to the development of both allo- and auto-antibodies directed against platelet antigens, leading to severe thrombocytopenia

(Jawkins J et al, *J Blood Med* 2019;10;405)

L.M. is a 47-year-old woman who is admitted for septic shock due to *Capnocytophaga canimorsus*, which she acquired from a dog bite. She is on broad spectrum antibiotic therapy and triple vasopressor support. One week into her hospitalization, she develops a lacy rash on her back, with dusking of her extremities, which soon progresses into ischemic gangrene of the upper and lower digits. Her hemoglobin is 8 g/dL and platelet count 52,000/mcL. Her LDH is 458 U/L and her haptoglobin undetectable. Her PT is 20.2 sec and her PTT 40.2 sec. Her fibrinogen is 50 mg/dL.

Which of the following interventions is (are) appropriate in managing this patient?

A. Intravenous heparin anticoagulation
B. Fresh frozen plasma transfusion
C. Cryoprecipitate transfusion
D. Intravenous vitamin K
E. Measurements of antithrombin and protein C activity and administration of antithrombin and/or protein C concentrate if these levels are low
F. All of these are appropriate

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E. Measurements of antithrombin and protein C activity and administration of antithrombin and/or protein C concentrate if these levels are low
F. All of these are appropriate

Teaching point

Treatment of purpura fulminans should incorporate therapeutic anticoagulation and replacement of fibrinogen and endogenous anticoagulant factors

(Goshua G et al, *Hematology Am Soc Hematol Educ Prog* 2022; Bendapudi PK and Losman JA, *Blood* 2025;134:1358)