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La CAPS e la HIT: condizioni rare ma da considerare nella diagnosi differenziale del paziente internistico acuto

Learning objectives

- Describe different possible clinical and laboratory features of **unwell patients** in medical and ITU wards
- List possible **haematology conditions** driving to severe and deteriorating clinical conditions

- Define Heparin Induced Thrombocytopenia (HIT)
- Describe clinical and laboratory picture of HIT
- Assess and manage patient with HIT and HIT with thrombosis

- Define Catastrophic Anti Phospholipid Syndrome (CAPS)
- Describe clinical and laboratory picture of CAPS
- Assess and manage patient with CAPS

Unwell, rapidly deteriorating patient

Unwell, rapidly deteriorating patient

Fever
(very high, remittent, uncontrolled)

Deranged
Liver function

Haemolysis

Worsening
Acute phase test
(CRP, Ferritine..)

Alteration
Clotting test

Bleeding

Worsening
Anaemia

Alteration in **vital signs**
(BP, RR, HR)

Multifocal
Thrombosis

Worsening
Thrombocytopaenia

Change in
mental state

Worsening
Neutropaenia

Worsening
AKI

Unwell, rapidly deteriorating patient

Medical ward

Deteriorating clinical conditions

Worsening lab alterations

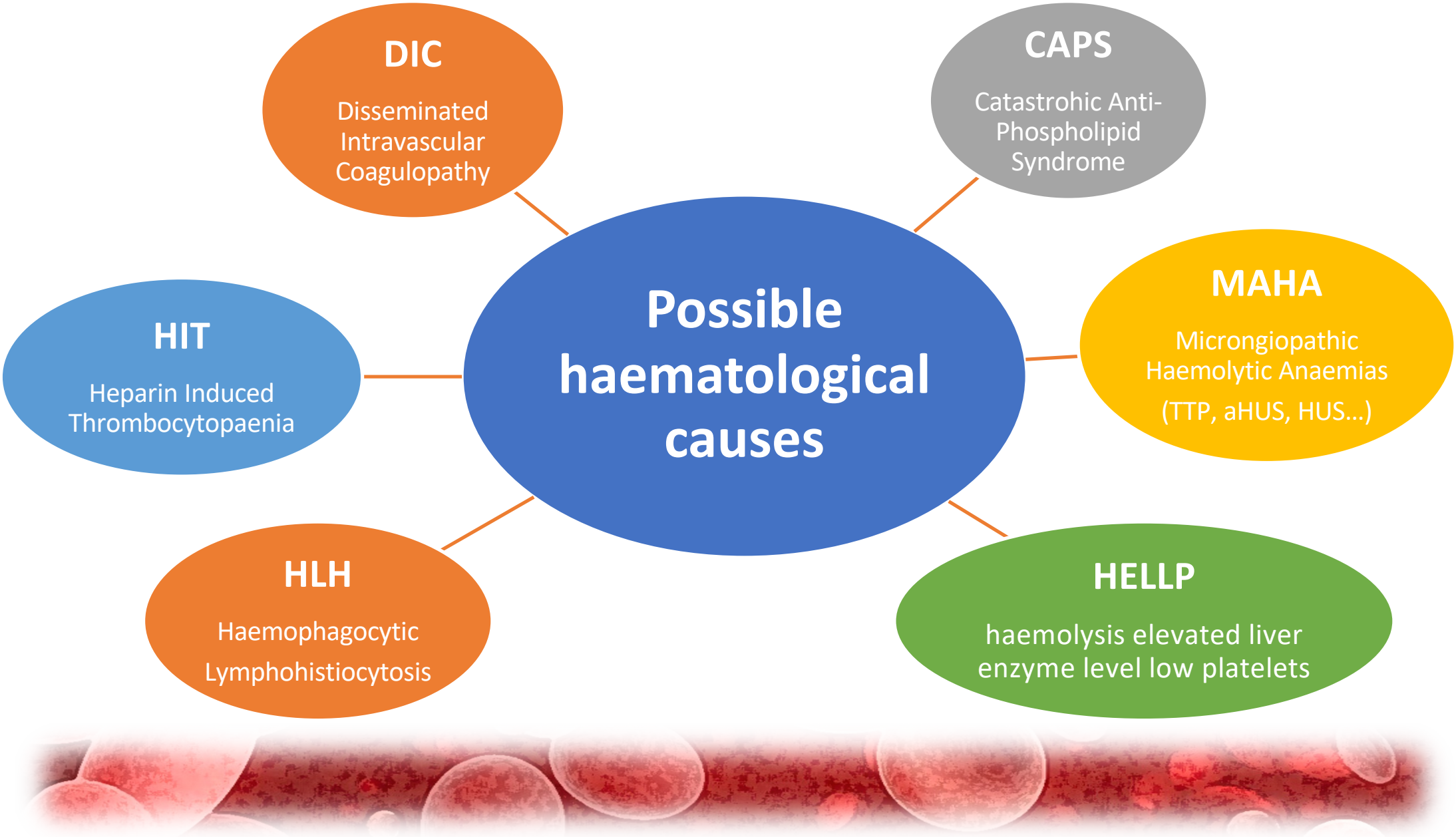
No clear explanation / diagnosis / trigger

Unwell, rapidly deteriorating patient

Medical ward

ITU

Unwell, rapidly deteriorating patient



Unwell, rapidly deteriorating patient

High mortality conditions!

Prompt recognition and treatment is key!

HIT
Heparin Induced Thrombocytopaenia

Case 1

82 yo F
Admission for pneumonia

LMWH prophylaxis during admission

PLT baseline 231.000/mmc

Day 23: PLT 83.000/mmc

No thrombosis
Patient well, ready for discharge

Case 2

69 yo M

Cardiosurgery with ECMO

UFH during and post op

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Day 2: PLT 67.000/mmc
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MOF, TEP, sternal bleeding

Case 3

49 yo M

LC Mycobacterial lymphadenopathy (surgery) + compression DVT

LMWH- TD

PLT baseline 129.000/mmc

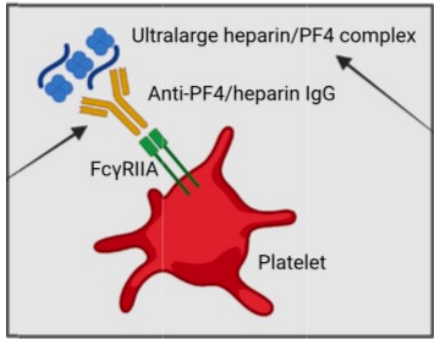
Day 9: PLT 87.000/mmc
Day 11: PLT 14.000/mmc

Pt well, no bleeding, no VTE

HIT - Definition

HIT is an immune-mediated highly pro-thrombotic **disorder of platelet activation** caused by pathogenic antibodies (mainly IgG) against Platelet Factor 4 (PF4)-heparin complexes.

It is the most frequent drug-induced immune thrombocytopenia and may lead to **life-threatening thrombosis.**



Arachchillage et al, BSH guidelines 2024

HIT - Incidence

- 12 million patients in USA are exposed to heparin each year
- Incidence of HIT < 0.1% - 7% / pts exposed to heparin / year depending on risk (type of heparin, duration, type of patient)
- 1/3 – 1/2 of HIT patients develop **thrombosis (HITT)** which may be venous, arterial or microvascular
- Mortality 5-10%

Cuker et al, ASH guidelines 2018

HIT – Risk factors

UFH > LMWH (differences in heparin chain length and level of sulphation)

- UFH 10 fold greater risk than LMWH
- 2-3% of pts receiving UFH for > 6 days
- risk with Fondaparinux is negligible

Major surgery / trauma > medical > obstetric pts

- 3 folder higher risk in major surgery / trauma patients
- **Cardiothoracic surgery supported with ECMO 6.6%**

Therapeutic dose > Prophylactic dose > CVC flashing

Longer duration > shorter duration

- Increased risk for duration > 6 days

Cuker et al, ASH guidelines 2018
Jori et al, RPTH 2023

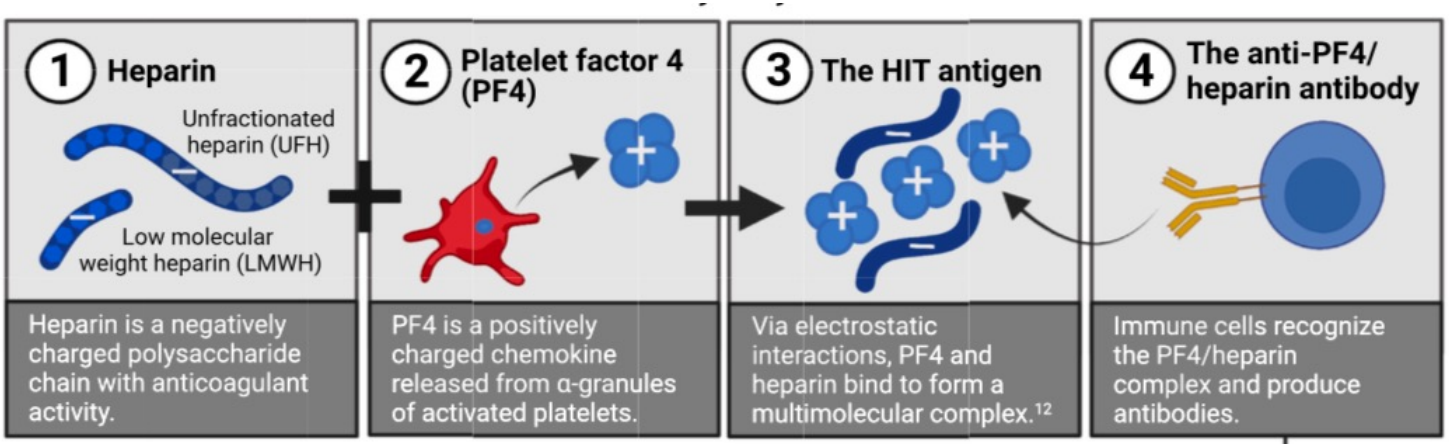
HIT – Screening strategies

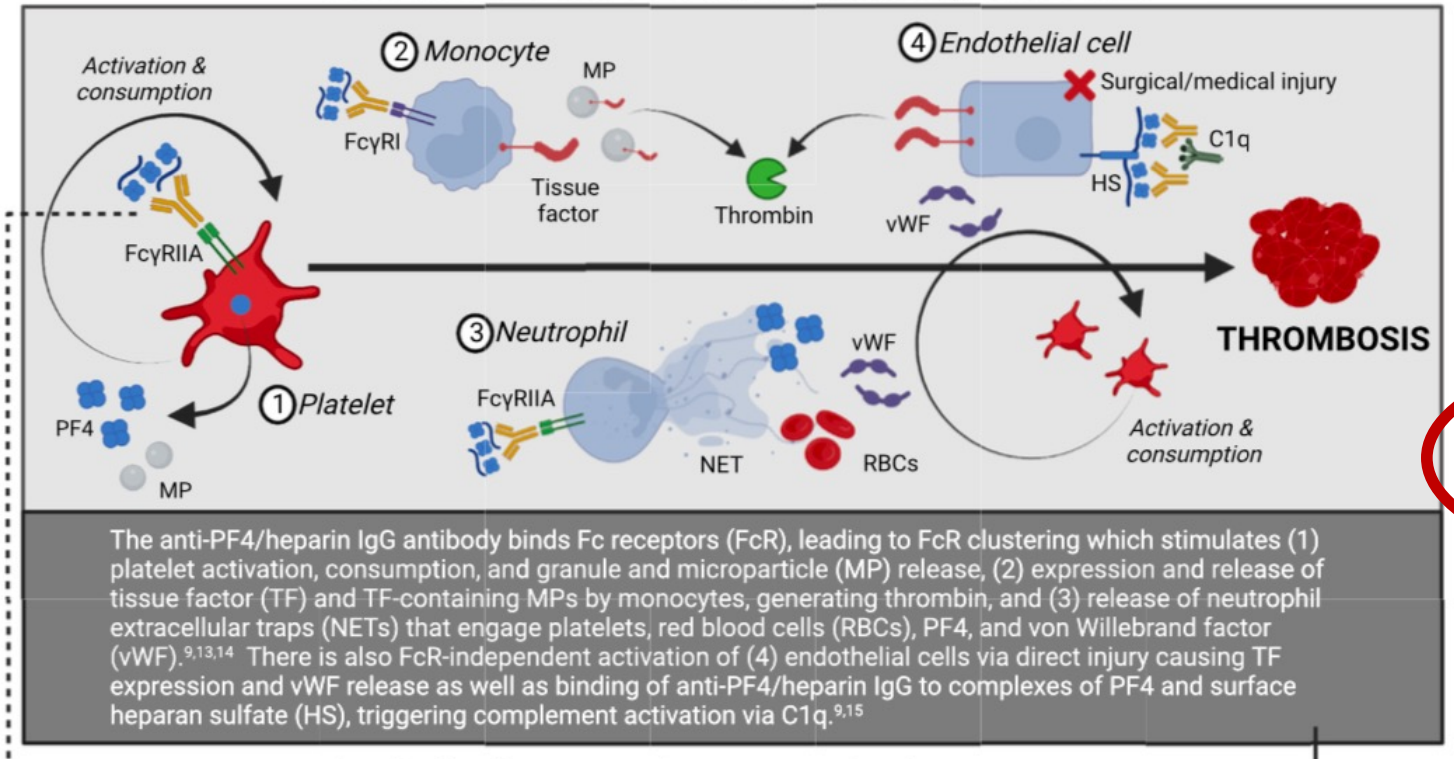
Risk category	Risk definitions	ASH guidelines 2018 and BSH guidelines 2024 recommendation on PLT count monitoring
Low	• Medical patients receiving LMWH	ASH panel suggest against PLT count monitoring
Intermediate	• Medical or obstetric pts receiving UFH • Major surgery / trauma pts receiving LMWH	PLT count monitoring every 2-3 days • From day 0 if heparin exposure in previous 30 days • From day 4 to 14 in heparin naïve patients
High	• Any surgery / trauma pts receiving UFH	PLT count monitoring **at least every other days** • From day 0 if heparin exposure in previous 30 days • From day 4 to 14 if 14 in heparin naïve patients

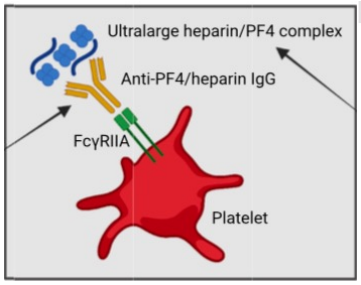
All patients should receive a **baseline PLT count** before receiving heparin.

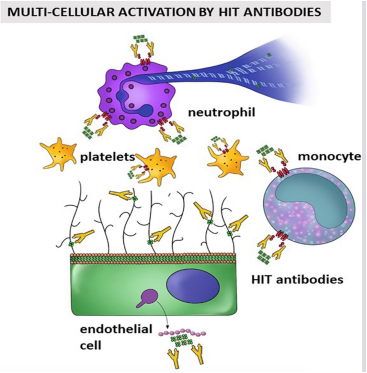
Cuker et al, ASH guidelines 2018
Whatson et al, BJH 2012
Arachchillage et al, BSH guidelines 2024

HIT – Pathophysiology









Multicellular activation:

- PLT
- Monocytes
- Neutrophils
- Endothelial cells

Intense thrombin generation

Role of Specific gene polymorphisms

HIT without heparin (other polyanions)

Role of infections / bacteria

Jori et al, RPTH 2023, Marchetti et al, JCM 2021

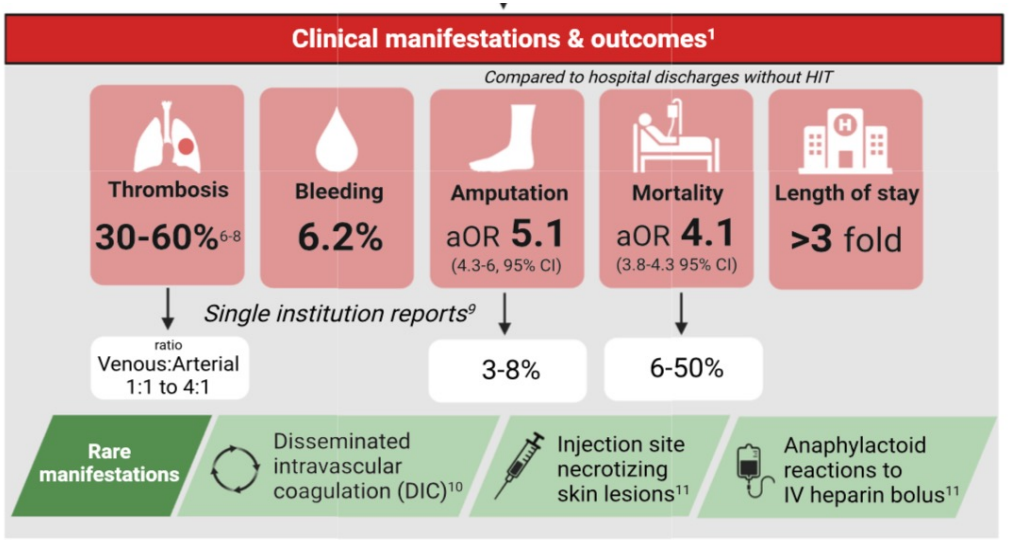
HIT – Clinical picture

Timing

Degree of thrombocytopenia

Thrombosis

Alternative explanation



M Hogan, Vascular Medicine 2020,
Arachchillage et al, BSH guidelines 2024
Jori et al, RPTH 2023

HIT – Clinical picture

Timing:

- Platelet drop 4-14 days since heparin start
- Early onset HIT: since the 1° day of heparin exposure if past exposure (last 100 days)
- Cardiopulmonary bypass surgery: initial PLT fall in the first 72 h with spontaneuos recover and secondary fall in day 4-14 related to HIT

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Arachchillage et al, BSH guidelines 2024

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Degree of thrombocytopenia

- Baseline PLT = highest PLT level before the fall
- Fall of by least 30-50% frm baseline
- Median nadir 55.000/mmc
- Severe thrombocytopaenia (< 15.000/mmc) is rare but associated with higher thrombotic risk

Thrombosis

Alternative explanation

Arachchillage et al, BSH guidelines 2024

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Thrombosis

- 50% HITT (HIT + Thrombosis)
- venous, arterial, microvascular
- Rare athypical thrombosis (adrenal, skin necrosis, gangrene)

Alternative explanation

Arachchillage et al, BSH guidelines 2024

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Thrombosis

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- venous, arterial, microvascular
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Alternative explanation

- Very unwell patients (often ITU, MOF)
- Possible alternative diagnosis: DIC, sepsis, etc

Arachchillage et al, BSH guidelines 2024

HIT – Diagnosis

- Clinical features: **heparin exposure + Thrombocytopenia**

Cuker et al, ASH guidelines 2018, Jori et al, RPTH 2023

HIT – Diagnosis

- Clinical features: **heparin exposure + Thrombocytopenia**
- Laboratory test
  - **Immunoassay** (ELISA HIT Ab test).
    Detects if Ab antiPF4/heparin are present and if their abundance.
    Screening test. Poor specificity (30-80%), high NPV.
  - **Functional assays** (ie. C-Serotonin Release Assay, SRA).
    Determine if Ab antiPF4/heparin are pathogenic in PLT activation.
    Confirmatory test. Measurement of platelet activation.
    High sensitivity (95%), high specificity (95%)

Cuker et al, ASH guidelines 2018, Jori et al, RPTH 2023

HIT – Lab Diagnosis

- Lab tests: not available everywhere
- Lab tests: may require time (days).
- 50% of patients have detectable anti-PF4 Ab but do not develop thrombosis or MOF
- Extensive use of low specificity assay can lead to overdiagnosis

Arachchillage et al, BSH guidelines 2024

HIT – Pretest score

- Pretest risk score (PTRS): 4T score or HEP score

HIT 4 T score

- **T**iming
- **T**hrombocytopaenia (PLT count)
- **T**hrombosis
- (other causes of) **T**rombocytopaenia

High NPV e poor PPV

Lo, GK, Warkentin E, JTH 2006

HIT – Pretest score

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

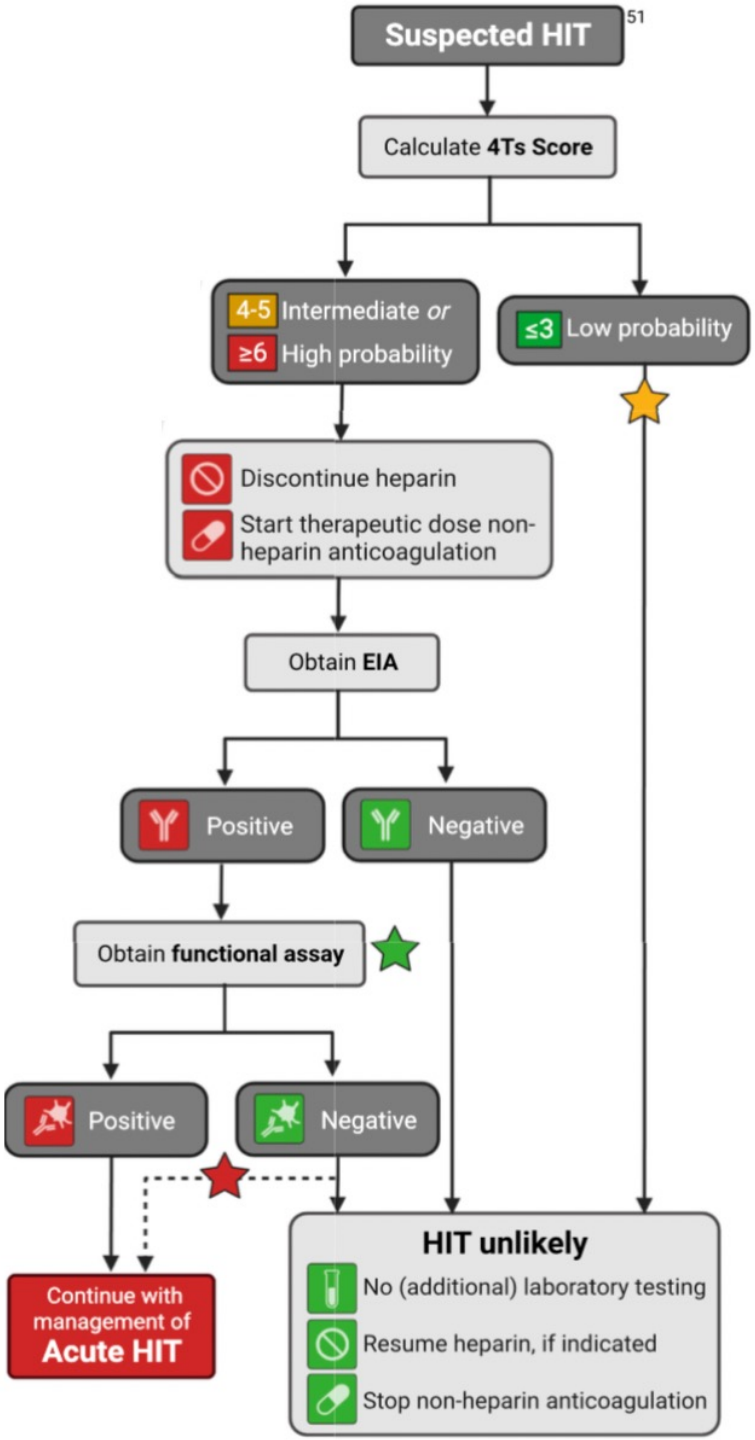
Lo, GK, Warkentin E, JTH 2006

HIT – Diagnostic pathway

ASH Guidelines 2018 recommend calculation 4T score BEFORE performing lab test

Low risk 0-3 points	•Laboratory testing NOT indicated •Monitor and repeat 4T score over time •Continue heparin if indicated
Intermediate risk 4-5 points	•Perform immunoassay if positive functional assay •Stop heparin •Start non-heparin anticoagulant: **at prophylactic dose** if high risk of bleeding and no indication to full anticoagulation, **at treatment dose** indication to full anticoagulation
High Risk > 6 points	•Perform immunoassay if positive functional assay •Stop heparin •Start non-heparin anticoagulant at treatment dose

HIT – Diagnostic **sequential** pathway



4 T pretest score

Immunoassay

Functional assay

Cuker et al, ASH guidelines 2018, Jori et al, RPTH 2023

HIT – Management of Acute HIT

Stop heparin

Start non-heparin anticoagulation

Duration of anticoagulation:

- HITT: 3-6 months (usually with DOAC)
- HIT without thrombosis: until PLT recovery

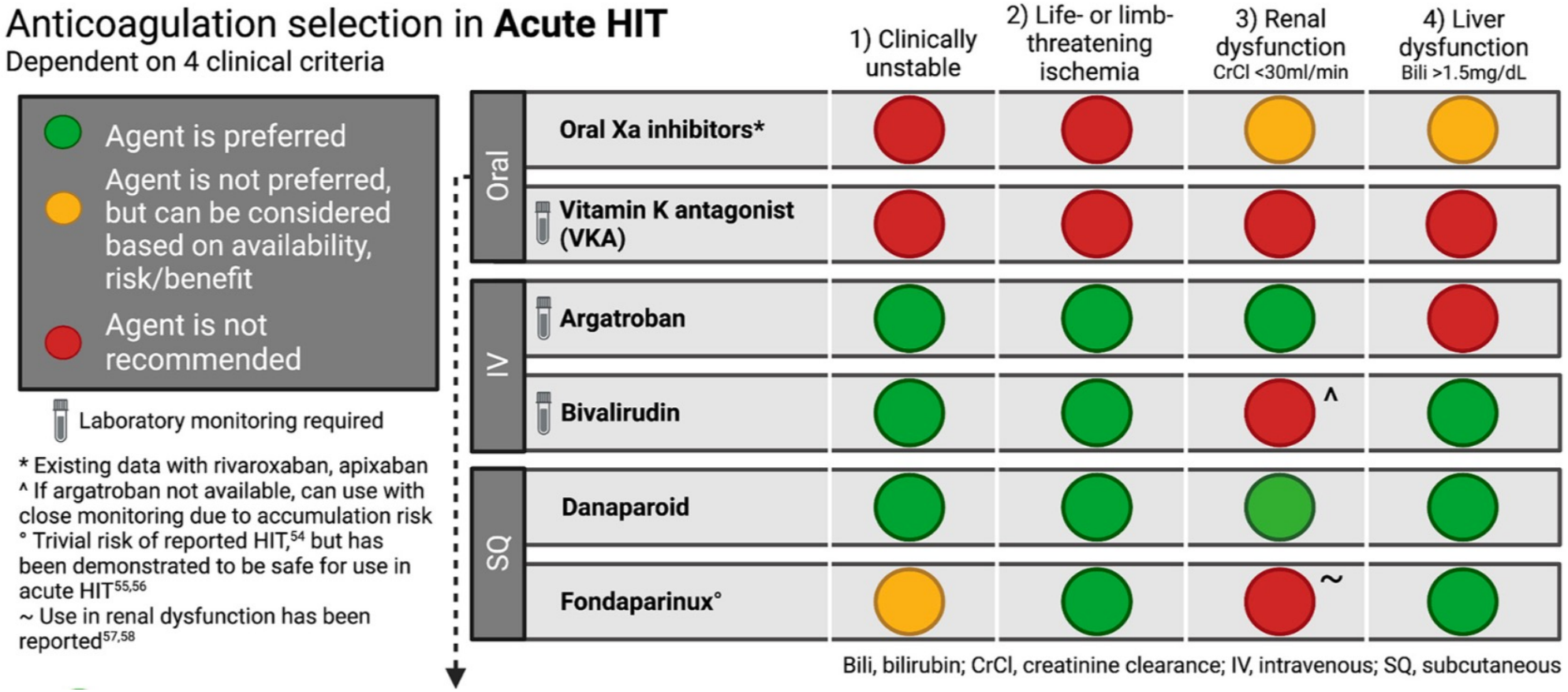
Non heparin anticoagulant choice:

- **Argatroban ***
- **Bivalirudin***
- **Danaparoid***
- Fondaparinux
- DOAC
- VKI (avoid in initial phase as skin necrosis risk)

**To be preferred in acute phase/ patient unstable*

Cuker et al, ASH guidelines 2018
Jori et al, RPTH 2023

HIT – Non Heparin Anticoagulation



Jori et al, RPTH 2023

HIT – PLT trasfusion

- Routine PLT transfusion in NOT recommended
- PLT transfusion to be considered only in ongoing major / life threatening bleeding or before mandatory procedure

Cuker et al, ASH guidelines 2018

HIT – Long term management

- HITT: anticoagulation for 3-6 months (DOAC first choice)

Heparin re-challenging (ie PCI, cardio surgery)

- In acute and subacute HIT A avoid UFH, consider delay procedure or bivalirudin
- In subacute HIT B and remote HIT consider UFH for cardio surgery and alternative anticoagulants for other procedure / anticoagulation

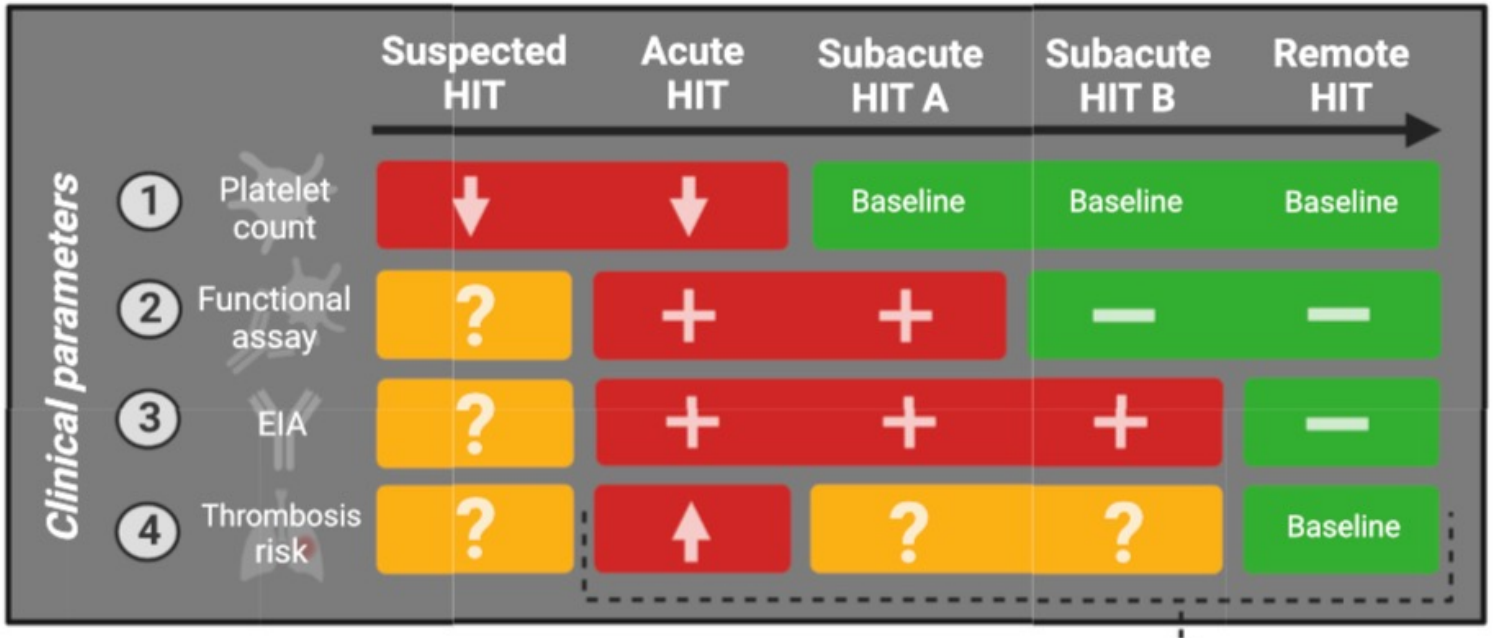
Cuker et al, ASH guidelines 2018

HIT – Predictable pattern and disease history

PLT count recovers in 7-8 days after discontinuation of heparin

Functional assay become negative at a median of 50 days

Immuneassay become negative at a median of 85 days



Cuker et al, ASH guidelines 2018
Jori et al, RPTH 2023

Suspected HIT:
- low PLT
- awaiting for test

Acute HIT:
- low PLT
- Functional assay +
- Immunoassay +
- +/- thrombosis (HITT)

Subacute HIT A:
- Normal PLT
- Functional assay -
- Immunoassay +

Subacute HIT B:
- Normal PLT
- Functional assay -
- Immunoassay –

Remote HIT:
- Normal PLT
- Ab no longer detectable

HIT – Conclusions

- HIT is a rare but potentially **severe** and life threatening condition
- HIT is a **prothrombotic condition**, often associated with VTE
- Risk stratification
- High rate of **misdiagnosis and overdiagnosis**
- **Sequential** diagnosis starting with **4T score** is key
- **Non heparin anticoagulation** in acute HIT is indicated
- **Parenteral non heparin anticoagulants** to be considered safe and effective in unwell /unstable patient

Case 1

82 yo F
Admission for pneumonia

LMWH prophylaxis during admission

PLT baseline 231.000/mmc

Day 23: PLT 83.000/mmc

No thrombosis
Patient well, ready for discharge

Case 2

69 yo M

Cardiosurgery with ECMO

UFH during and post op

PLT baseline 307.000/mmc

Day 2: PLT 67.000/mmc
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MOF, TEP, sternal bleeding

Case 3

49 yo M

LC Mycobacterial lymphadenopathy (surgery) + compression DVT

LMWH- TD

PLT baseline 129.000/mmc

Day 9: PLT 87.000/mmc
Day 11: PLT 14.000/mmc

Pt well, no bleeding, no VTE

HIT - Definition

- Type I HIT: non immunological
- Type II HIT: immune mediated

- Autoimmune HIT (aHIT)
- Spontaneous HIT
- VITT and VITT-like disorders

Arachchillage et al, BSH guidelines 2024

HIT - Definition

- **HIT type I: heparin-associated thrombocytopenia**

Non immunological response to heparin treatment
Mediated by a direct interaction between heparin and circulating PLT
More frequent than type II (10-30% of heparin patients)
Occurs within 48-72 hours
Transient mild thrombocytopenia (normal within 4 days of heparin discontinuation)
Benign, not associated with thrombosis

- **Type II HIT: immune mediated**

Often associated with thrombosis
Occurs day 4-14 from first heparin exposure
Severe clinical picture

Arachchillage et al, BSH guidelines 2024

HIT - Definition

- **Autoimmune HIT (aHIT)**

PLT activating antibodies
Both heparin-dependent and heparin-independent
Similar IgG autoAb reactive against heparin-PF4 complex but able to activate PLT even in absence of pharmacological heparin
°delayed onset HIT (begin and worsed despite heparin cessation)
°persistent HIT (beyond a week after heparin cessation)

- Spontaneous HIT
- VITT and VITT-like disorders

Arachchillage et al, BSH guidelines 2024

HIT - Definition

- Autoimmune HIT (aHIT)

- **Spontaneous HIT**

High level of PF4 dependent Ab detected with both ELISA and PLT activation assay
No exposure to heparin
Unexplained thrombocytopenia and/or thrombosis
Following surgery, trauma, bacterial infection
Possible Ag stimulating Ab formation (bacterial wall, inflammation/endothelial Ag during surgery/trauma)

- VITT and VITT-like disorders

Arachchillage et al, BSH guidelines 2024

HIT - Definition

- Autoimmune HIT (aHIT)
- Spontaneous HIT

- **VITT and VITT-like disorders**

Highly pathogenic Anti-PF4 Ab
Heparin-independent PLT-activating properties
Antigen site(s) on PF4 that support anti-PF4 Ab are distinct in heparin-dependent and heparin-independent reactivity

1. Following adenovirus-based COVID-19 vaccine (VITT)
2. Following recent adenovirus infection (VITT-like)
3. MGUS patients

Arachchillage et al, BSH guidelines 2024

CAPS
Catastrophic Anti Phospholipid Syndrome

CAPS - Definition

- Life threatening condition
- Rapid development (“catastrophic”)
- Clinical evidence of multiorgan involvement (three or more organs)
- Multiple small vessels thrombosis
- Laboratory confirmation of the **presence of aPL**, usually in high titers
- aPL: positive lupus anticoagulant (LAC), anticardiolipin (aCL) ar anti-β2-glycoprotein I (aβ2GPI) antibodies, in isolation or in any combination.

Cervera et al, 2018

CAPS – Incidence and prognosis

- Rare condition
- **Easily misdiagnosed**
- 1% of APL patients
- 50% of patients develops CAPS ”de novo” as first APL manifestation
- 40% have an associated autoimmune disease
- **Mortality** described ad high as 50% (37-50%)
- 69 % female (CAPS registry)
- Mean age 38 years

Cervera et al, 2018
Rodriguez-Pinto et al, 2016

APS - Diagnostic Criteria

Criterio clinico

- Trombosi vascolari (arteriose/venose) e/o
- Complicanze gravidanza:

1. Morte fetale inspiegata dopo la 10°settimana
2. Parto prematuro < 34°WGA
3. 3 o + aborti spontanei < 10 settimana

Criterio laboratoristico

- LAC
- Ab anticardiolipina (IgG/IgM)
- Ab antiB_2GPI (IgG/IgM)

Due positività a distanza di 12 settimane

APS se un criterio clinico e uno di laboratorio presenti

Miyakis S, JTH 2006

APS - Diagnostic Criteria

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- Complicanze gravidan
1. Morte fetale i dopo la 1
2. P

C

ttività a distanza di 12 settimane

linico e uno di laboratorio presenti

Miyakis S, JTH 2006

Arthritis & Rheumatology
Vol. 0, No. 0, Month 2023, pp 1–16
DOI 10.1002/art.42624

2023 ACR/EULAR Antiphospholipid Syndrome Classification Criteria

Medha Barbhaiya,[1*] Stephane Zuily,[2*] Ray Naden,[3†] Alison Hendry,[4] Florian Manneville,[5] Mary-Carmen Amigo,[6]

American College of Rheumatology
Empowering Rheumatology Professionals

Box 2 Preliminary criteria for classification of catastrophic antiphospholipid syndrome.[11]

1 Evidence of involvement of three or more organs, systems or tissues
2 Development of manifestations simultaneously or in less than 1 week
3 Confirmation by histopathology of small-vessel occlusion in at least one organ or tissue
4 Laboratory confirmation of the presence of antiphospholipid antibodies (lupus anticoagulant or anticardiolipin antibodies, or both, on two or more occasions at least six weeks apart

Definite catastrophic antiphospholipid syndrome

- All four criteria

Probable catastrophic antiphospholipid syndrome

- All four criteria, but with only two organs affected and/or tissue involvement
- All four criteria, but with the absence of laboratory confirmation at least six weeks apart (e.g. because of the early death of a patient never tested for antiphospholipid antibodies before onset of the catastrophic antiphospholipid syndrome)
- 1, 2 and 4
- 1, 3 and 4 and the development of a third event in more than 1 week but less than 1 month despite anticoagulation

CAPS – Diagnostic Criteria

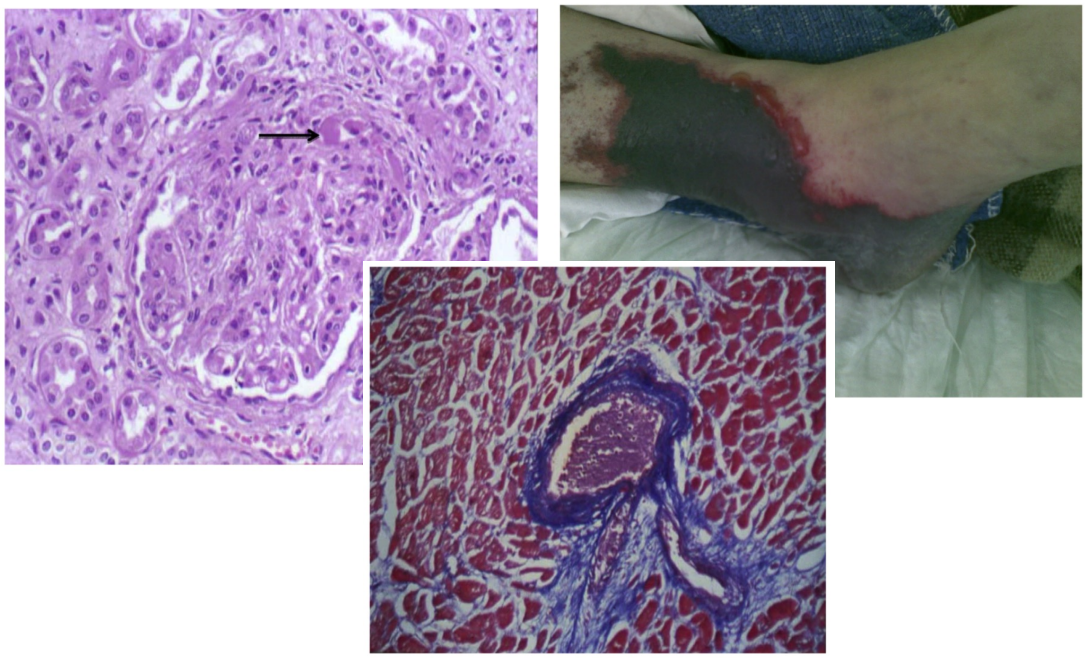
1. Multi organ / system involvement (>=3)
2. Timing (simultaneous)
3. Histology confirmation
4. aPL positivity

Often a ”PROBABLE” diagnosis as biopsy not feasible

Taormina preliminary criteria, 2002

CAPS – CAPS Pathophysiology

- Multifactorial pathogenesis
- Precipitating factors (drug? Infection?)
- Endothelial damage



Cervera et al, 2018, Nayer et al, 2014

Table 2. Putative Pathogenic Mechanisms in CAPS

Cellular activation
Endothelial cell activation
Immune cell activation
Platelet activation
Inhibition of anticoagulants
Inhibition of the protein C pathway
Disruption of annexin A5 shield
Inhibition of fibrinolysis
Inhibition of plasminogen activator inhibitor-1
Blocking of β_2-glycoprotein I
Blocking of annexin A2
Complement activation
Endothelial cell activation by C5a and MAC
Immune cell activation by C5a
Platelet activation by C3a and MAC
Inhibition of fibrinolysis by C5a

MAC, membrane attack complex. Modified from reference 1.

CAPS – Clinical picture

Manifestations associated with Thrombosis (venous, arterial, microvascular)

Manifestations associated with SIRS (cytokine storm, MOF)

Cervera et al, 2018

CAPS – Clinical picture

Cervera et al, 2018

Intra-abdominal:	kidney, adrenal glands, splenic, intestinal, mesenteric, pancreatic thrombosis
Pulmonary:	pulmonary emboli, ARDS, pulmonary hemorrhage, pulmonary oedema, infiltrates.
Cardiac:	valvular defects, miocardial infarction
Cerebral:	microthrombosis, stroke, seizure, cerebral venous occlusion, encephalopathy.
Skin:	livedo reticularis, purpura, skin necrosis
Haematology:	DIC, thrombocytopenia, haemolytic anaemia
Other:	Gastric ulceration, pancreatitis, adrenal infarction, testicular/ovarian infarction, acalculous cholecystitis, bone marrow necrosis

CAPS – Differential diagnosis

- **Severity** of the clinical picture
- Difficult differential diagnosis with other condition (ie. microangiopathic vasculopathy) with **overlapping** clinical presentation
- Often **difficult to obtain biopsy** (low PLT, coagulation factor consumption, unstable patient, etc.)
- Lab results for **aPL may require time**
- Positive aPL in other clinical conditions
- False positive results of LAC in anticoagulation/inflammation

Cervera et al, 2018

CAPS – Differential diagnosis

Table 2
Common disorders associated to microangiopathic hemolytic anemia that should be included in the differential diagnosis of patients with catastrophic antiphospholipid syndrome.

- Systemic infection
- Malignancy
- Preeclampsia, eclampsia, HELLP syndrome
- Malignant hypertension
- Thrombotic thrombocytopenic purpura
- Hemolytic uremic syndrome
- Drug-related microangiopathic syndromes (i.e. clopidogrel, ticlopidine, chemotherapy, alendronate…)
- Heparin-induced thrombocytopenia

- Past medical history (40% known autoimmune disease)
- Drugs (ticlopidine? Heparin?)
- Infections?
- Pregnancy?
- Diarrhea?

Cervera et al, 2018

Table 3
Diagnostic work-up in front of a patient with suspicion of thrombotic microangiopathy (TMA).

1) To establish the suspicion of TMA
   - Thrombocytopenia (< 150 × 10^9/l or > 25% of decrease)
   - Signs of microangiopathic hemolysis
   - Anemia (± increase in mean corpuscular volume)
   - Reticulocyte count raised
   - Lactate dehydrogenase (LDH) increased with haptoglobin decreased
   - Direct Coomb's test negative
   - Blood smear searching schistocytes
2) To look for organ involvement
   - Neurological: Confusion, headache, seizures, encephalopathy, focal deficits
   - Renal: ARF, arterial hypertension, proteinuria, hematuria
   - Cardiac: Cardiac failure, hypotension, ischemic cardiopathy
   - Pulmonary: ARDS, respiratory insufficiency
   - Gastrointestinal: Abdominal pain, intestinal angina, diarrhea, vomiting
   - Hematological (thrombocytopenia): epistaxis, hemoptysis, menorrhagia, retinal haemorrhage, gastrointestinal bleeding, petechiae
3) To confirm organ involvement
   - Blood analysis including renal function, cellular blood count, LDH, liver and pancreatic enzymes, creatinkinase, and troponin I
   - Renal biopsy: to confirm glomerular microthrombosis
   - CT/MRI brain: to determine neurological involvement
   - Electrocardiogram/Echocardiogram: to document or monitor cardiac damage
   - Chest radiograph/CT: to document lung involvement
   - Echography/CT: to document hepatic/pancreatic/intestinal involvement
   - Fundoscopic examination: to document retinal vessel involvement
4) To investigate the etiology
   - ADAMTS 13 activity: < 5–10% (TTP)
   - If gastroenteritis (bloody diarrhea): Shiga toxin/STEC: positive (HUS)
   - If ADAMTS13 > 10%: secondary or associated TMA
   - Fundoscopic examination (malignant hypertension)
   - Immunologic profile: ANA, ANCA, and aPL (autoimmune diseases)
   - Pregnancy test (pregnancy-related)
   - CT toracoabdominal or PET: (cancer-associated)
   - Clinical history looking for drugs/heparin and anti-PF4 antibodies (HIT)
   - Complement study FH, FB, FI, anti-FH antibodies, genetic study (aHUS)

Abbreviations: aHUS: atypical HUS, ANA: antinuclear antibodies, ANCA: antineutrophil cytoplasmic antibodies, aPL: antiphospholipid antibodies, CT: computed tomography, HIT: heparin-induced thrombocytopenia; HUS: hemolytic uremic syndrome, PET: positron emission tomography, STEC: Shiga toxin *Escherichia coli*, TTP: thrombotic thrombocytopenic purpura.

CAPS – Management

High mortality rate: early and aggressive therapeutic approach is needed

Importance of finding and treating **precipitating factors** (ie. infection)

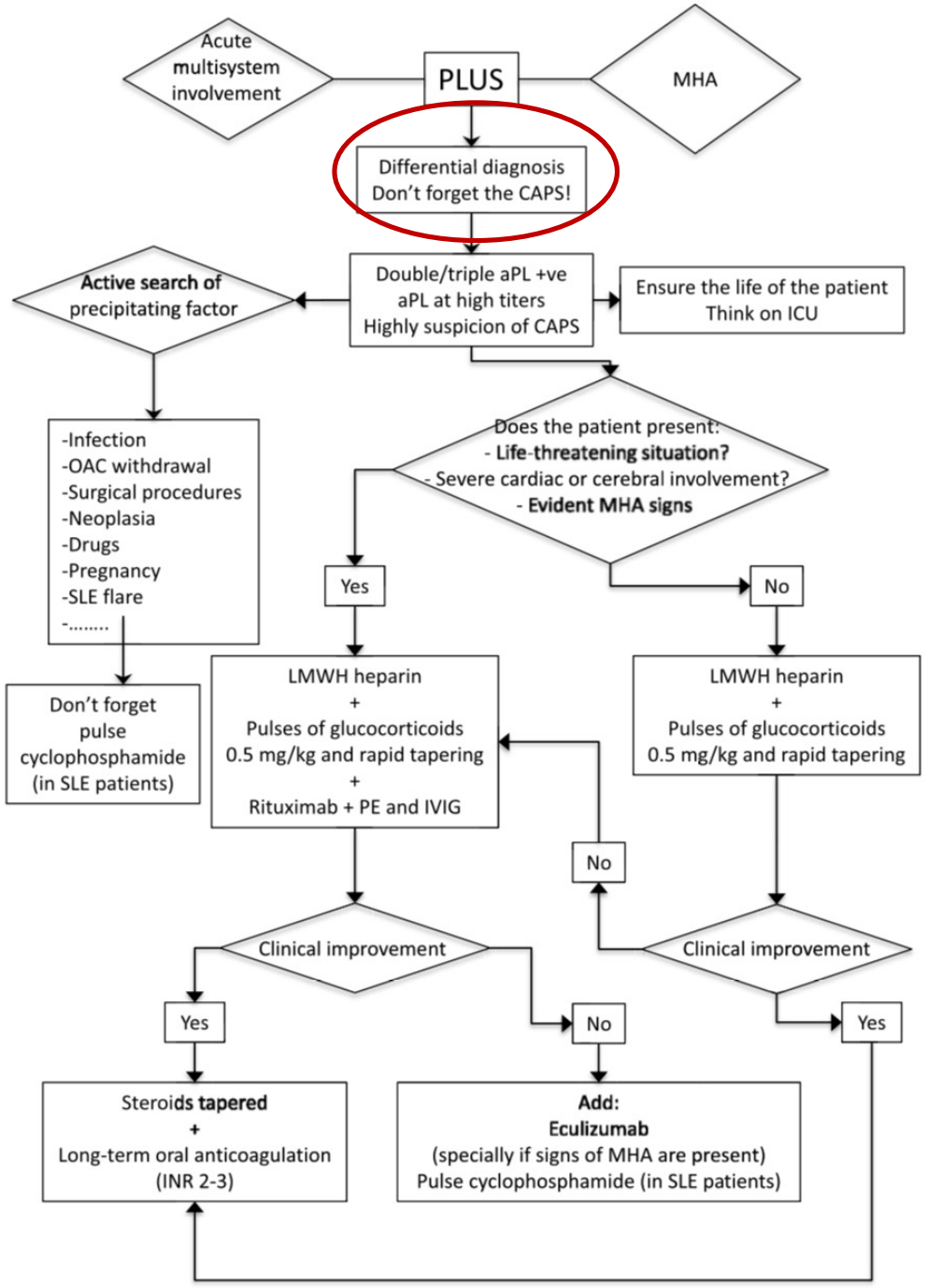
Intensive support needed (often ICU admission): external ventilation, inotropic drugs, hemodialysis.

Cervera et al, 2018

CAPS – Management

Anticoagulation (UFH, LMWH)	To be started asap, alone is the only factor improving prognosis. Consider switch to oral anticoagulation if improvement
Glucocorticoids	Rational: overcoming the excessive inflammatory response
Plasma Exchange	Rational: removing aPL e cytokines, replacement of clotting factors
Intravenous Immunoglobulins	Regimen: 400 mg/kg for 5 days or 1-2 gr/kg in 1-2 days
Cyclophosphamide	Particularly useful in SLE (es regimen: 750 mg/m2 monthly or 500 mg fortnightly)
Rituximab	Four weekly doses (375 mg/m2)
Eculizumab	In severe/refractory CAPS. Role in preventing recurrence?
Antibiotics	Infection as precipitating agent?
Intensive support	ITU?

Cervera et al, 2018, Siniscalchi et al 2024, BSH guidelines 2024



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Cervera et al, 2018

CAPS - Conclusions

- Extremely severe condition, high mortality
- **Need to think about it!**
- Challenging differential diagnosis (other MAHA)
- Difficult to achieve a definitive diagnosis (biopsy often not feasible)
- Lab diagnosis is key (aPL)
- **Multidisciplinary intensive** management
- Need to start prompt intensive treatment (included immunosuppression)
- Anticoagulation as a key point for management

Grazie per l’attenzione