Thrombopenie bei Intensivpatienten

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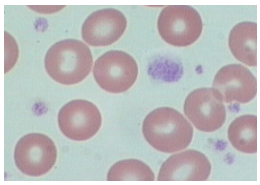
Thrombozyten

ANZAHL:
150 – 350 G/l = 150.000 – 350.000 /µl

GRÖSSE:
2 - 3 µm



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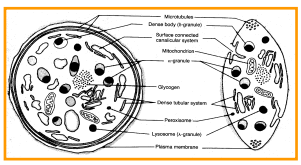
Thrombozyten-Funktion

Primäre Hämostase

- **Anlagerung an Kollagen**
  über von Willebrand Faktor und GP Ib/IX
- **Aktivierung:**
  Expression von GP IIb/IIIa
  Freisetzung von Granulainhalt
  (Phospholipide, ADP, Ca, Fibrinogen, Serotonin, F V, Protein S, Fibronectin, etc.)
- **Aggregation**
  über GP IIb/IIIa und Fibrinogen



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Bildung der Thrombozyten

- im blutbildenden Knochenmark
- Abschnürungen von Megakaryozyten
- unter dem Einfluß von Thrombopoietin

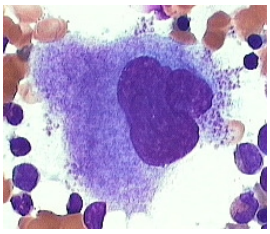
IPF = Immature Platelet Fraction =
Jugendformen von Thrombozyten

Lebensdauer

8-12 Tage, bei Krankheiten oft viel kürzer

Abbau

Milz, RES



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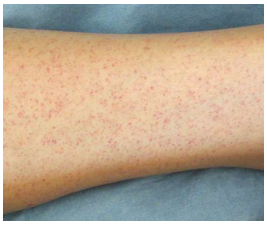
Thrombopenie

= ERNIEDRIGTE THROMBOZYTENZAHL

BLUTUNGSNEIGUNG:

Petechien
Rumpel-Leede Phänomen
Epistaxis
Wet purpura
Schleimhautblutungen



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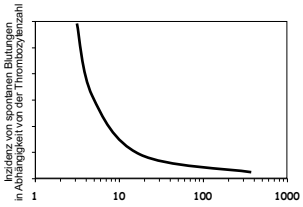
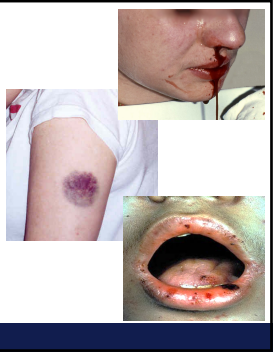
Thrombopenie und Blutungsneigung





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Ursachen für Thrombopenie

Vermehrter Verbrauch Immunologisch	Autoimmunthrombopenie (ITP)	
	ITP in der Schwangerschaft	
	posttransfusionelle Purpura	
	neonatale Purpura; ITP im Kindesalter	
	medikamenteninduzierte Purpura (Haptene):	Chinin/Chinidin, Sulfonamide, Penizilline, Gold, Rifampizin, u.v.a.m.
	Heparin-induzierte Thrombopenie (HIT II)	
	Antiphospholipid-Syndrom	
	Andere Systemerkrankungen (SLE, etc.)	

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	Heparin-induzierte Thrombopenie (HIT II)	
	Antiphospholipid-Syndrom	
	Andere Systemerkrankungen (SLE, etc.)	
Vermehrter Verbrauch Nicht-immunologisch	Hypersplenismus:	Splenomegalie, Leberzirrhose, portale Hypertension, Osteomyelofibrose, Speicherkrankheiten
	Disseminierte intravasale Gerinnung (DIC)	
	Von Willebrand Syndrom Typ 2b	
	Mechanische Sequestrierung:	Extrakorporale Zirkulation (CVVHF, ECMO, HLM, etc.), künstliche Herzklappen, IABP, Pulmonalis-Katheter, etc.
	Thrombotische Mikroangiopathie:	thrombotisch-thrombopenische Purpura (TTP), hämolytisch-urämisches Syndrom (HUS), HELLP Syndrom, EPH-Gestose, schwere Vaskulitis, maligne Hypertension
	Aktivierung und Abbau Interaktionen mit Zellen oder Fremdoberflächen	Thrombin, Zytokine, Hypoxie, Selectine, Fibronectin, Vitronectin, ICAM, PECAM, Leukozyten, Endothel, Willebrand Faktor, Kollagen, etc.....

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Ursachen für Thrombopenie

Verminderte Bildung	Knochenmarks-Suppression	Zytostatika, Medikamente, Chemikalien, Alkohol
	Knochenmarks-Infiltration	Leukämie, Lymphome, Myelom, myelodysplastisches Syndrom, Infiltration mit anderen Tumorzellen (Knochenmarkskarzinose)
	Aplastische Anämie	
	Vitamin B12 Mangel, Folsäuremangel	
	paroxysmale nächtliche Hämoglobinurie	
	Virusinfekte	Hepatitis C, HIV, EBV, CMV, andere

Knöbl P. [Thrombocytopenia in the intensive care unit : Diagnosis, differential diagnosis, and treatment]. Med Klin Intensivmed Notfmed. 2016 Jun;111(5):425-33.

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	Aplastische Anämie	
	Vitamin B12 Mangel, Folsäuremangel	
	paroxysmale nächtliche Hämoglobinurie	
	Virusinfekte	Hepatitis C, HIV, EBV, CMV, andere
Sonstige Ursachen:	Hämodilutionsthrombopenie	
	Pseudothrombopenie	
	Präanalytische Fehler, Laborfehler	
	Schwangerschaft	
	Vaskulitis	

Knöbl P. [Thrombocytopenia in the intensive care unit : Diagnosis, differential diagnosis, and treatment]. Med Klin Intensivmed Notfmed. 2016 Jun;111(5):425-33.

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Thrombopenie bei Intensivpatienten

TABLE I.— *Differential diagnosis of thrombocytopenia in the ICU.*

Differential diagnosis	Relative incidence	Additional diagnostic clues
Sepsis	52.4%	Positive (blood) cultures, positive sepsis criteria, hematophagocytosis in bone marrow aspirate
DIC*	25.3%	Prolonged aPTT and PT, increased fibrin split products, low levels of physiological anticoagulant factors (antithrombin, protein C)
Massive blood loss	7.5%	Major bleeding, low hemoglobin, prolonged aPTT and PT
Thrombotic microangiopathy	0.7%	Schistocytes in blood smear, Coombs-negative hemolysis, fever, neurologic symptoms, renal insufficiency
Heparin-induced thrombocytopenia	1.2%	Use of heparin, venous or arterial thrombosis, positive HIT test (usually ELISA for heparin-platelet factor IV antibodies), rebound of platelets after cessation of heparin
Immune thrombocytopenia	3.4%	Anti-platelet antibodies, normal or increased number of megakaryocytes in bone marrow aspirate, thrombopoeitin (TPO) decreased
Drug-induced thrombocytopenia	9.5%	Decreased number of megakaryocytes in bone marrow aspirate or detection of drug-induced anti-platelet antibodies, rebound of platelet count after cessation of drug

Seven major causes of thrombocytopenia (platelet count <150x109/L) are listed. Relative incidences are based on two studies in consecutive ICU patients.1, 6 Patients with hematological malignancies were excluded. * Patients with sepsis and DIC are classified as DIC.

Levi M, et al: Coagulopathy and platelet disorders in critically ill patients. Minerva Anestesiol 2010;76:851-9

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Thrombopenie als Prädiktor der Mortalität

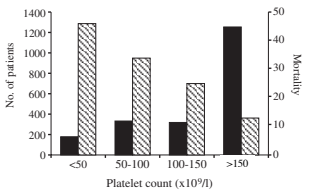

Figure 1.—Distribution of nadir platelet count (black bars) and survival (striped bars) in a pooled analysis of four clinical studies of consecutive groups of patients admitted to the ICU.[1, 3, 4, 6]

Levi M, et al: Coagulopathy and platelet disorders in critically ill patients. Minerva Anestesiol 2010;76:851-9

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Box 2. Questions to ask when evaluating thrombocytopenia in the ICU patient

Past:
- What is the context of the patient's ICU admission?
- Is there evidence of a preexisting illness or the use of a drug known to cause thrombocytopenia?
- Could the ICU admission have been precipitated by a catastrophic illness associated with thrombocytopenia, such as thrombotic thrombocytopenic purpura, hemophagocytic syndrome, or acute leukemia?
- Was there major trauma or surgery that would consume platelets, or transfusion and fluid resuscitation that would cause dilution?

Present:
- What is the trajectory of the platelet count, and how does it relate to the patient's clinical course?
- How low is the platelet count?
- Is there thrombosis?

Future:
- Is the platelet count following the expected trajectory, given your analysis of the cause?

Zarychanski R. et al. Assessing thrombocytopenia in the intensive care unit: the past, present, and future. Am Soc Hematol Educ Program. 2017 Dec 8;2017(1):660-666.

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Differentialdiagnosen der Thrombopenie bei kritisch Kranken

Platelet count less than 100 x 10^9/l	Exclude laboratory artefacts
Acute drop (more than 50% in 24-48 h)	Drug-induced ITP, HIT, PTP
Surgery less than three days ago	Postoperative drop
Clear evidence of sepsis (e.g., culture +ve)	Sepsis-associated thrombocytopenia
Abnormal coagulation profile (PT/APTT)	Sepsis, DIC, Liver disease
Blood contact with devices	Dialysis, Cardiac assist device or ECMO-related
Blood film shows microangiopathy	Thrombotic microangiopathy
Large amount of fluids given	Haemodilution
Recent extensive thrombosis	Clot thrombocytopenia
Recent blood transfusion	Post-transfusion purpura

Fig 2. Clues for the diagnosis of thrombocytopenia in critically-ill patients. ITP, immune thrombocytopenia; HIT, heparin-induced thrombocytopenia, PTP, post-transfusion purpura; PT, prothrombin time; APTT, activated partial thromboplastin time; DIC, disseminated intravascular coagulation.

Thachil J. et al. How do we approach thrombocytopenia in critically ill patients? British Journal of Haematology. 2017; 177: 27–38

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Medikamenteninduzierte Thrombopenie

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Table 3—*Nonchemotherapeutic Drugs Commonly Used in the ICU Associated With Thrombocytopenia*

Drugs	Mechanism (If Known)
Antibiotics	
Penicillins	Hapten-dependent antibody
Vancomycin	Drug-dependent antibody
Linezolid	Myelosuppression
Daptomycin	Unknown
Meropenem	Interference with folate metabolism by inhibition of dihydrofolate reductase and/or drug-specific antibody
Trimethoprim/sulfamethoxazole	
Nitrofurantoin	Unknown
Ganciclovir	Unknown
Valganciclovir	Unknown
Fluconazole	Unknown
Rifampin	Drug-dependent antibody
Heparins and low-molecular-weight heparins	
Unfractionated heparin	Forms immune complex with platelet factor 4
Enoxaparin	
Histamine 2 receptor blockers	
Cimetidine	Drug-specific antibody
Ranitidine	Drug-specific antibody
Salicylates/nonsteroidal antiinflammatory drugs	
Aspirin	Drug-dependent antibody
Diclofenac	Drug-dependent antibody
Ibuprofen	Drug-dependent antibody
Glycoprotein IIb/IIIa inhibitors	
Abciximab	Preexisting antibodies specific for murine structural elements of abciximab
Tirofiban	Reacts with glycoprotein IIb/IIIa to induce neoepitope
Eptifibatide	
Ticlopidine	Thrombotic microangiopathy
Clopidogrel	
Antiarrhythmics	
Procainamide	Induction of autoantibodies
Amiodarone	Drug-dependent antibody/bone marrow granulomas
Antiepileptics	
Valproate	Drug-dependent antibody
Carbamazepine	Drug-dependent antibody
Phenytoin	Drug-dependent antibody
Miscellaneous	
Digoxin	Unknown
Furosemide	Drug-dependent antibody
Thiazides	Drug-dependent antibody
Haloperidol	Unknown
Morphine	Drug-dependent antibody

Rice TW, Wheeler AP (2009) Coagulopathy in critically ill patients: part 1: platelet disorders. Chest 136:1622-30

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Table 1. Mechanisms of immune-mediated drug-induced thrombocytopenia

Mechanism	Description	Clinical Consequence	Special Laboratory Testing[a]	Prototype Drugs
Hapten-dependent	Drug (hapten) binds covalently to platelet membrane glycoprotein producing a neoepitope recognized by antibody	Hemorrhage	Drug-dependent platelet antibody assay	Penicillin, cephalosporins
Drug-glycoprotein complex (quinine-type)	Drug interacts noncovalently with platelet membrane glycoprotein; antibody bonds	Hemorrhage	Drug-dependent platelet antibody assay	Quinine, quinidine, nonsteroidal anti-inflammatory drugs, sulfonamides
Ligand-induced binding site (fiban-type)	Drug binds to platelet GPIIb/IIIa complex inducing conformational change elsewhere and formation of a neoepitope recognized by antibody	Hemorrhage	Drug-dependent platelet antibody assay	Eptifibatide, tirofiban, lotrafiban
Drug-specific antibody	Drug consists of chimeric Fab fragments against GPIIIa with a murine component that is recognized by antibody	Hemorrhage	Drug-dependent platelet antibody assay	Abciximab
Autoantibody	Drug induces an autoantibody that reacts with a platelet surface glycoprotein in the absence of the drug	Hemorrhage	Anti-platelet antibody assay (nonspecific)	Gold salts, procainamide
Immune complex	Drug reacts with platelet factor 4 to produce an antigenic complex against which antibodies react; resultingimmune complexes bind to platelet Fc receptors resulting in platelet activation	Thrombosis	Heparin-platelet factor 4 antibody assay	Unfractionated heparin, low- molecular-weight heparins

Priziola JL et al: Drug-induced thrombocytopenia in critically ill patients. Crit Care Med 2010; 38[Suppl.]:S145-S154

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Immunologische Thrombopenien

- Immunologische Begleitphänomene bei Infektionen oder Autoimmunerkrankungen (entspricht einer typ. **Autoimmunthrombopenie** (ITP))
- **Transfusionsthrombopenie** (Antikörperbildung gegen HPA-1a als Reaktion auf Erythrozyten- oder Thrombozyten-Transfusionen):
  oft sehr niedrige Thrombozytenzahlen (< 1G/l) und schwere klinische Blutungsneigung, hohe Mortalität, keine Behandlungsmöglichkeit.
  Dauer: ca. 2-3 Wo.

Knöbl P. [Thrombocytopenia in the intensive care unit : Diagnosis, differential diagnosis, and treatment]. Med Klin Intensivmed Notfmed. 2016 Jun;111(5):425-33.

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Theapiemöglichkeiten für immunologische Thrombopenien

- Wait & watch
- Steroide
- Hochdosierte iv. Immunglobuline
- Thrombopoietinrezeptor-Agonisten
- Rituximab
- Splenectomie

Knöbl P. [Thrombocytopenia in the intensive care unit : Diagnosis, differential diagnosis, and treatment]. Med Klin Intensivmed Notfmed. 2016 Jun;111(5):425-33.

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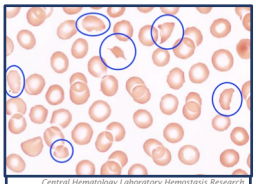
Thrombotic microangiopathy (TMA)

Hemolysis
- Low hemoglobin and RBC counts
- High reticulocyte counts
- High LDH
- Low (consumed) haptoglobin
- Red cell fragmentation (schistocytes) in blood smear
- Non-immunologic, direct antiglobin test (DAT) negative

Thrombocytopenia
- Consumption thrombocytopenia
- any range of platelet counts, but rarely very low
- "hyperactive" platelets, bleeding symptoms rare



Central Hematology Laboratory Hemostasis Research, Laboratory Bern University Hospital & University of Bern [CC BY-SA 4.0 (http://creativecommons.org/licenses/by-sa/4.0)], via Wikimedia Commons

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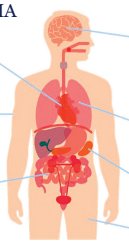
Organ involvement in TMA



Cardiovascular:
Cardiomyopathy, myocardial infarction, myocarditis and arhythmia, heart failure
ECG deviations, sudden cardiac death

Skin:
Purpuric rash

GI:
Diarrhea, abdominal colics, constipation, abdominal distension, strictures, occlusions, intestinal perforations, pancreatitis, intestinal bleeding, hepatic cytolysis

CNS:
Irritability, drowsiness, convulsions, encephalopathy, diplopia, cortical blindness, hemiparesis or hemiplegia, stupor and coma
agitation, psychosis

Pulmonary:
Pulmonary hypertension, pulmonary hemorrhage, pulmonary edema

Renal:
Renal impairment, end stage renal disease
Elevated creatinine, reduced urine output

Skeletal muscle:
Rhabdomyolysis

Figure 3 – *Frequency of organ involvement in atypical hemolytic uremic syndrome.*[9] *See Figure 2 legend for expansion of abbreviations.*

Modified from Azoulay E, et al. Expert Statements on the Standard of Care in Critically Ill Adult Patients With Atypical Hemolytic Uremic Syndrome. Chest. 2017 Aug;152(2):424-434.

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Pathophysiology-based classification of TMA

TMA with ADAMTS13 deficiency = TTP	
Genetic defects causing ADAMTS13 deficiency	Upshaw-Schulman Syndrome
Autoantibodies causing ADAMTS13 deficiency	Spontaneous autoimmune TTP
= M. Moschcowitz	Secondary autoimmune TTP (after infections, pregnancy, drugs, cancer, etc.)
TMA with complement dysregulation(some of them called atypical HUS, aHUS)	
Genetic defects causing complement overexpression	Familial HUS
Antibodies blocking complement factors	Spontaneous autoimmune HUS
= Autoimmune-type of acquired HUS	Secondary autoimmune HUS (after infections, pregnancy, drugs, cancer, etc.)
Other forms of TMA	
Idiopathic / spontaneous	No trigger identified
Organ transplantation	kidneys, hematopoetic stem cells, lung, heart, liver, etc.
Infections	EBV, CMV, HIV, etc.
Drugs	clopidogrel, ticlopidine, cyclosporin, quinine, mitomycine C, etc.
Malignancy	Disseminated cancer, bone marrow infiltration
Pregnancy	HELLP Syndrome, preeclampsia
Toxines	Diarrhea-associated HUS: E.Coli, Shigella, etc.
Sytemic diseases	SLE, Antiphospholipid syndrome, hypertension, vasculitis, etc.

P. Knöbl, Inherited and Acquired Thrombotic Thrombocytopenic Purpura (TTP) in Adults, Semin Thromb Hemost 2014, p.493-502

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Therapie der TTP

- Plasma-Austausch (1 – 1,5 faches Plasmavolumen) täglich bis Thrombozyten >150 G/L
- Cortison (1 mg/kg/d)
- Caplacizumab (Cablivi®) 10 mg/d sc. bis ADAMTS13 normalisiert
- Rituximab zur Immunsuppression
- Symptomatische Organprotektion (Intensivmedizin)

- KEINE Thrombozytenkonzentrate

P. Knöbl, Inherited and Acquired Thrombotic Thrombocytopenic Purpura (TTP) in Adults, Semin Thromb Hemost 2014, p.493-502

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Other therapy for TMA

Therapeutic option	Indication	Dose	Mechanism of action
Immunomodulators (bortezomib, MMF, cyclosporine, cyclophosphamide)	Autoantibody-induced TTP (4th line immunotherapy)	As indicated	Immunosuppression
Anti-platelet agents (ASS, clopidogrel, prasugrel, ticagrelor)	TTP with severe organ damage	Clopidogrel: 75-150 mg/d	Inhibition of platelet aggregation
Splenectomy	Refractory TTP (after rituximab failure)		unknown. elimination of memory cells?
Eculizumab	Complement-mediated TMA	900 mg weekly	Complement inhibition
Supportive therapy	Anemia: RBC transfusion organ failure: ICU	As indicated	(details: see text)

P. Knöbl, Inherited and Acquired Thrombotic Thrombocytopenic Purpura (TTP) in Adults, Semin Thromb Hemost 2014, p.493-502

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Heparin-assoziierte Thrombopenie

4T Score für HIT

	Points (0, 1, or 2 for each of four categories: maximum possible score = 8)		
	2	1	0
Thrombocytopenia	> 50% platelet fall to nadir ≥ 20	30–50% platelet count fall (or > 50% directly resulting from surgery); or nadir 10–19	< 30% platelet fall; or nadir < 10
Timing* of platelet count fall, thrombosis, or other sequelae (1st day of putative immunizing exposure to heparin = day 0)	Days 5–10 onset* (typical/delayed-onset HIT); or ≤ 1 day (with recent heparin exposure within past 30 days (rapid-onset HIT)	Consistent with days 5–10 fall, but not clear (e.g., missing platelet counts); or, ≤ 1 day (heparin exposure within past 31–100 days) (rapid-onset HIT); or, platelet fall after day 10	Platelet count fall ≤ 4 days (unless picture of rapid-onset HIT—see two left boxes)
Thrombosis or other sequelae (e.g., skin lesions, anaphylactoid reactions)	Proven new thrombosis; or skin necrosis (at injection site); or postintravenous heparin bolus anaphylactoid reaction	Progressive or recurrent thrombosis; or erythematous skin lesions (at injection site); or suspected thrombosis (not proven); hemofilter thrombosis	None
Other cause for thrombocytopenia	No explanation for platelet count fall is evident	Possible other cause is evident	Definite other cause is present
Pretest probability score: 6–8 = high; 4–5 = intermediate; 0–3 = low			

Warkentin TE. Heparin-Induced Thrombocytopenia in Critically Ill Patients. Semin Thromb Hemost 2015;41:49–60.

Probleme des 4T-Scores bei kritisch Kranken

- Niedrige Sensitivität und Spezifität bei kritisch Kranken, oft können Kriterien nicht klar definiert werden
- Patienten haben oft viele andere Gründe für Thrombopenie (100% aller Pat. mit nachgewiesener HIT)
- Patienten haben oft andere Gründe für Thromboembolie
- Art des Heparins und Verlauf der Thrombozyten oft unklar / nicht definierbar
- Nur 7,5 % von kritisch kranken Patienten mit Verdacht auf HIT haben tatsächlich eine HIT

Harada MY, et al. Overtreatment of Heparin- Induced Thrombocytopenia in the Surgical ICU. Crit Care Med 2017; 45:28–34.
Knoebl P. Is It HIT? Crit Care Med. 2017 Jan;45(1):132–134.

HIT - Algorithmus

Table 3. Probability of HIT in the intensive care unit

Probability of HIT	Clinical and Laboratory Findings	Recommended Action
Very unlikely	No TCY or other clinical features Positive PF4 EIA	Maintain heparin Monitor platelet counts Avoid antibody testing with low probability
	TCY and/or new thrombosis Negative PF4 EIA	Check other causes of TCY Ensure adequate anticoagulation Avoid repeat antibody testing unless TCY worsens
HIT is not ruled out	Platelet decrease may be explained by comorbidity Weak positive PF4 EIA (optical density <1.0)	Switch to alternate anticoagulant in prophylactic dose If DTI used start with 25%–50% of expected dose, adjust by aPTT Functional assay result negative or not available Guide treatment by response to alternate anticoagulant Confirm HIT with functional assay
HIT is probable	Unexplained platelet decrease	Stop heparin Initiate therapeutic dose PF4 EIA optical density >1.0, alternate anticoagulation Reduce dose if high bleeding risk Confirm HIT with functional assay
HIT very likely	New thrombosis and TCY with appropriate timing and without other causes Positive PF4 EIA	Stop heparin Initiate therapeutic dose, alternate anticoagulation Reduce dose if high bleeding risk Confirm HIT with functional assay

HIT, heparin-induced thrombocytopenia; TCY, thrombocytopenia; PF4, platelet factor 4; EIA, enzyme immunoassay; DTI, direct thrombin inhibitors; aPTT, activated partial thromboplastin time. Adapted from Selleng et al (14).

Pirzada JL, et al. Drug-induced thrombocytopenia in critically ill patients. Crit Care Med. 2010; 38(suppl.):S145–S154

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HIT - Algorithmus

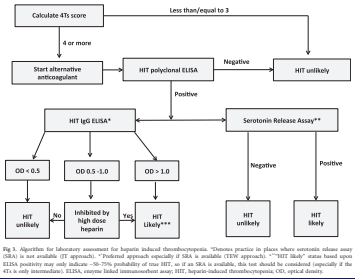

Fig 3. Algorithm for laboratory assessment for heparin induced thrombocytopenia. *Denotes practice in places where serotonin release assay (SRA) is not available (IT approach). **Preferred approach especially if SRA is available (TEW approach). ***"HIT likely" status based upon ELISA positivity may only indicate ~50–75% probability of true HIT, so if an SRA is available, this test should be considered (especially if the 4Ts is only intermediate). ELISA, enzyme linked immunosorbent assay; HIT, heparin-induced thrombocytopenia; OD, optical density.

Thachil J, et al. How do we approach thrombocytopenia in critically ill patients? British Journal of Haematology, 2017, 177, 27–38

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Persönliche Empfehlung

- Klinische Situation und HIT-Wahrscheinlichkeit abschätzen
- Typischen Zeitverlauf beachten (HIT unwahrscheinlich <5d oder >20 d nach Beginn von Heparin
- HIT-Ak Testung in >80% falsch positiv. Wenn negativ oder nur niedrige OD dann ist HIT praktisch ausgeschlossen
- Bei hoher klinischer Wahrscheinlichkeit für HIT frühzeitiger Wechsel auf alternatives Antikoagulans, vor allem bei kritischen Konditionen (ECMO, CVVHF, VAD, etc.)
- Argatroban (Argatra®) ist auf der ICU gut zu managen und meist die beste Wahl, Fondaparinux (Arixtra®) oder Danaparoid (Orgaran®) als Alternativen für sc. Therapie

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Therapeutische Möglichkeiten bei Thrombopenie

	DOSIS	INDIKATION	KONTRAINDIKATION
Thrombozyten-Konzentrate	1-2/d	Bildungsstörung, Hämodilution, DIC, prä-interventionell	Absolute KI: TTP, TMAs, HIT Relative KI: ITP
Thrombopoietinrezeptor-Agonisten Romiplostin Elthrombopag	1-9 µg/kg/Wo. sc. 50-150 mg/d po.	ITP, Bildungsstörung	Relative KI: alle off-label Anwendungen
Corticosteroide	1 mg/kg/d	ITP, TTP	
Immunglobuline	1 g/kg iv d1+2	ITP und lebensbedrohliche Blutungen	
Immunsuppression, Rituximab	?	ITP, TTP	
Splenectomie		ITP, TTP, TMA	
Desmopressin	0,4 µg/kg KI direkt vor Thrombozyten-Konzentrat	Refraktäre Thrombopenie und lebensbedrohliche Blutungen	Nierenversagen, akutes Coronarsyndrom
Rek. FVIIa (Novoseven)	90 µg/kg iv (alle 2 h)	Ultima Ratio bei lebensbedrohlichen Blutungen	

DIC=disseminierte intravaskuläre Koagulopathie; HIT=Heparin-induzierte Thrombopenie; TMA=thrombotische Mikroangiopathie; TTP=thrombotisch-thrombopenische Purpura

Knöbl P.: Thrombocytopenia in the intensive care unit. Med Klin Intensivmed Notfmed. 2016 Jun;111(5):425-33

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Table 1. Thresholds for platelet transfusion in critical illness[21,38,42]

Indication	Platelet threshold*	Strength of recommendation	Quality of evidence
Severe bleeding	Maintain PLT > 50 × 10^9/L; consider using an MTP	Strong	Low
Prophylaxis in adults	10 × 10^9/L	Moderate	Low
Prior to elective central venous catheter	20 × 10^9/L†	Weak	Low
Prior to chest tube insertion or thoracentesis	50 × 10^9/L	Weak	Low
Prior to bronchoscopy with lavage	20 × 10^9/L	Weak	Low
Prior to paracentesis	Not routinely required	Weak	Low
Prior to bone marrow biopsy	Not routinely required	Weak	Low
Prior to elective diagnostic lumbar puncture	50 × 10^9/L	Weak	Very low
Prior to urgent diagnostic lumbar puncture	20 × 10^9/L	Weak	Very low
Prior to major elective surgery (excluding neurosurgery)	50 × 10^9/L	Weak	Very low
Prior to neurosurgery	100 × 10^9/L	Weak	Very low
Traumatic brain injury, intracranial hemorrhage	100 × 10^9/L	Weak	Low
Prior to insertion of an intraventricular drain	100 × 10^9/L	Weak	Very low

MTP, massive transfusion protocol; PLT, platelet count.
*May be modified by several factors including platelet dysfunction or other risk factors for bleeding, indication for the procedure, urgency, and medical comorbidities.
†Inserted with bedside ultrasound and by experienced personnel. Avoid noncompressible vessels if platelets are <50 × 10^9 per liter. Choosing a compressible site is preferable to platelet transfusion.

Zarychanski R. et al: Assessing thrombocytopenia in the intensive care unit: the past, present, and future. Am Soc Hematol Educ Program. 2017 Dec 8;2017(1):660-666.

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Table 1. The impact of platelet transfusions on platelet-count increment in critically ill patients with thrombocytopenia

Reference	N	Population	Study design	Results	Study quality*
Adults					
4	1923	Medical ICU	Prospective cohort	Median increase was 15 × 10^9/L (IQR, 2-35 × 10^9/L)	Low
12	350	Dengue fever	Prospective cohort	Median PLT count yield† was 12.4% higher than baseline after transfusion (range, −3.9%-67.1%)	Low
9	216	Medical/surgical ICU	Retrospective cohort	Median increase after single PLT transfusion was 14 × 10^9/L (IQR, −2-30 × 10^9/L)	Moderate
11	147	Surgical ICU	Prospective cohort	PLT count rose above 40-50 × 10^9/L (but never >100 × 10^9/L) after transfusion	Low
10	72	Surgical ICU	Case-control study	Platelet transfusion led to sustained correction of thrombocytopenia in 8/16 patients; the remainder had only transient improvement	Low
Neonates					
15	422	Preterm neonates	Retrospective cohort study	Platelet transfusion resulted in good, but less sustained, rise in platelet count for neonates with severe thrombocytopenia (data not shown)	Low
14	194	Neonates	Prospective cohort	Fifty-nine percent of transfusions increased counts >40 × 10^9/L; 8% of transfusions increased counts <20 × 10^9/L; median platelet count increase from 27 × 10^9/L (IQR, 19-36 × 10^9/L) to 79 × 10^9/L (IQR, 47-126 × 10^9/L)	Moderate
8	152	Preterm neonates	RCT	Significant increase by 95 × 10^9/L in the intervention group (PLT transfusions for platelets <150 × 10^9/L)	Low

Lieberman L, et al. Platelet transfusions for critically ill patients with thrombocytopenia. Blood. 2014 Feb 20;123(8):1146-51

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Zusammenfassung

- Eine Thrombopenie ist häufig bei kritisch kranken Patienten und kann eine Vielzahl von Ursachen haben.
- Nur ein strukturiertes Aufarbeiten der Differenzialdiagnosen ermöglicht eine sinnvolle Behandlung.
- Die Konsultation von erfahrenen Hämatologen/Hämostaseologen ist dabei oft hilfreich.
- Das unbedingte Erzielen von bestimmten Thrombozytengrenzwerten ist nicht durch klinische Studien belegt.
- Die unkritische Substitution von Thrombozytenkonzentraten kann lebensbedrohliche Nebeneffekte haben.

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