23° corso di aggiornamento per il medico di base

15 – 16 – 17 ottobre 2025
Palazzo dei Congressi Lugano

organizzato dal Gruppo Medico Formazione

Diatesi emorragica: Quello che deve sapere il medico di famiglia

Lorenzo ALBERIO

Médecin chef
Hématologie générale et Hémostase
Service et Laboratoire centrale d'Hématologie
CHUV, Lausanne

UNIL | Université de Lausanne
Faculté de biologie et de médecine

Disclosures

Company name	Advisory board	Consultant	Hemophilia nurse	Research support	Speakers fees	Stockholder	Travel grant
Amgen							√
CSL-Behring			√	√	√		√
Bayer	√	√	√	√	√		√
Biotest					√		
Boehringer Ingelheim	√						
Daiichi Sankyo	√						
Novartis				√			√
Novo Nordisk	√		√	√			√
Octapharma			√				√
OM					√		
OrPha Swiss	√						
Pfizer							√
Roche	√		√	√			√
Sanofi-Aventis					√		
Sanofi-Genzyme		√					
Shire / Takeda	√		√	√			
Siemens					√		
Sobi	√		√	√			√
Werfen				√	√		

Medicina di base & Diatesi emorragiche

- Campanelli d'allarme nello studio medico (15')
- Presa a carico di pazienti con diatesi emorragica (5')
- Trombocitopenia (10')
- Come prevenire il rischio emorragico (10')

Campanelli d’allarme

La storia di Tommaso

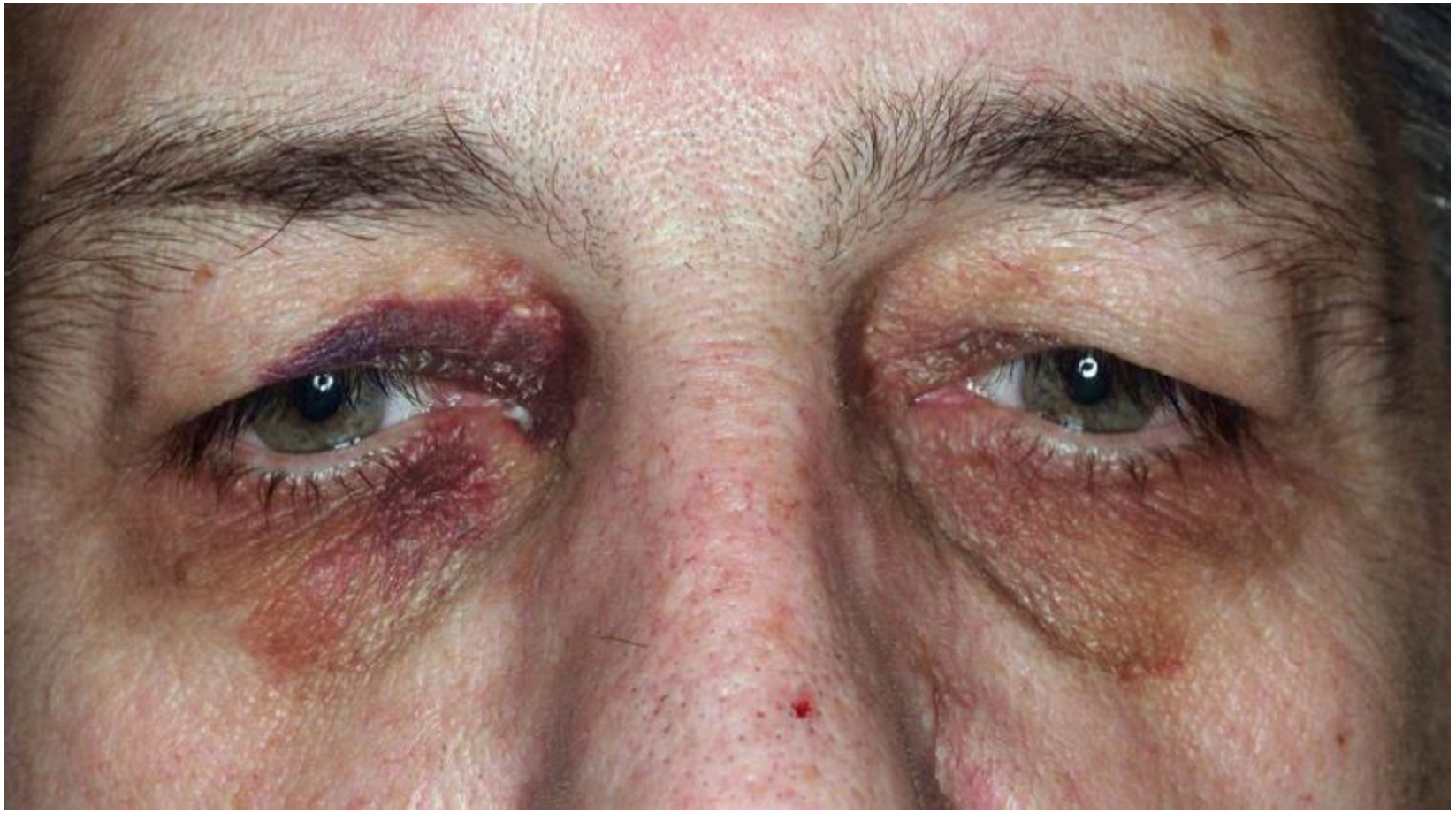
58-year-old man

La storia di Tommaso

Complaint:
recurrent, bilateral, spontaneous
peri-orbital haematomas

Hämostaseologie 2014;34:249

Clinical inspection



Hämostaseologie 2014;34:249

La storia di Tommaso

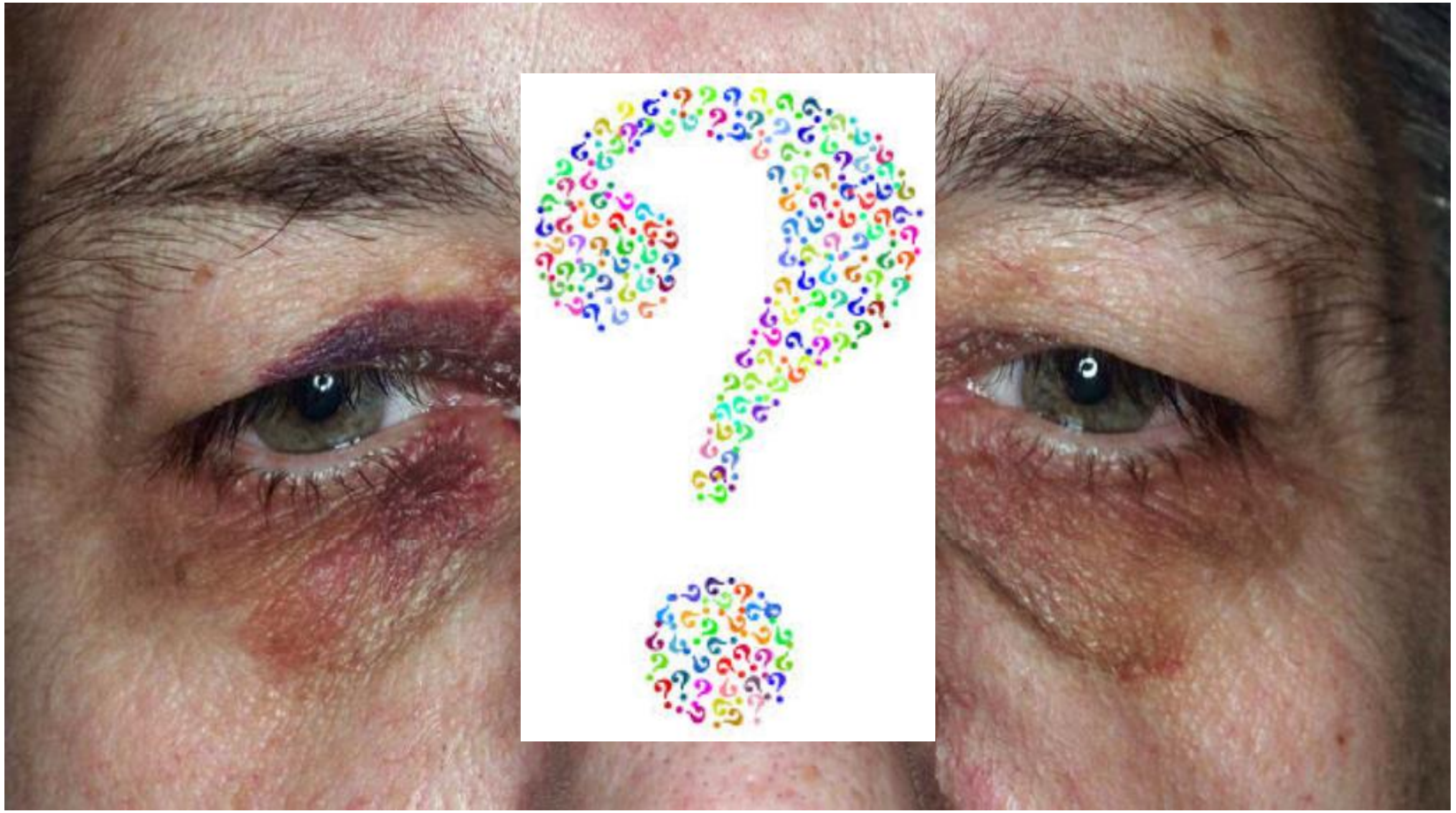
Complaint:
recurrent, bilateral, spontaneous
peri-orbital haematomas

Present for one year

Involved physiciancs: General practitioner (GP), Ear-Nose-Throat (ENT) physician, angiologist, radiologist

Excluded pathologies: local tumor, fracture, vascular malformation, thrombosis

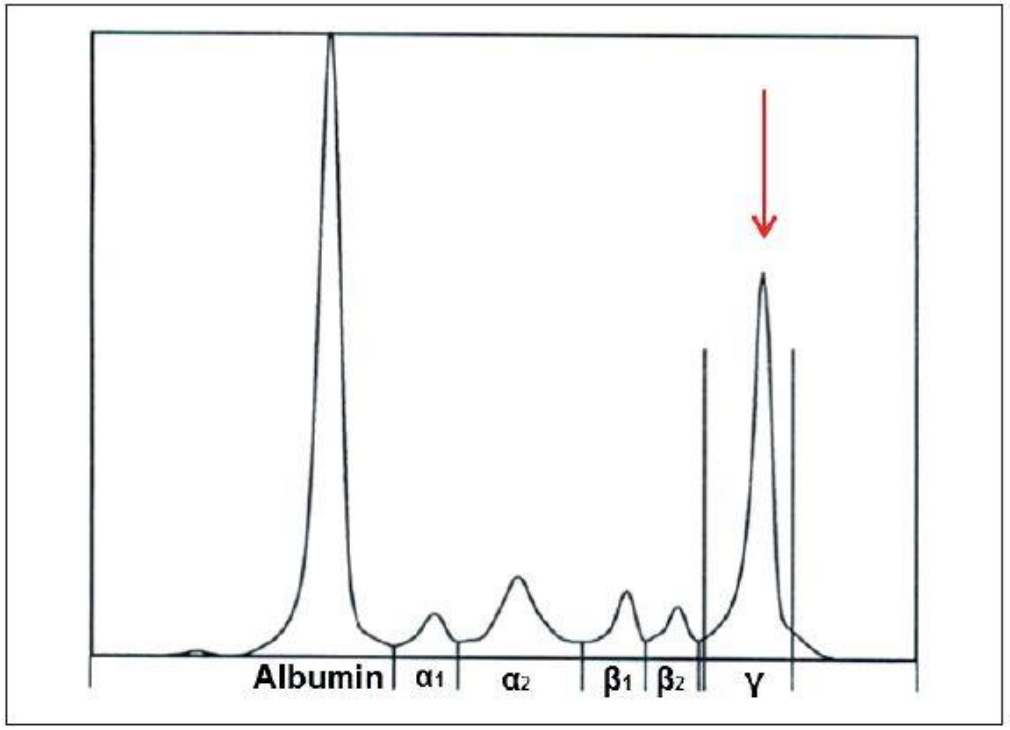
Hämostaseologie 2014;34:249



Working hypothesis ?

Diagnostic procedure ?

Serum free light chains & protein electrophoresis

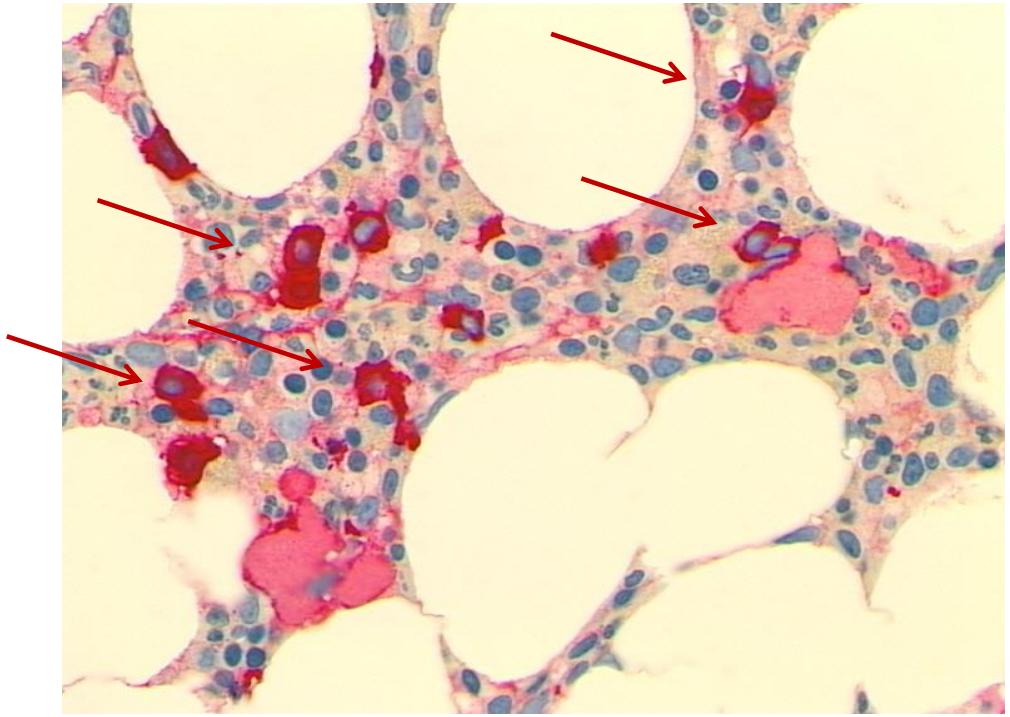


Paraprotein: 11.8 g/l (IgG)

Immunofixation :
Monoclonal lambda light chain

Hämostaseologie 2014;34:249

Bone marrow biopsy



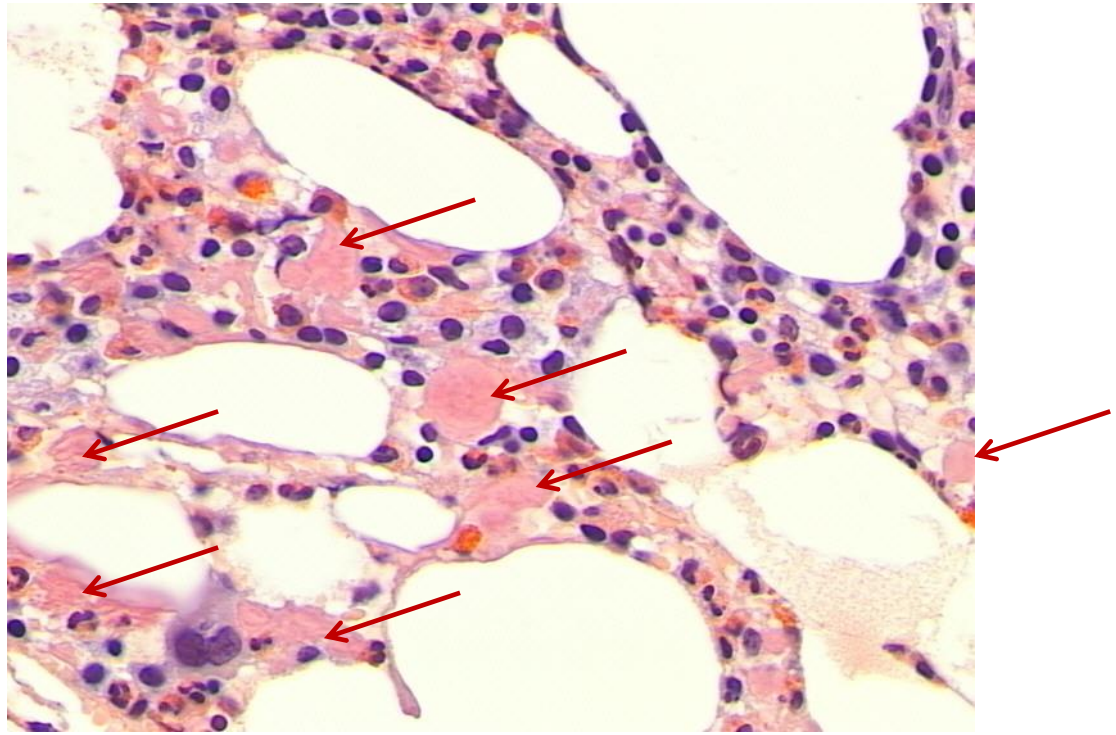
Infiltration 15-20% plasma cells
with lambda light-chain restriction

Hämostaseologie 2014;34:249

Bone marrow biopsy

Amorphous congo red positive deposits (amyloid)

Immunohistochemistry lambda light-chains



Hämostaseologie 2014;34:249

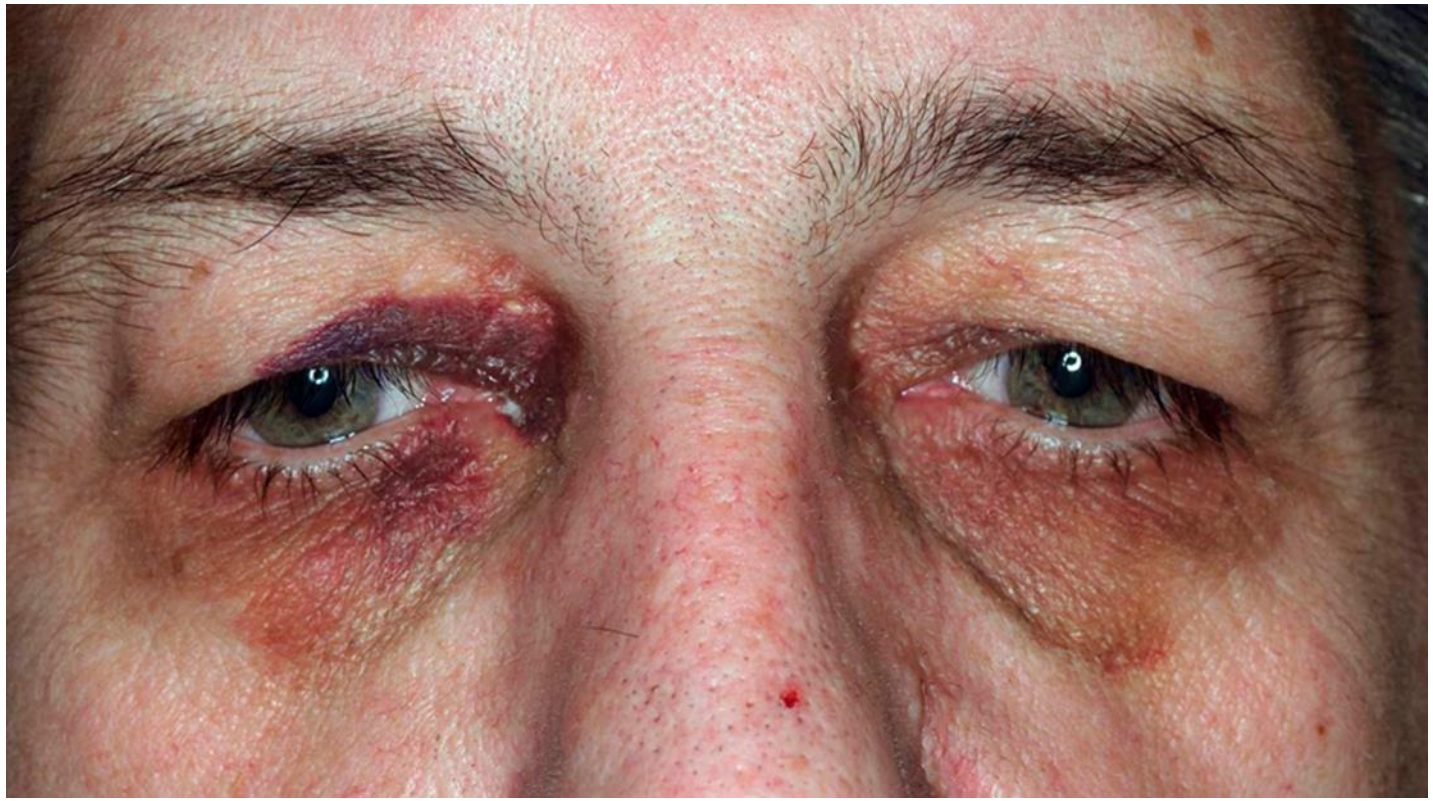
La storia di Tommaso

Final diagnosis

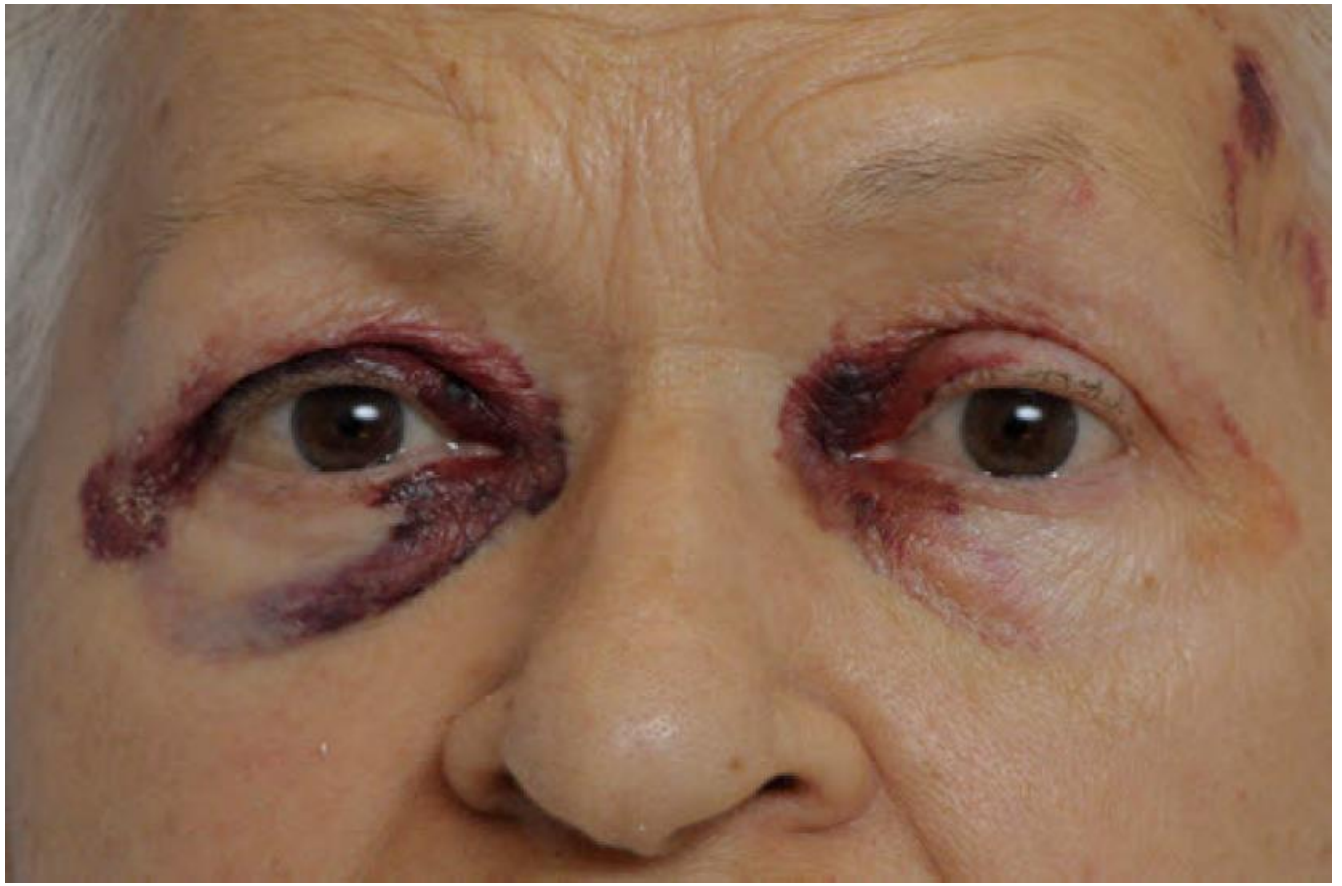
Multiple myeloma IgG Lambda
with
Amyloid purpura in the context of secondary monoclonal immunoglobulin light-chain amyloidosis

Hämostaseologie 2014;34:249

Diagnosis at first sight

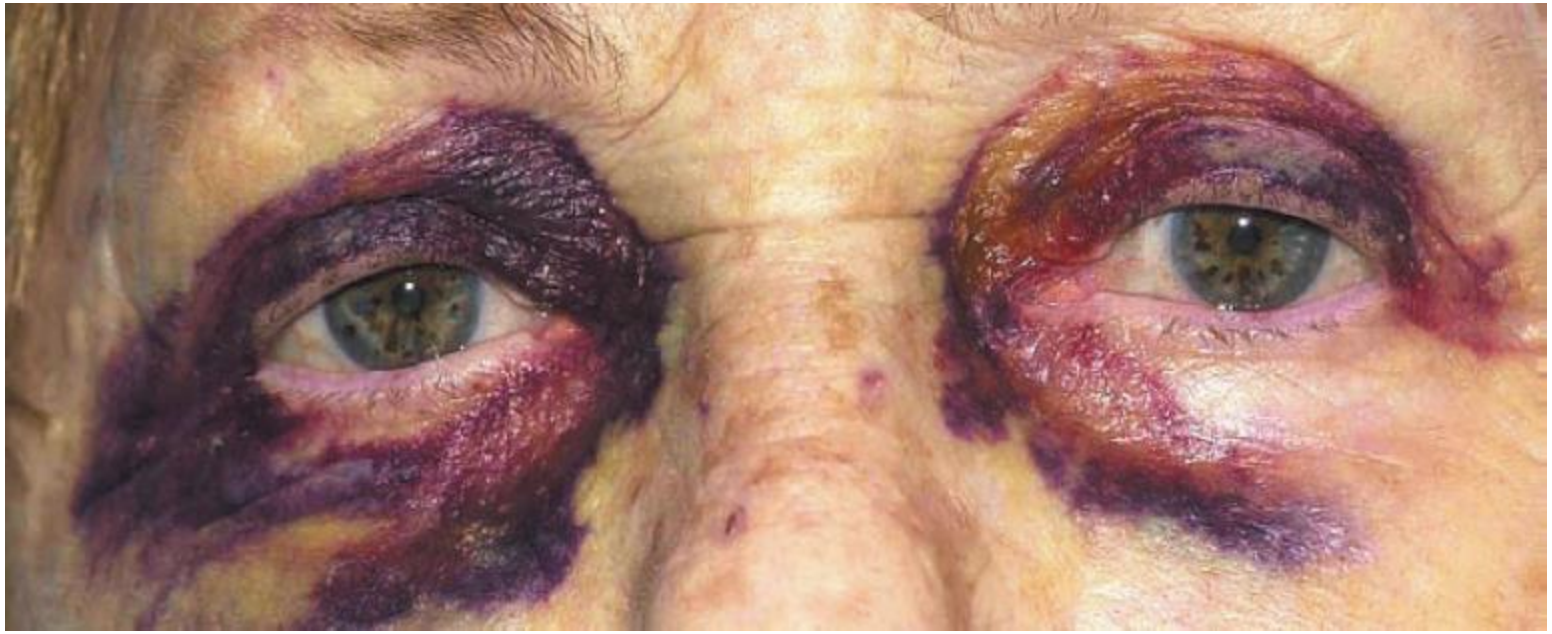


Diagnosis at first sight



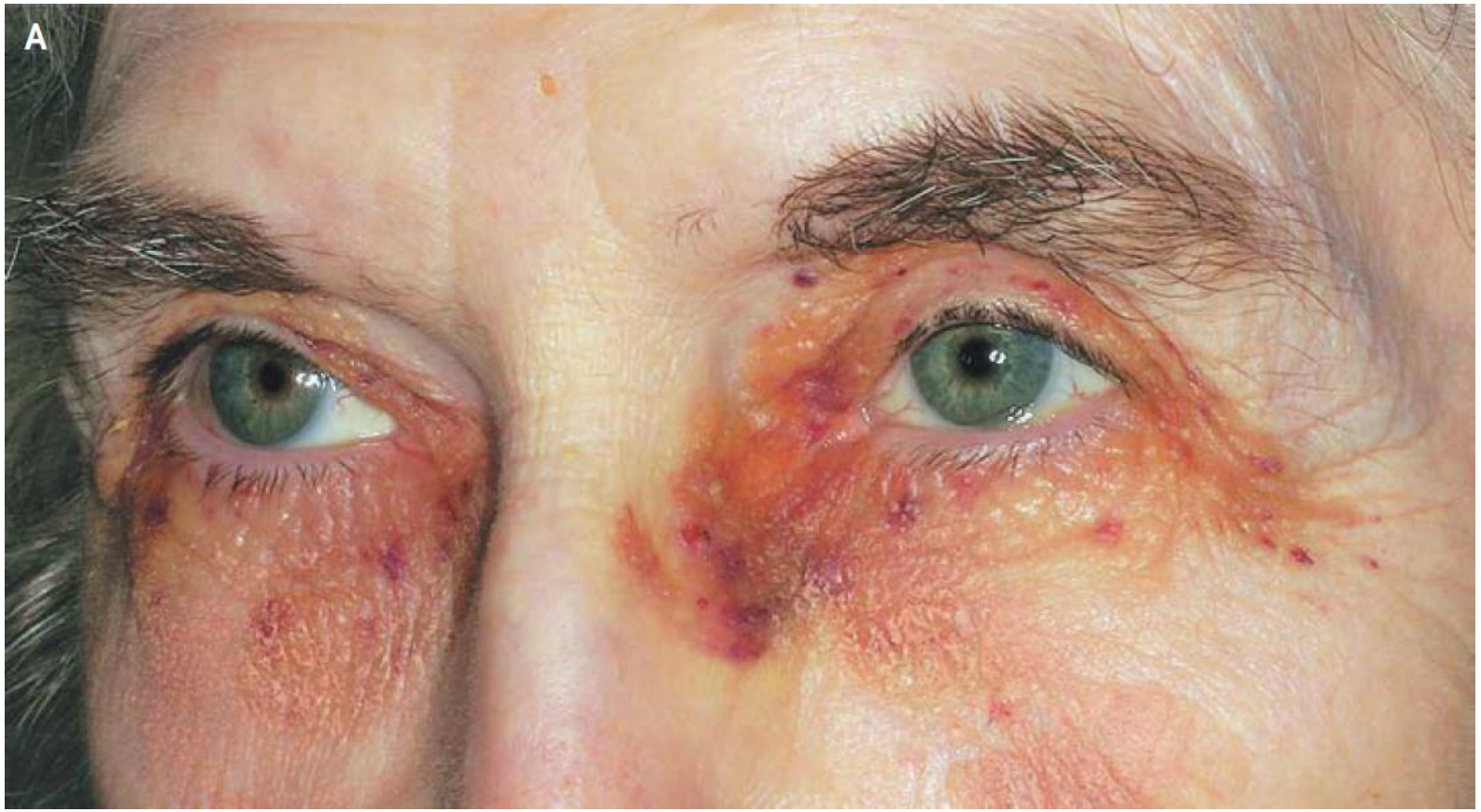
The New Zealand Medical Journal 2013

Diagnosis at first sight



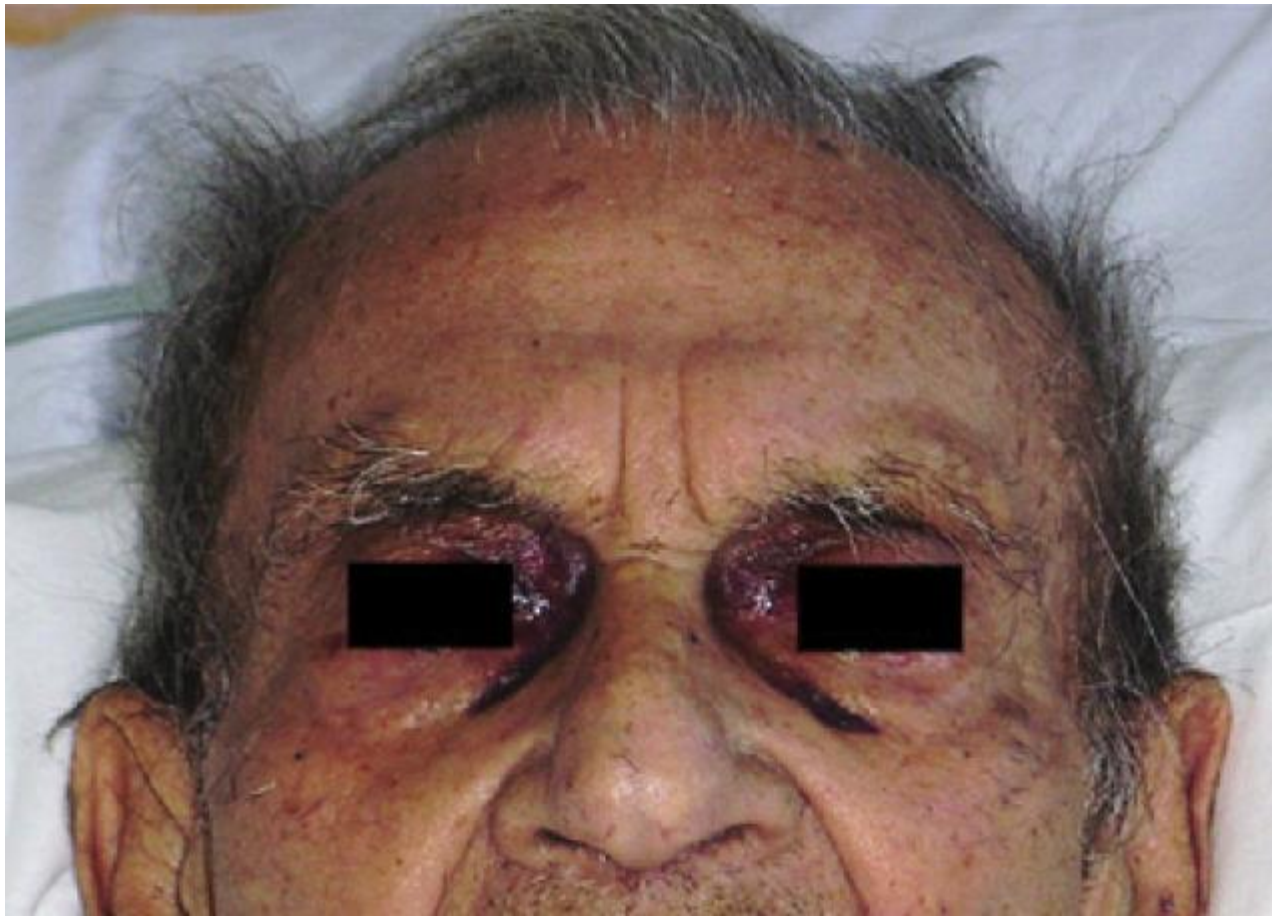
The New England Medical Journal 2017

Diagnosis at first sight



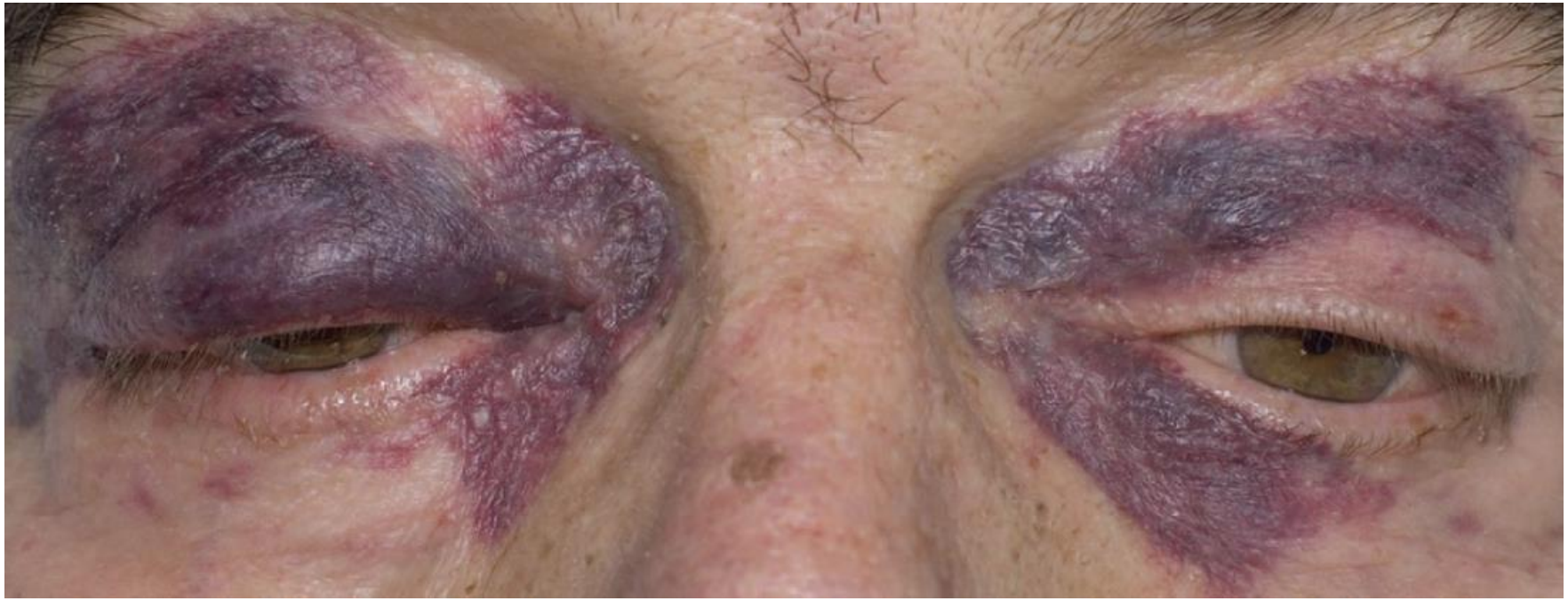
The New England Medical Journal 2011

Diagnosis at first sight



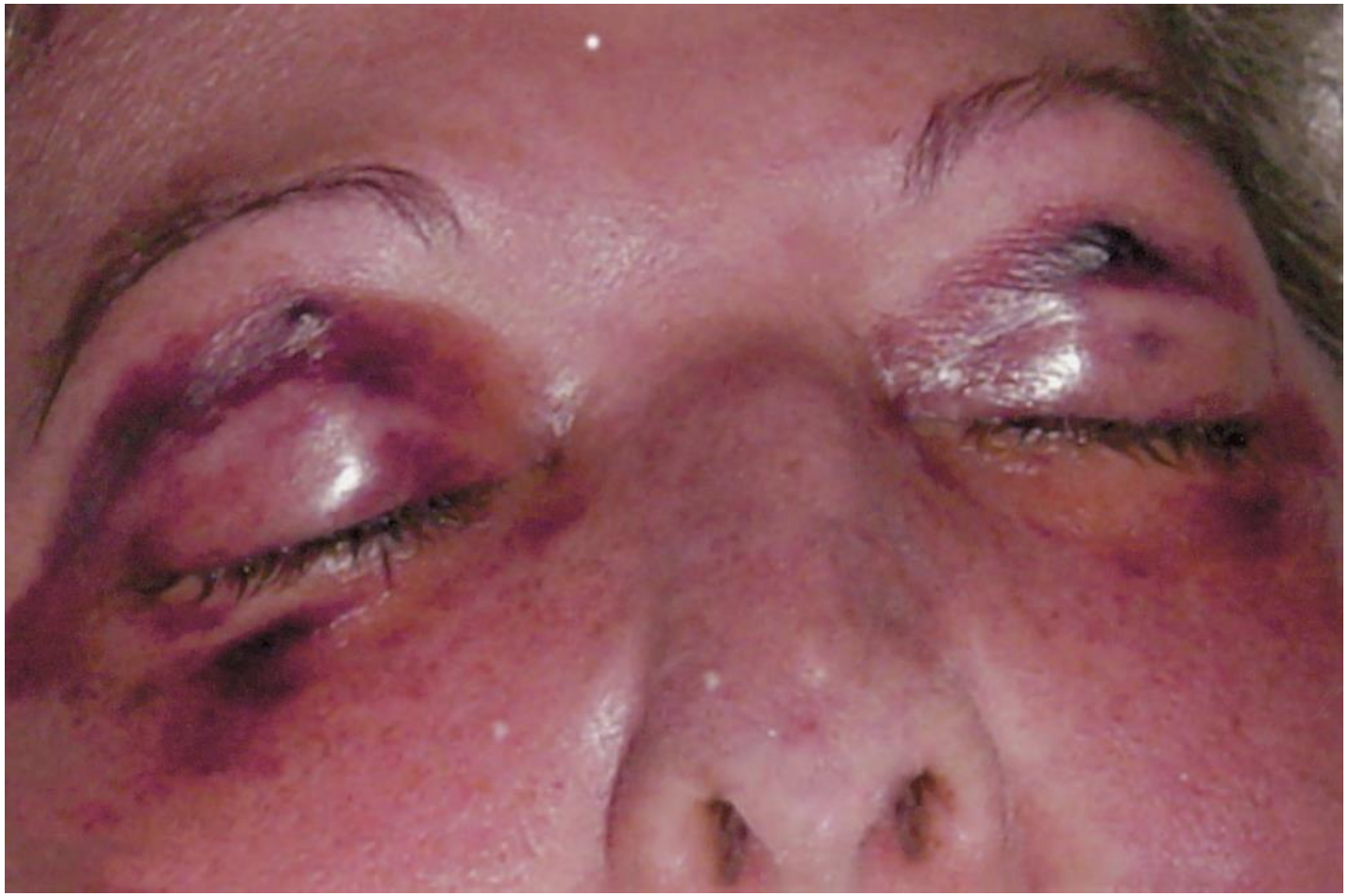
The American Journal of Medicine 2009

Diagnosis at first sight



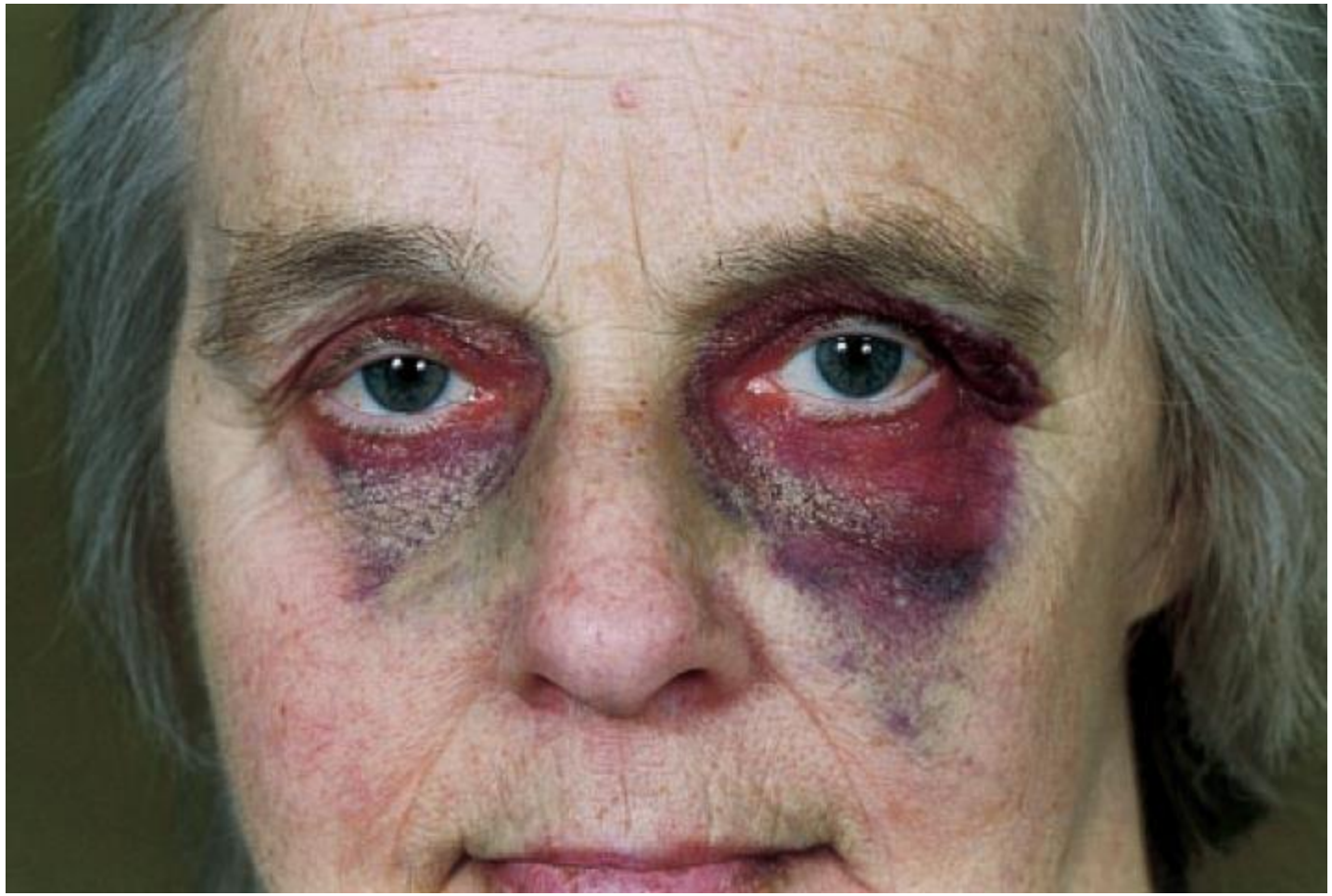
Anesthesia & Analgesia 2007

Diagnosis at first sight



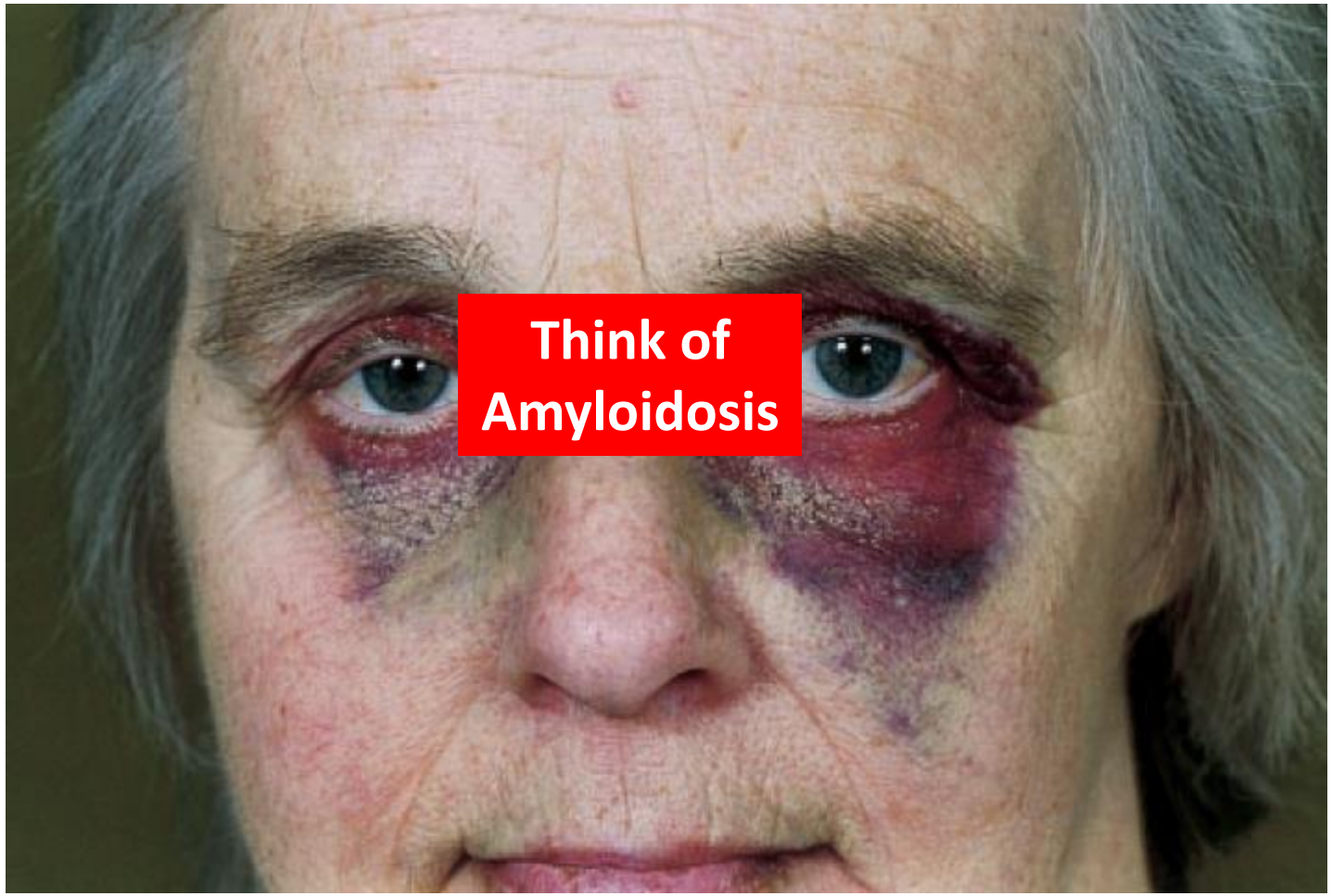
Arthritis & Rheumatology 2006

Diagnosis at first sight



Nephrol Dial Transplant 2000

Bilateral, spontaneous peri-orbital haematomas



La storia di *Falco*

66-year-old man

Acquired bleeding diathesis

Isolated prolonged aPTT

Confirmed several times over several weeks

Medical records: "*Administer FFP & check aPTT afterwards*"

Emergency room

Intracerebral haemorrhage

Exitus letalis

Legend:
aPTT, activated partial-thromboplastin time; FFP, fresh frozen plasma

Oh … La coagulazione !

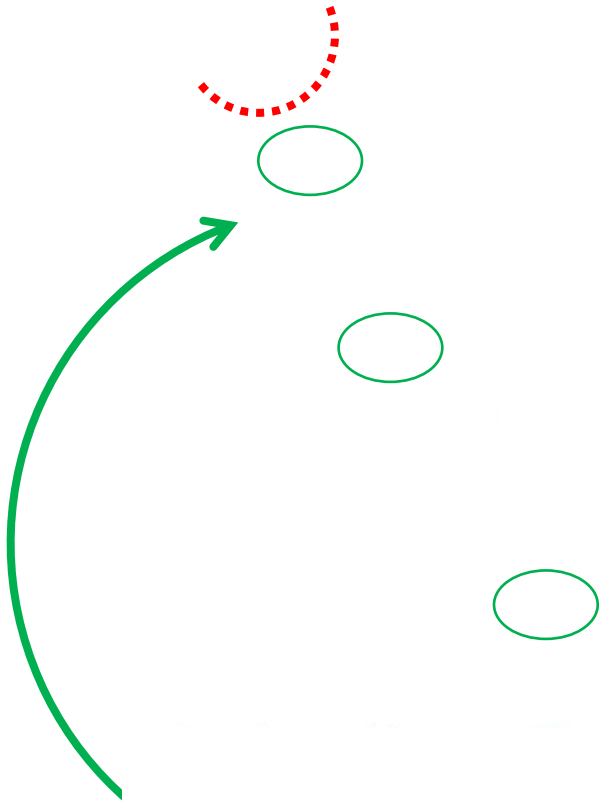
Coagulation

INtrinsic pathway

EXtrinsic pathway

97% of *in vivo* thrombin generation

3% of *in vivo* thrombin generation

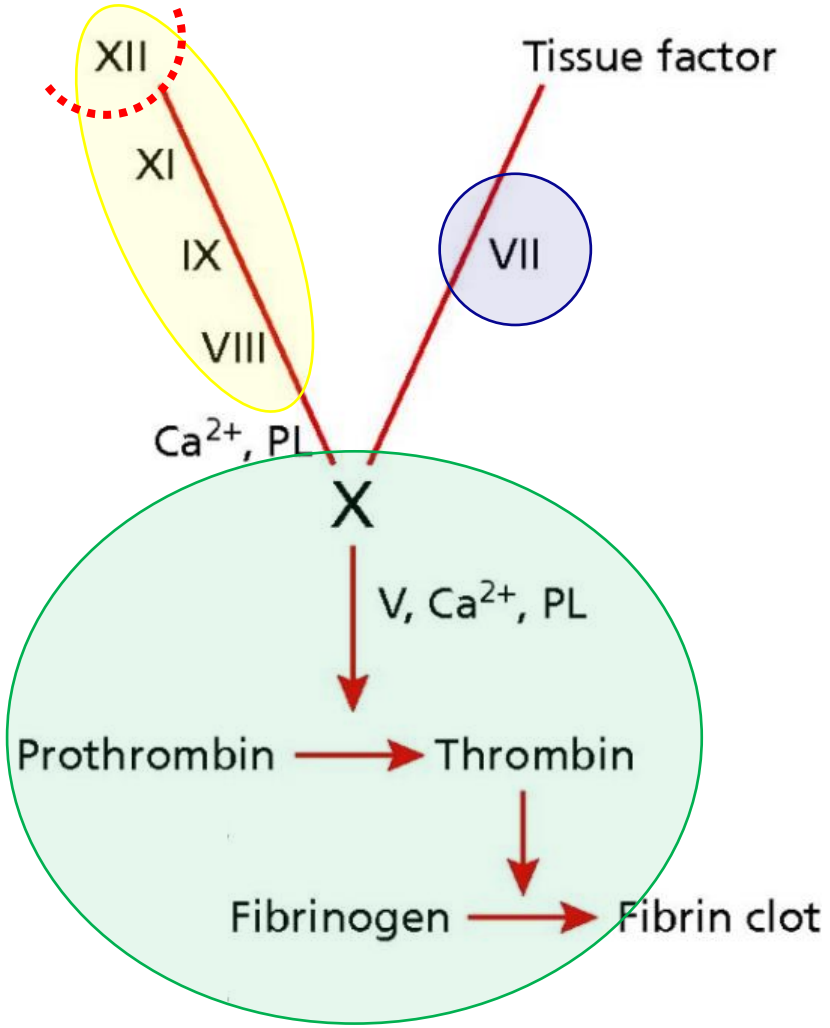


Positive feed-back mediated by thrombin
→ Activates the "amplification/propagation" pathway of coagulation.

Legend:
PL, phospholipids (negatively charged)

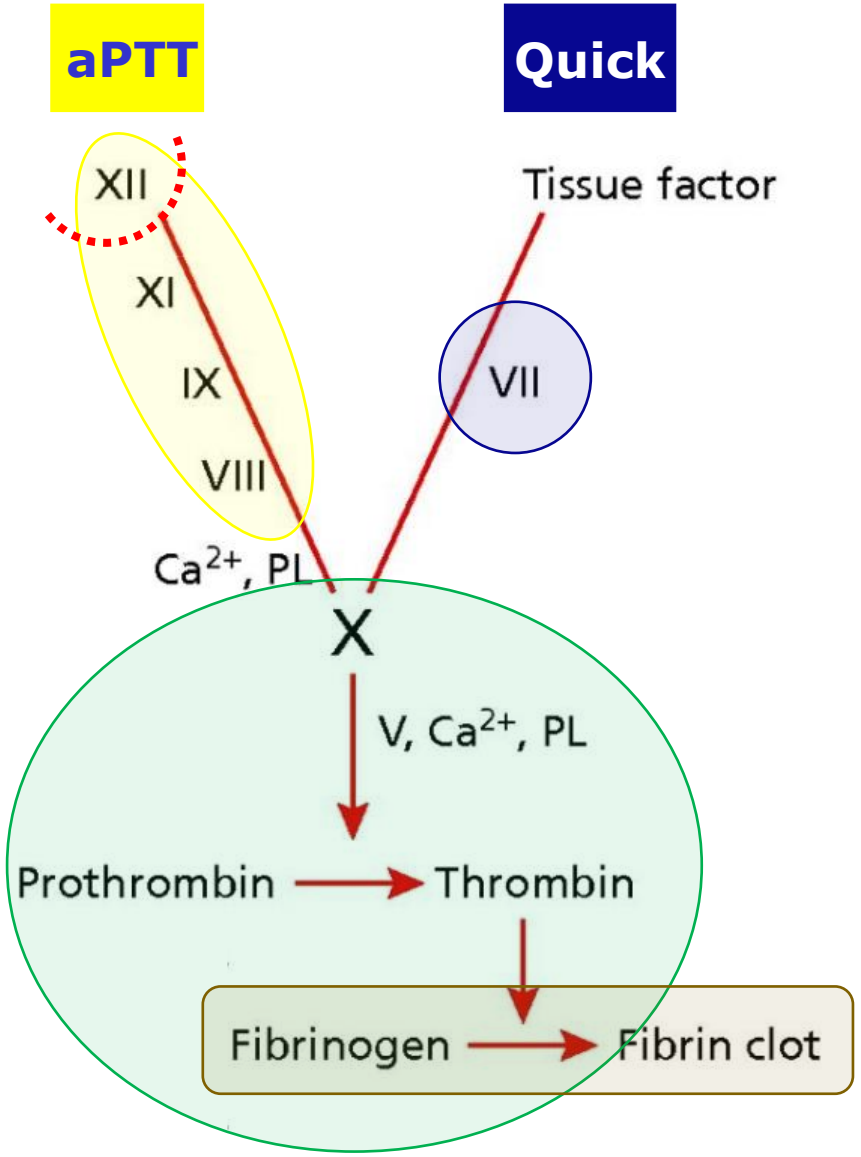
Coagulation assays

aPTT (INtrinsic pathway) (EXtrinsic pathway) **Quick**



Legend:
aPTT, activated partial-thromboplastin time; PL, phospholipids (negatively charged)

Coagulation assays



Thrombin time

Legend:
aPTT, activated partial-thromboplastin time; PL, phospholipids (negatively charged)

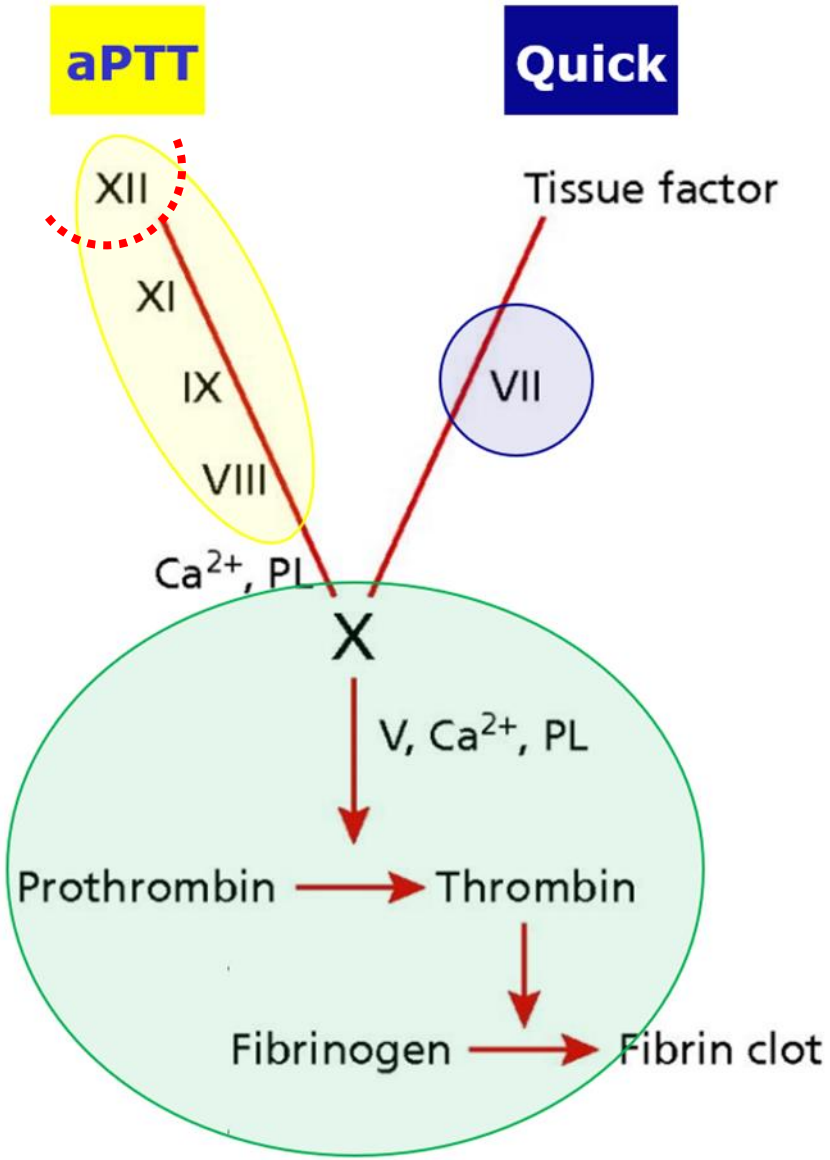
Isolated prolonged aPTT

DD:
- Factor deficiency
- Inhibitors

DD:
- aPTT mixing-test

La storia di Falco
- Slow inhibitor

Acquired haemophilia



Normal Quick
- VII ✓
- X ✓
- V ✓
- Prothrombin ✓
- Fibrinogen ✓

Normal Thrombin time
- Fibrinogen ✓
- **No** thrombin inhibitors

Legend:
aPTT, activated partial-thromboplastin time; PL, phospholipids (negatively charged)

New-onset bleeding + isolated prolonged aPTT

Think of Acquired Haemophilia

La storia di *Giorgio*

72-year-old man

Present complain:
- Fatigue (recent onset, progressive)
- Colchicine (because of gout, diagnosed 1 month ago)

Personal history:
- Hyperferritinemia (3 phlebotomies/year)
- Arterial hypertension

La storia di *Giorgio* – Complete Blood Count

Hb	122	g/l	(133 – 177)
Hk	0.34	l/l	(0.40 – 0.52)
Ec	3.87	T/l	(4.4 – 5.8)
MCV	88	fl	(81 – 99)
MCH	31.5	pg	(27 – 34)
MCHC	360	g/l	(310 – 360)
Retics	42.2	G/L	(20 – 120)
Lc	1.3	G/l	(4.0 – 10.0)
Neutro	1.12	G/l	(1.8 – 7.5)
Lympho	0.16	G/l	(1.5 – 4.0)
Mono	0.01	G/l	(0.2 – 0.8)
Eos	0.01	G/l	(0.05 – 0.3)
Tc	50	G/l	(150 – 350)

Pancytopenia

What is the most relevant  … next diagnostic step ?

Coagulation studies !

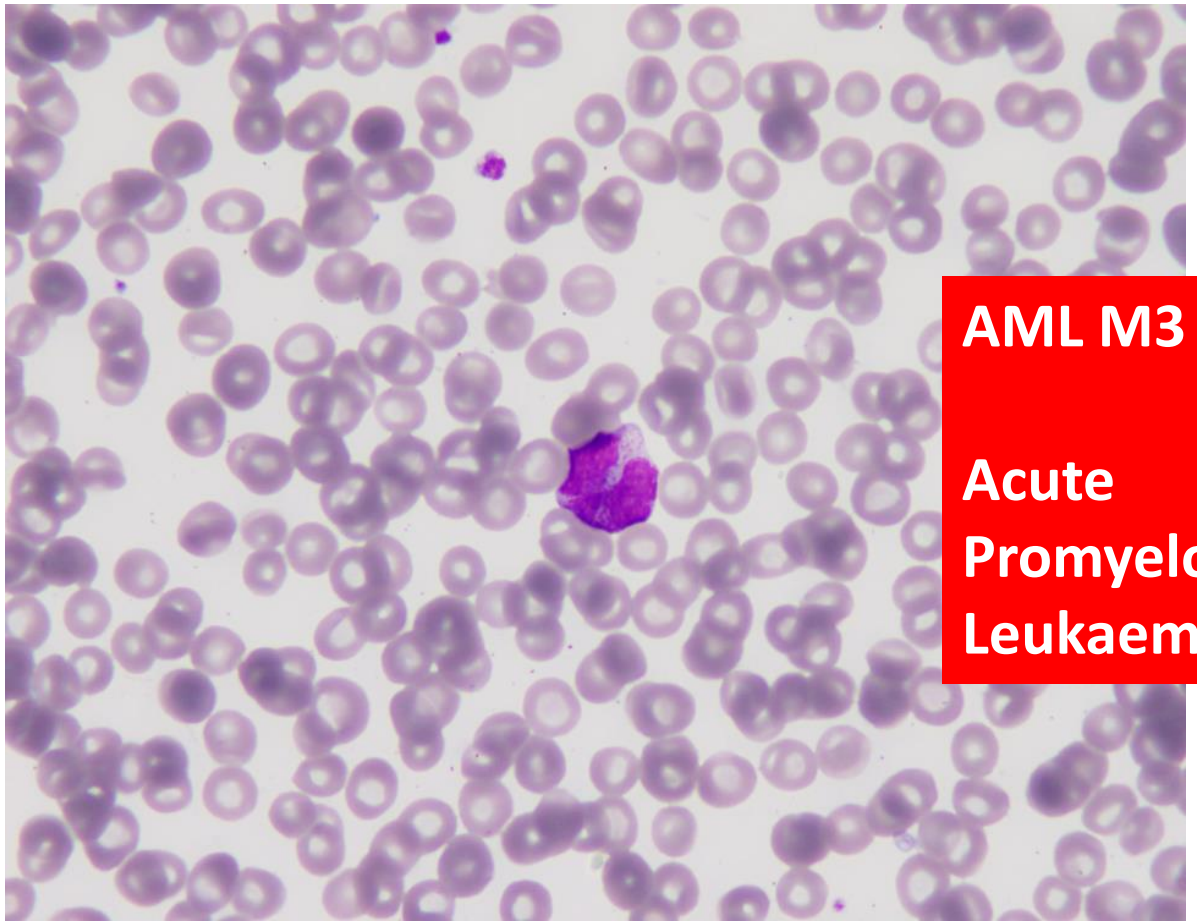
La storia di *Giorgio* – Coagulation studies

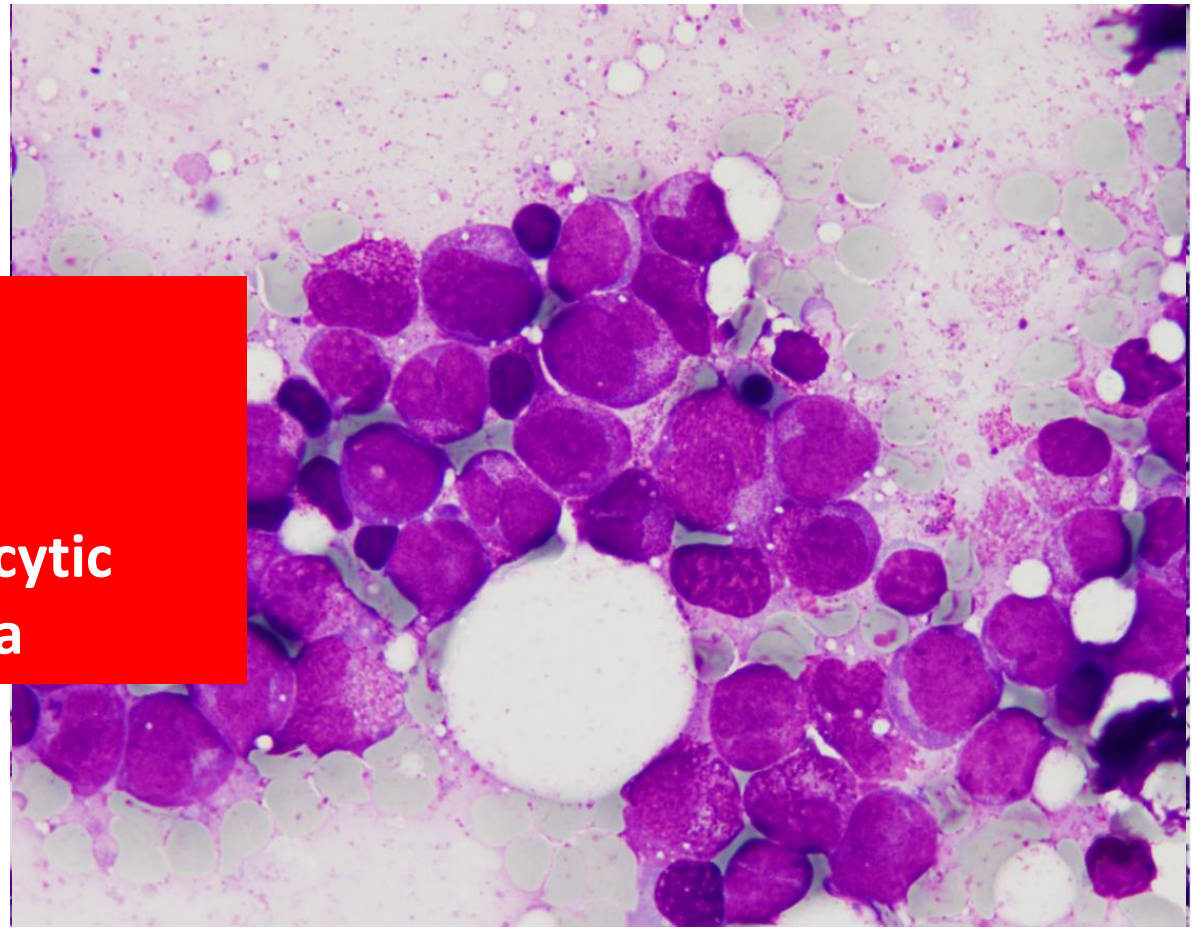
PT	30	%	(80 – 120)
aPTT	33	sec	(26 – 37)
Thrombin time	20	sec	(14 – 19)
Fibrinogen	0.5	g/l	(2.0 – 4.0)
D-dimers	50’600	ng/ml	(<500)

Disseminated Intravascular Coagulation

Legend:
aPTT, activated partial-thromboplastin time; PT, prothrombin time (Quick)

La storia di *Giorgio* – Blood film & bone marrow





AML M3

Acute Promyelocytic Leukaemia

Pancytopenia & DIC

AML M3

Acute Promyelocytic Leukaemia

Legend:
AML, acute myeloid leukaemia

Alcuni « campanelli d'allarme » ematologici

- *Tommaso: Purpura amiloide secondaria a mieloma multiplo*
  Ematomi periorbitali spontanei → Catene leggere ?

- *Falco: Emofilia acquisita*
  Nuova tendenza a sanguinare → aPTT ? Mix !

- *Giorgio: Leucemia promielocitica*
  Pancitopenia → DIC ?

Presa a carico del paziente con diatesi emorragica

History

- It’s the key step
- Structured & semi-quantitative
- Inherited *versus* acquired bleeding tendency
- Exacerbating events (e.g., drugs!, concomitant diseases, ...)

ISTH-Bleeding Assessment Tool

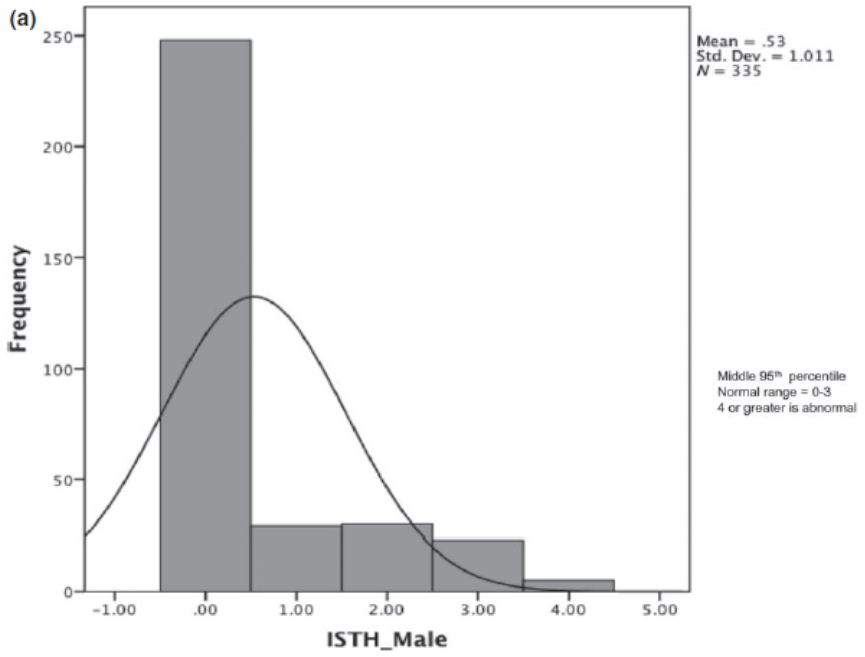
Symptom
Epistaxis
Cutaneous
Bleeding from minor wounds
Oral cavity
GI bleeding
Tooth extraction
Surgery
Menorrhagia
Post-partum haemorrhage
Muscle haematomas
Haemarthrosis
Additional items
Drugs
Time axis
Family history

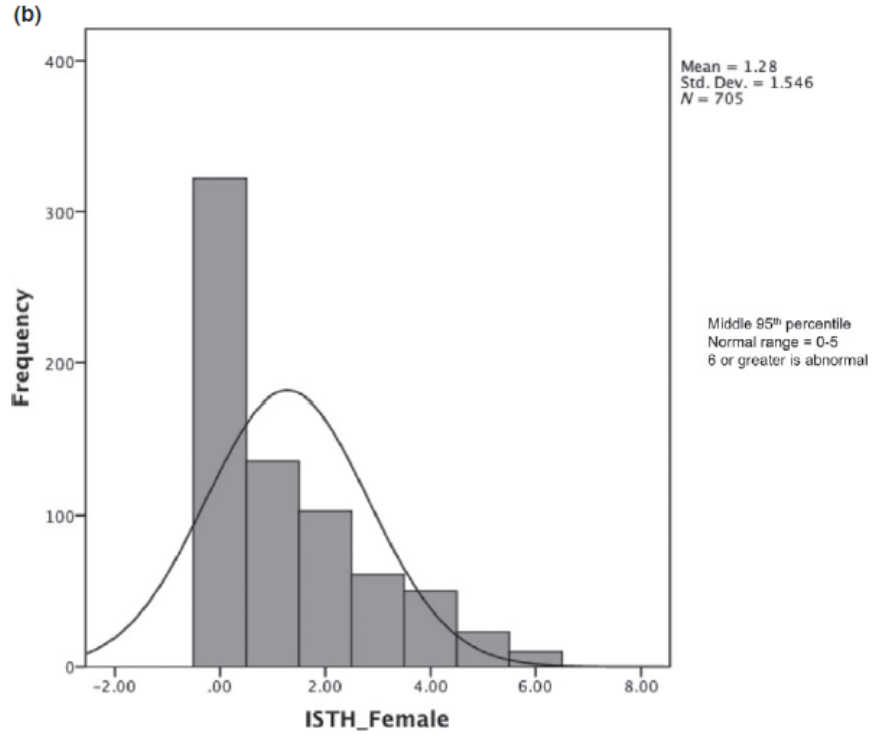
Legend:
ISTH, International Society on Thrombosis and Haemostasis

www.practical-haemostasis.com
→ Risk Assessment Algorithms → Bleeding Assessment → ISTH-BAT

Swiss Med Wkly 2009;139:327

ISTH-Bleeding Assessment Tool





Male
Score ≥4 : abnormal

Female
Score ≥6 : abnormal

www.practical-haemostasis.com
→ Risk Assessment Algorithms → Bleeding Assessment → ISTH-BAT

Haemophilia 2014;20:831

Legend:
ISTH, International Society on Thrombosis and Haemostasis

ISTH-Bleeding Assessment Tool

- PROBLEM : It takes 20-30 minutes to go trough the ISTH-BAT
- A POSSIBLE SOLUTION : Ask the patient to fill in a form ...

Patient questionnaire

Bitte beantworten Sie folgende Fragen durch Ankreuzen:

Starkes Nachbluten nach Operationen	☐ Ja	☐ Nein
Bluttransfusionen während oder nach Operationen	☐ Ja	☐ Nein
Verzögerte, schlechte Wundheilung	☐ Ja	☐ Nein
Grosse blaue Flecken nach leichten Verletzungen	☐ Ja	☐ Nein
Langes Nachbluten nach Schnittverletzungen	☐ Ja	☐ Nein
Auffällig langes Nachbluten nach Zähneziehen oder Dentalhygiene	☐ Ja	☐ Nein
Wiederholte Einblutungen in Gelenke	☐ Ja	☐ Nein
Blutungsneigung bei Eltern, Geschwistern, Grosseltern, sonst. Verwandten, z.B. Nachbluten nach Operationen, Verletzung oder Zähneziehen, Hämatome, starke Menstruationsblutungen	☐ Ja	☐ Nein
Häufiges Nasenbluten	☐ Ja	☐ Nein

Starke und/oder verlängerte Monatsblutungen Mehr als 3 Tampons/Vorlagen pro Tag und/oder Dauer mehr als 6 Tage	☐ Ja	☐ Nein
Nachbluten nach Geburten oder Fehlgeburten	☐ Ja	☐ Nein
Haben Sie Kinder?	☐ Ja	☐ Nein

Physical examination

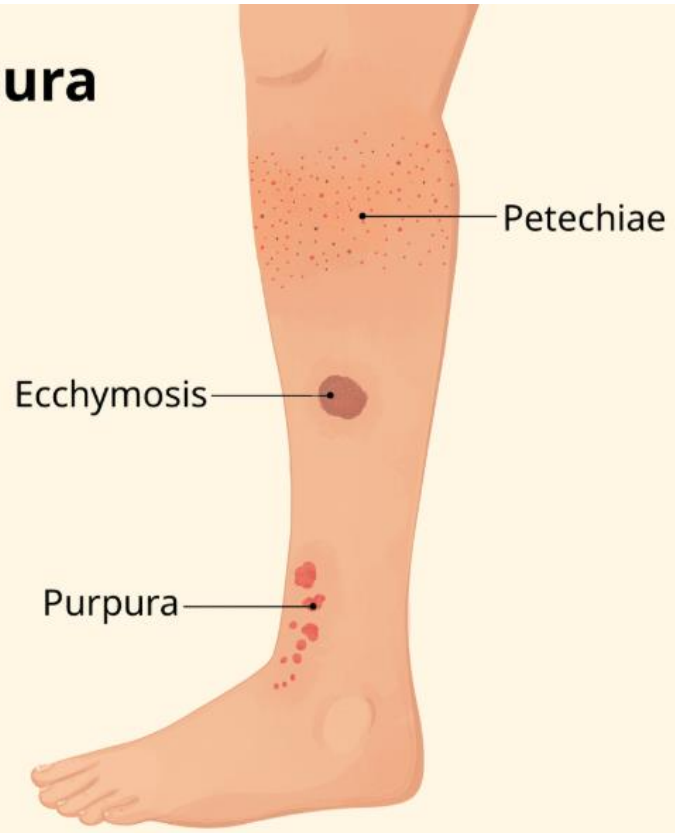
Inspection of the **skin and mucous** membranes for:

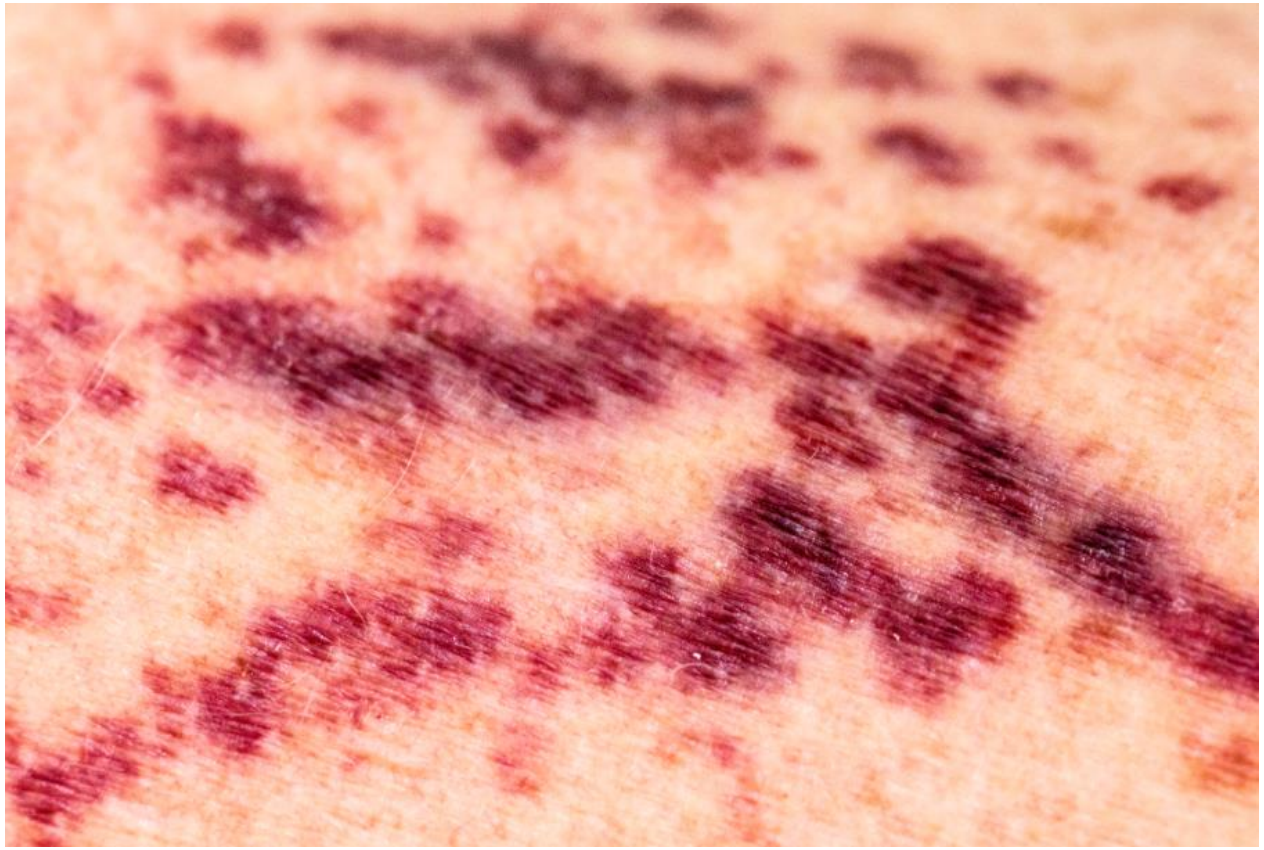
- Petechiae / Purpura
- Ecchymoses
- Haematomas
- Abnormal blood vessels (telangiectasia)
- Jaundice or pallor

Petechiae / Purpura / Ecchymosis

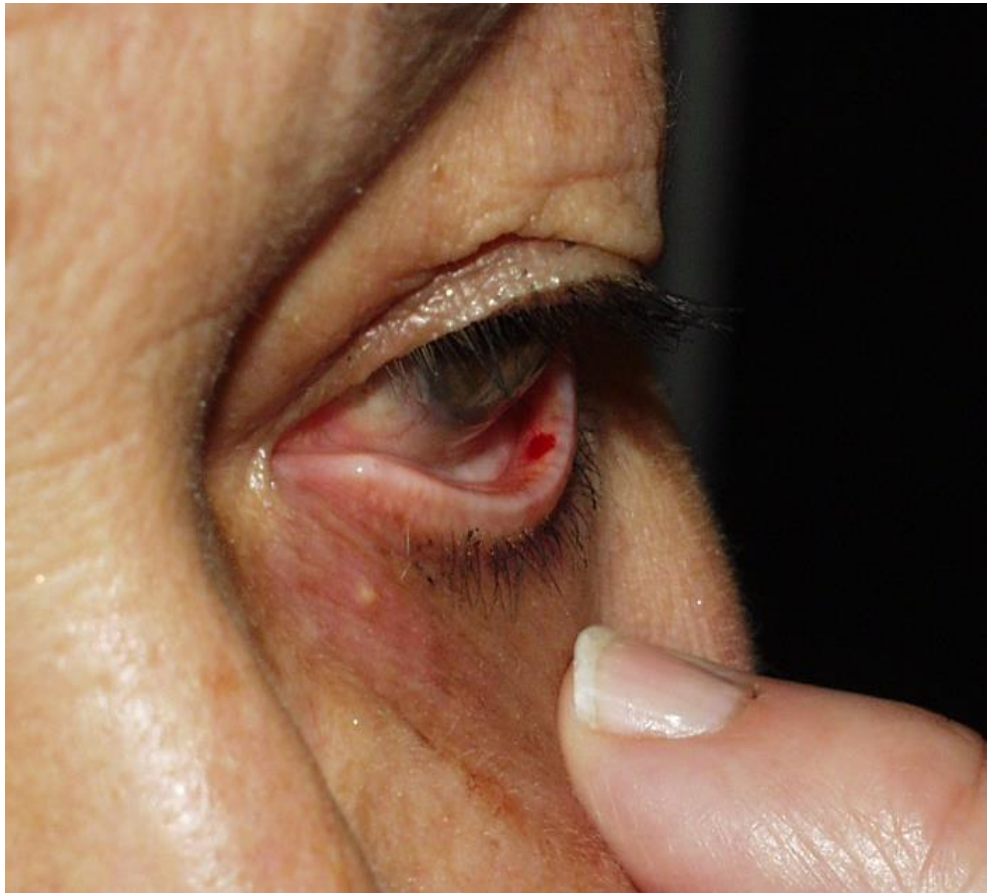
Petechiae vs. Purpura vs. Ecchymosis

- Petechiae are less than 4 mm in diameter.
- Purpura are between 4 mm and 10 mm in size.
- Ecchymosis, also known as bruising, are areas that are larger than 10 mm.

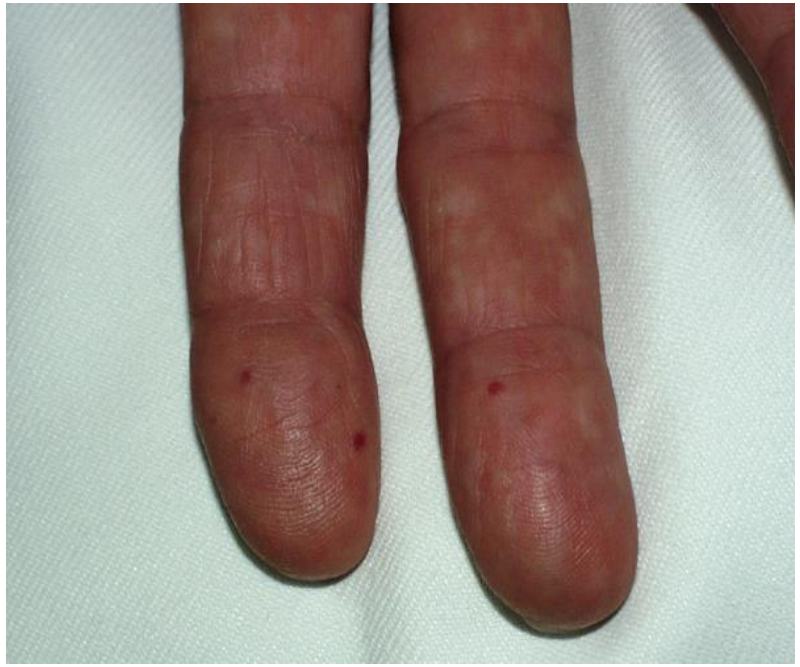


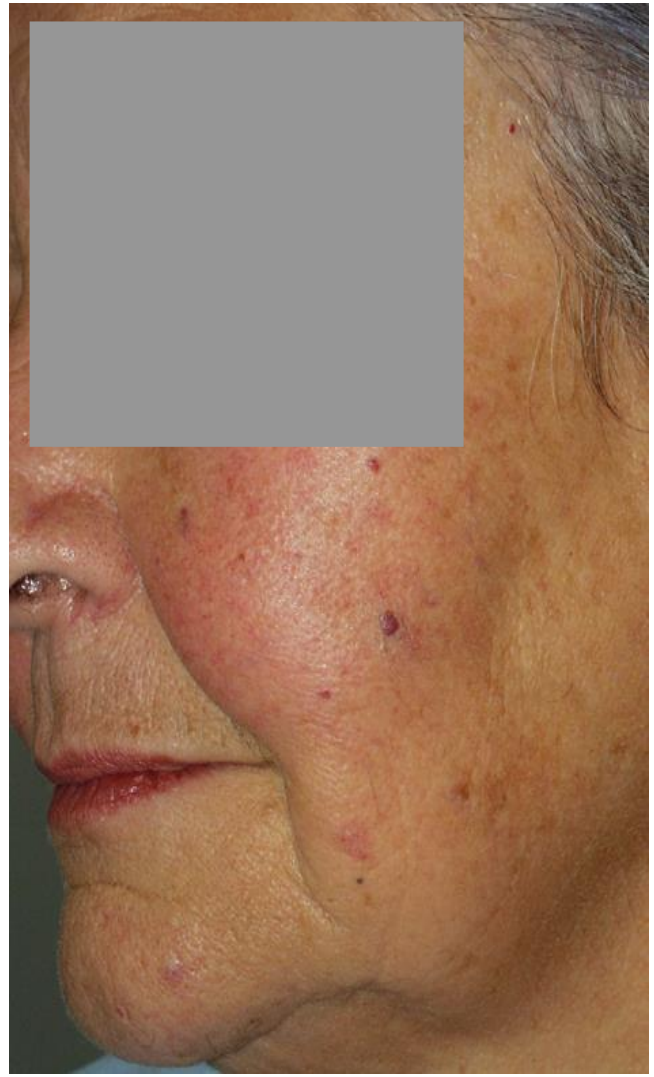


Abnormal blood vessels

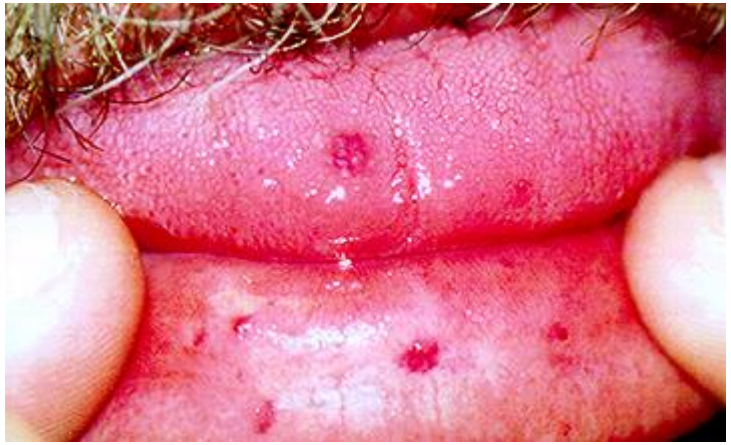


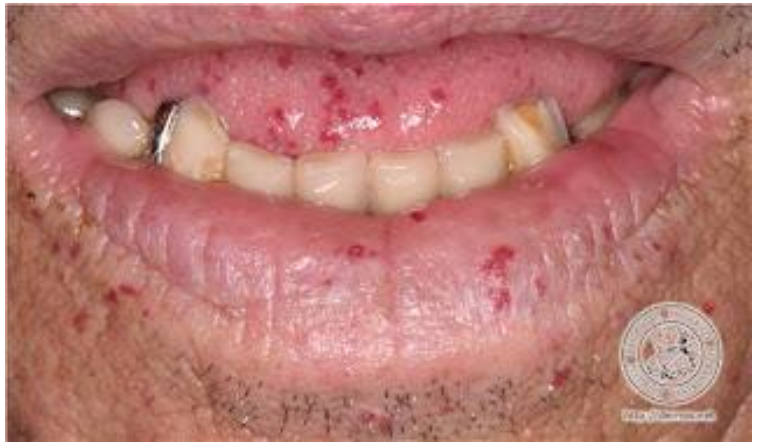
Anna, diagnosed with **Morbus Osler**
at age 67
after a life-long journey of iron-replacements, blood transfusions and haemostasis work-ups.

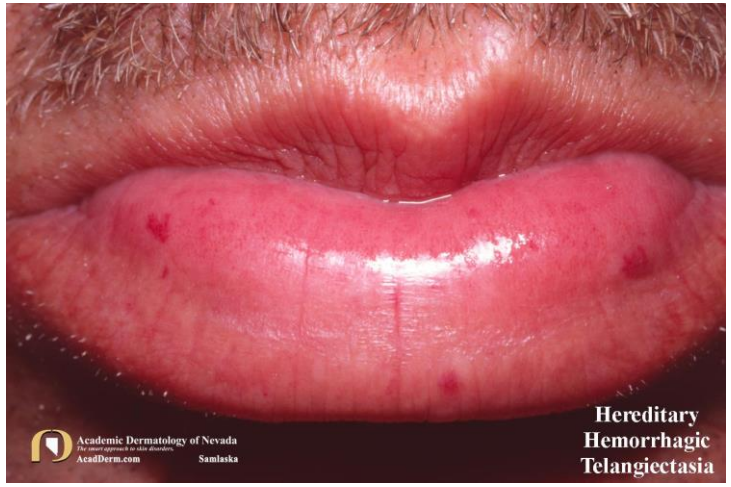


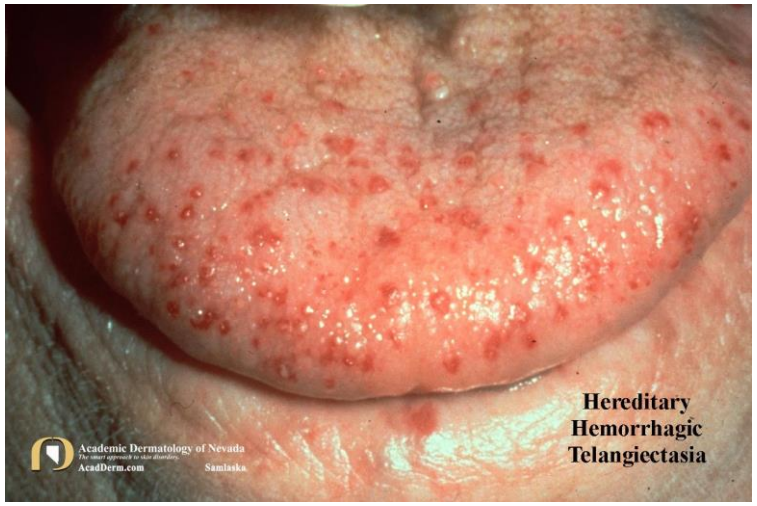


Hereditary Haemorrhagic Telangectasia









Physical examination

Inspection of the **skin and mucous** membranes for:	Petechiae / Purpura Ecchymoses Haematomas Abnormal blood vessels (telangiectasia) Jaundice or pallor
Examination of **oral and nasal mucosa** for:	Bleeding, ulcers, or gum bleeding
Palpation of **lymph node regions** for:	Lymphadenopathy
Palpation of the **abdomen** for:	Hepatosplenomegaly
Evaluation of **joints** for:	Swelling or tenderness
Consideration of a **rectal examination** to check for:	Occult or gross blood in stool

Laboratory analyses

- Complete blood count including a peripheral blood smear
- Prothrombin time, aPTT, TT, fibrinogen (and D-dimers)
- Renal function tests
- Liver function tests

Legend:
TT, thrombin time

Am Fam Physician 2016;93:279

Referral to a hematologist

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
The ISTH-BAT should be used during the initial evaluation of patients with a suspected bleeding disorder.	C	11, 12
A peripheral blood smear, complete blood count, prothrombin time, partial thromboplastin time, and renal and liver function tests should be obtained in patients with an abnormal ISTH-BAT score or in whom a bleeding disorder is suspected.	C	18-20
Patients should be referred to a hematologist for further evaluation if suspicion for a bleeding disorder remains high despite a negative workup.	C	15

ISTH-BAT = International Society on Thrombosis and Hemostasis Bleeding Assessment Tool.

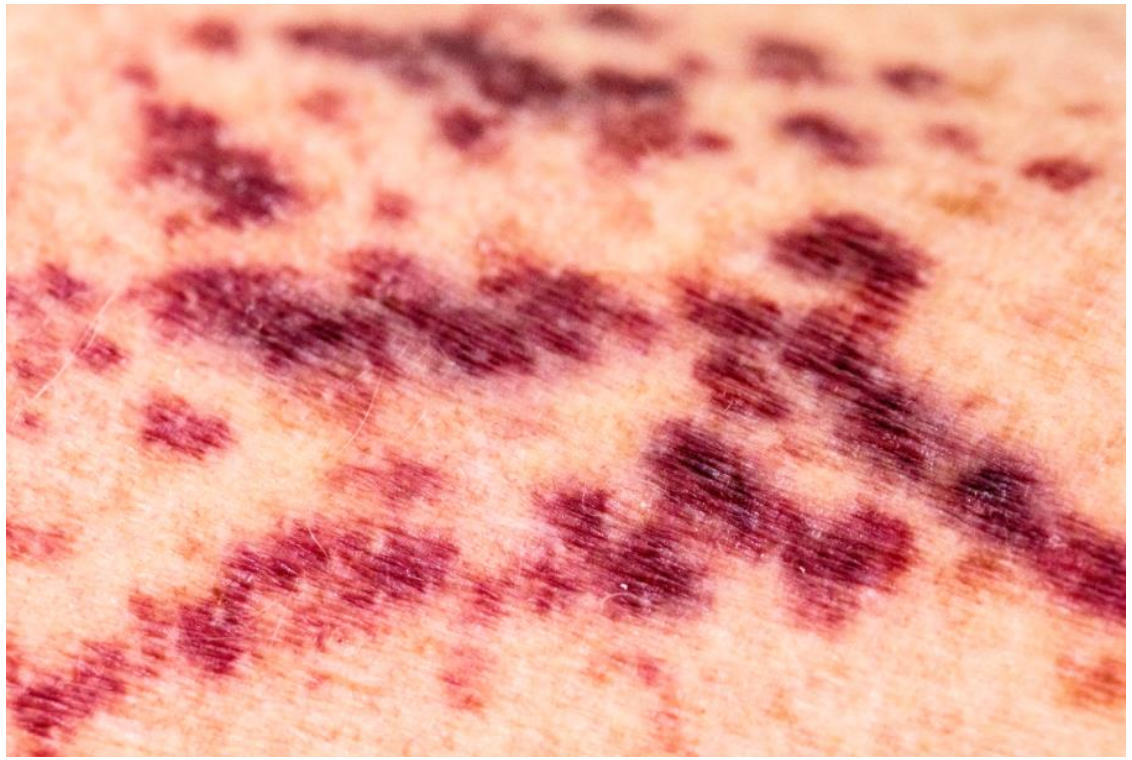
A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to http://www.aafp.org/afpsort.

Am Fam Physician 2016;93:279

Trombocitopenia

Thrombocytopenia

- Asymptomatic ← "routine" complete blood count
- Symptomatic ← petechiae / purpura

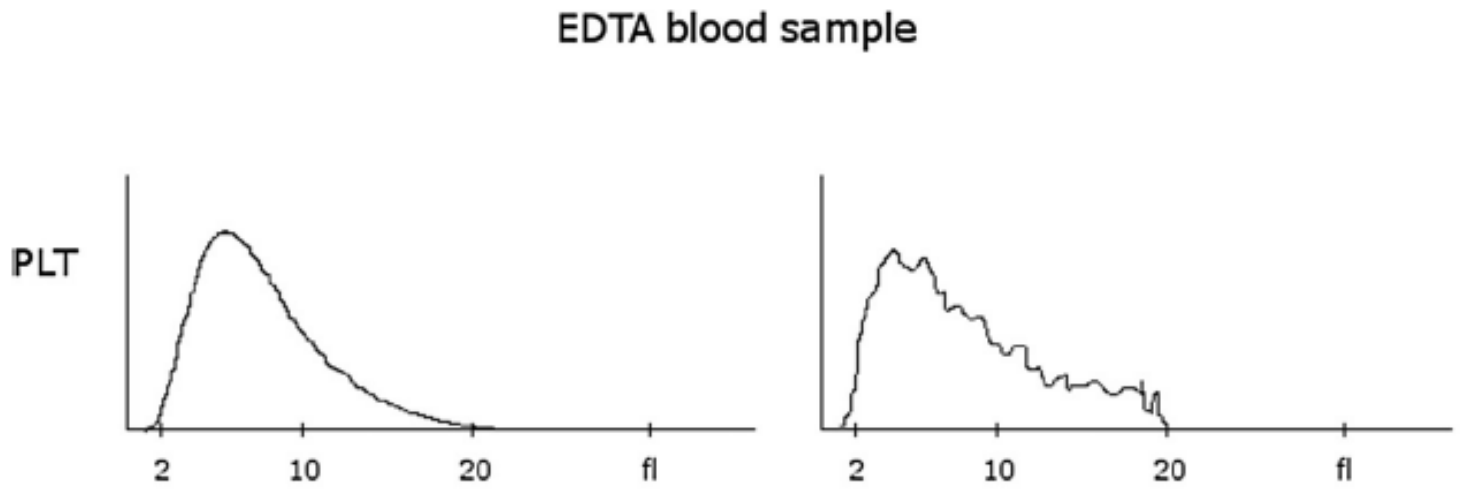


Asymptomatic thrombocytopenia

- 1st question: Real or pseudo ?
- 2nd question: Cause ?
- 3rd question: Urgent treatment needed ?

How can I recognize a pseudo-thrombocytopenia ?

- Review the platelet scattergram :



Normal

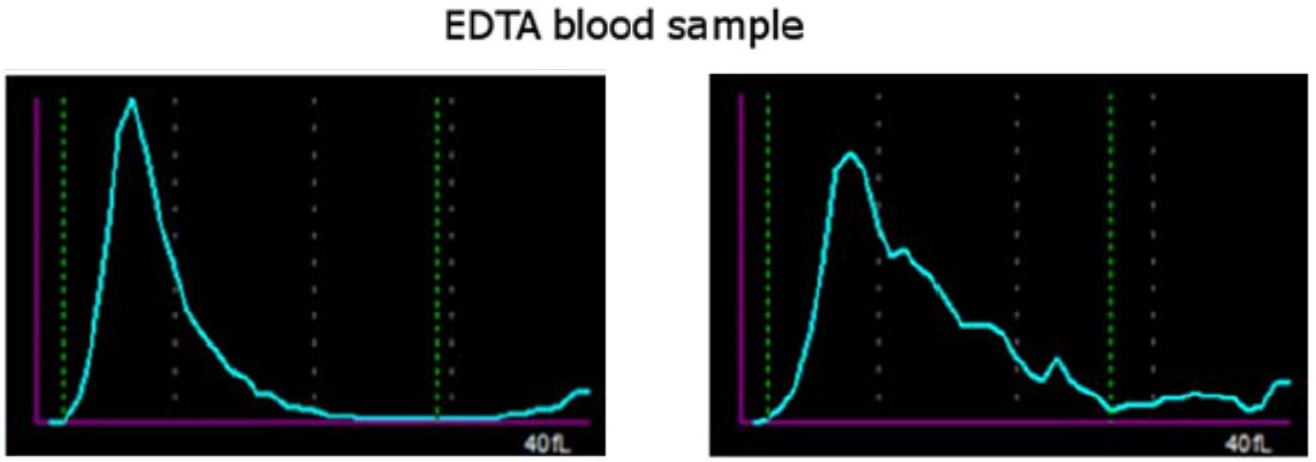
Abnormal

Legend:
PLT, platelets

BMC Clin Pathol 2014;14:19

How can I recognize a pseudo-thrombocytopenia ?

- Review the platelet scattergram :



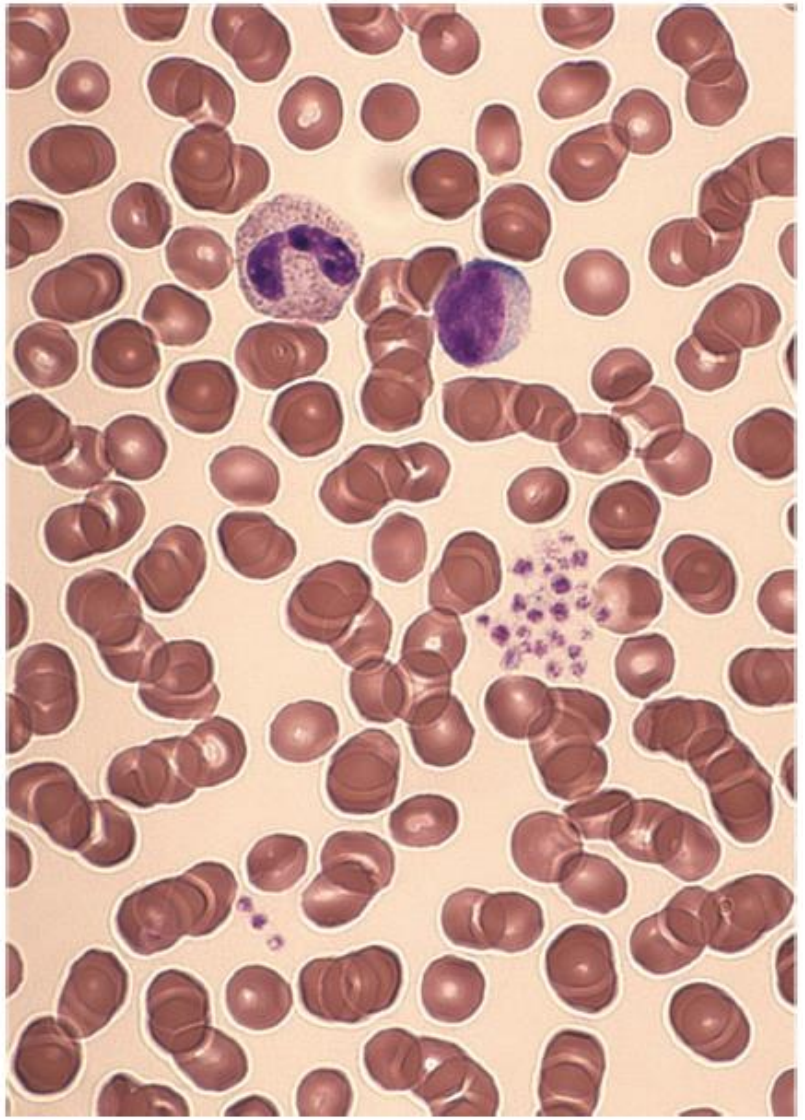
Normal

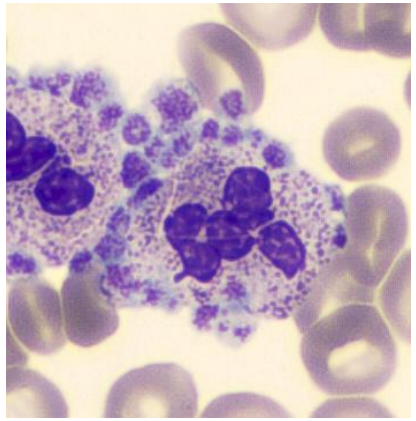
Abnormal

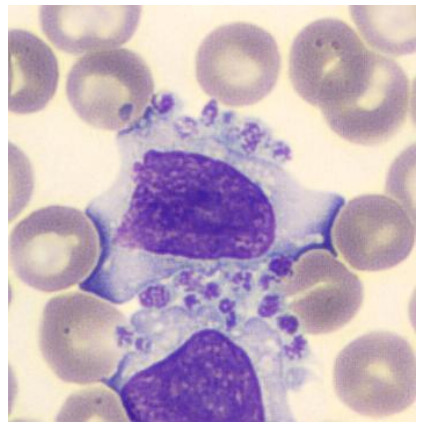
Am J Hematol 2018;93:1192

How can I confirm a pseudo-thrombocytopenia ?

- Review the blood film :





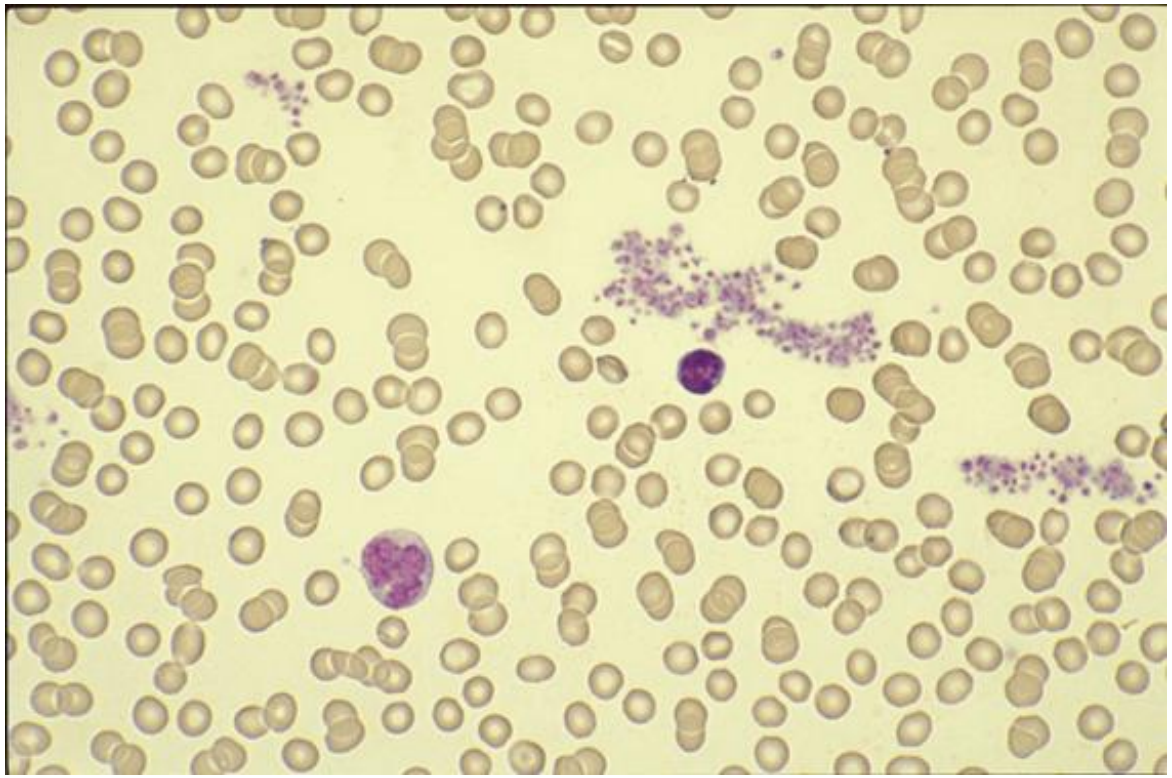


EDTA blood

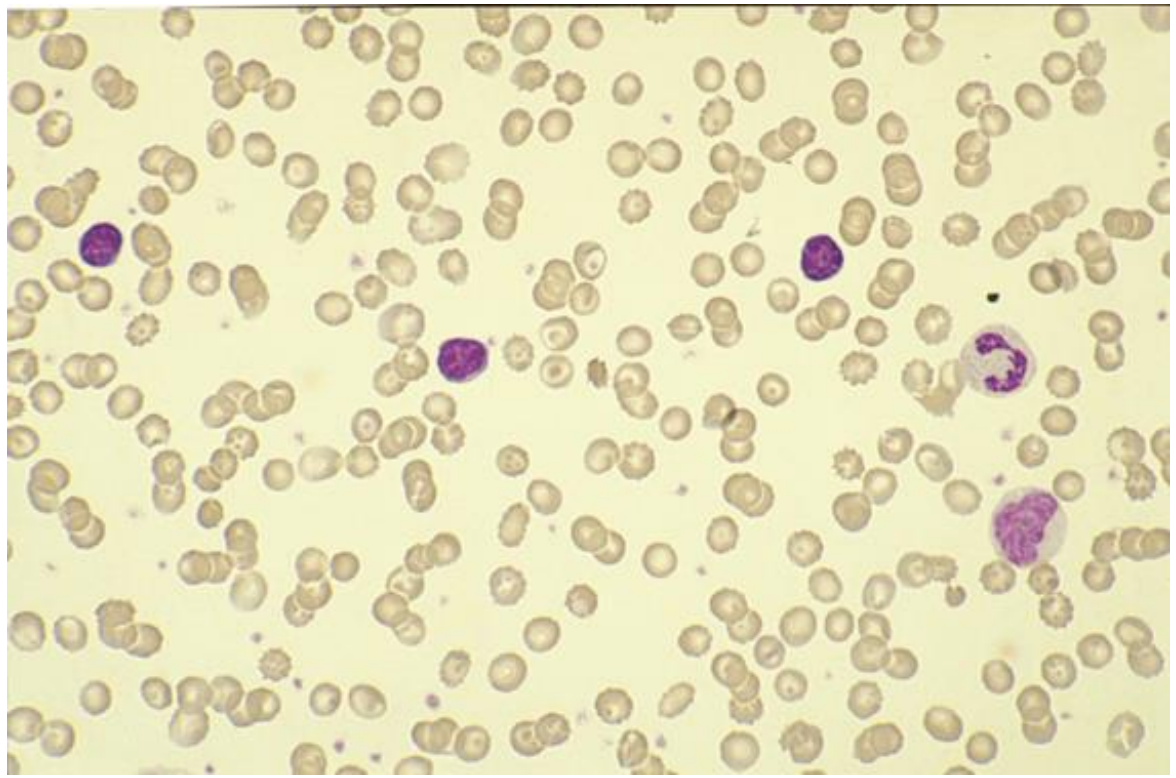
BMC Clin Pathol 2014;14:19

How can I measure the real platelet count ?

- Avoid EDTA



EDTA



Citrate or Magnesium (ThromboExact® tube)

BMC Clin Pathol 2014;14:19

Asymptomatic thrombocytopenia

- 2nd question: Cause ?

Asymptomatic thrombocytopenia

- History

questions to be asked	information
previous blood counts	pre-existing versus acquired thrombo-cytopenia
bleeding history	
family history of thrombo-cytopenia / bleeding	congenital thrombocytopenia (▶Tab. 5)
recurrent infections	syndromic thrombocytopenia (▶Tab. 5), CVID
cataracts, deafness, nephropathy	syndromic thrombocytopenia ▶(Tab. 5)

Legend:
CVID, common variable immunodeficiency

Hämostaseologie 2013;33:83

Asymptomatic thrombocytopenia

- History

questions to be asked	information
autoimmune disorders	acquired thrombocytopenia, CVID
previously diagnosed haematologic diseases	acquired thrombocytopenia
recent vaccination	
recent new drug / medications	
recent infection	
recent travel	
pregnancy	

Legend:
CVID, common variable immunodeficiency

Hämostaseologie 2013;33:83

Asymptomatic thrombocytopenia

- History

questions to be asked	information
dietary habits	alcohol?, quinine?, substrate deficiency?

Hämostaseologie 2013;33:83

Possible causes of (asymptomatic) thrombocytopenia

clinical scenario	most frequent aetiologies	consider
ambulatory patients	*DITP, *ITP	Infections, connective tissues disorders, hypersplenism, primary marrow disorders, *congenital thrombocytopenias, CVID
patients with thrombosis	*HIT, antiphospholipid syndrome	paroxysmal nocturnal haemoglobinuria
pregnant women	gestational thrombocytopenia, *ITP	HELLP, preeclampsia, TTP/HUS

Legend:
DITP, drug-induced thrombocytopenia
CVID, common variable immunodeficiency
HELLP, haemolysis, elevated liver (enzymes), low platelets
HIT, heparin-induced thrombocytopenia
HUS, haemolytic-uremic syndrome
ITP, immune thrombocytopenia
TTP, thrombotic thrombocytopenic purpura

Hämostaseologie 2013;33:83

Asymptomatic thrombocytopenia

- 3rd question: Urgent treatment needed ?

→ Heparin-induced thrombocytopenia

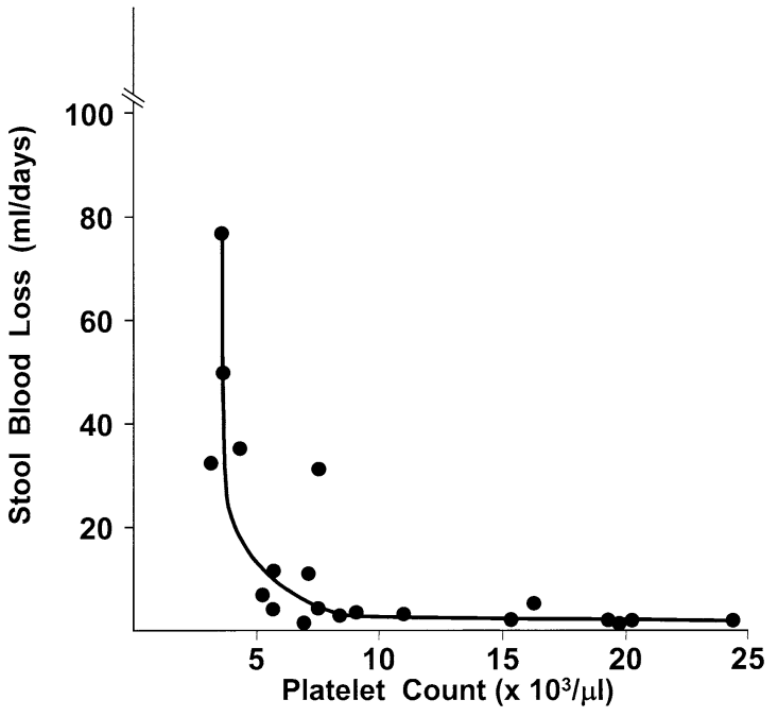
→ Remove identified cause, if possible

→ Treat underlying disease, if indicated

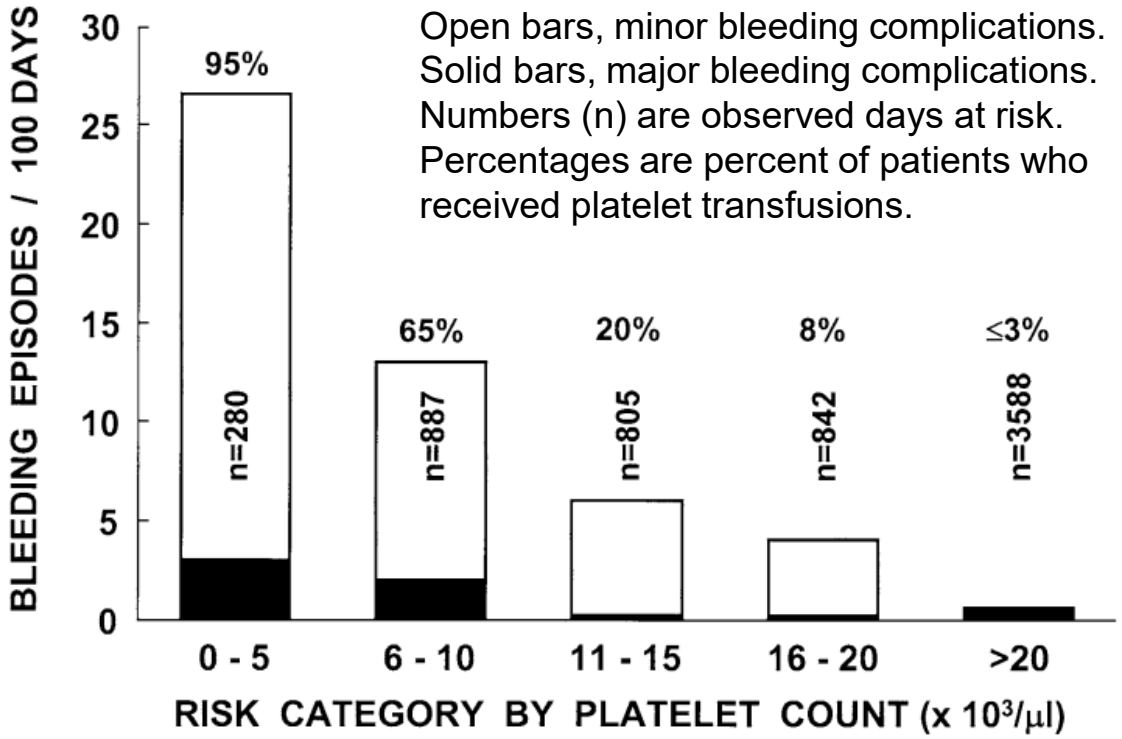
→ High bleeding risk

Hämostaseologie 2013;33:83

Thrombocytopenia and Bleeding risk



Fecal blood loss in thrombocytopenic patients.
When fecal blood loss (expressed as mL of blood/d) was determined in 20 aplastic thrombocytopenic patients, blood loss was <5 mL/d at platelet counts >10 x 10^9/L.



Open bars, minor bleeding complications.
Solid bars, major bleeding complications.
Numbers (n) are observed days at risk.
Percentages are percent of patients who received platelet transfusions.

In clinically stable patients, major bleeding is unusual unless the platelet count is <10 x 10^9/L.

Transfus Med Rev 2004;18:153

Symptomatic thrombocytopenia

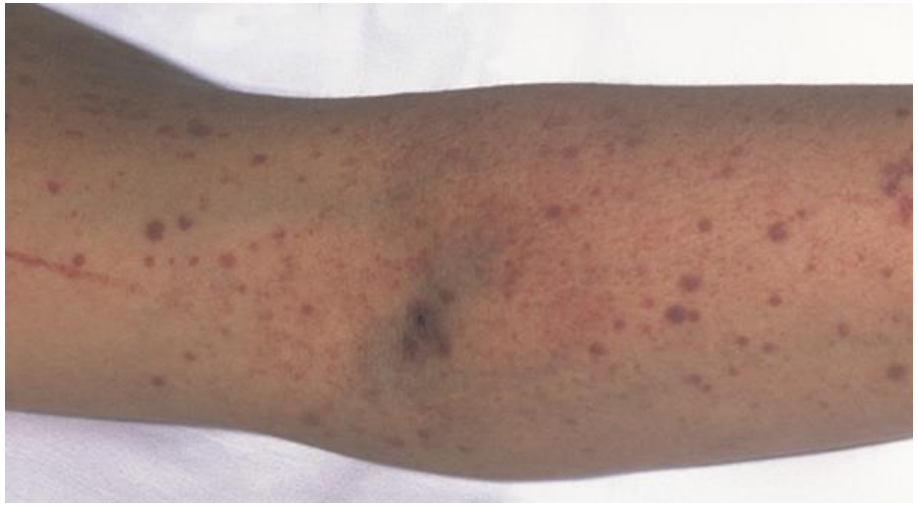
La storia di *Domenica*

41-year-old woman

La storia di *Domenica*

History:	1 week before hospitalization	dark urine
	3 days before hospitalization	petchiae (perimalleolar)
		abdominal pain
	2 days before hospitalization	nausea
		frontal haedache
	Reason for hospitalization	bicytopenia (Hb, Tc)
		suspected pancreatic mass

Status: general conditions: decreased
abdomen: epigastric sensitivity, no defence or relaxation
derma: petechiae on the limbs



La storia di *Domenica*

Laboratory:

Hb	63	g/l	(117 – 157)
Hct	18	%	(35 – 47)
MCV	87	fl	(81 – 99)
MCH	31	pg	(27 – 34)
MCHC	350	g/l	(310 – 350)

Tc	13	G/l	(150 – 350)

Severe thrombocytopenia

Reflex:
Blood film ?
(microscope)

Lc	13.2	G/l	(4.0 – 10.0)
- neutrophiles	10.1	G/l	(1.8 – 7.5)
- lymphocytes	2.4	G/l	(1.5 – 4.0)
- monocytes	0.7	G/l	(0.2 – 0.8)
- eosinophiles	0.0	G/l	(0.05 – 0.3)
- basophiles	0.0	G/l	(0.01 – 0.05)

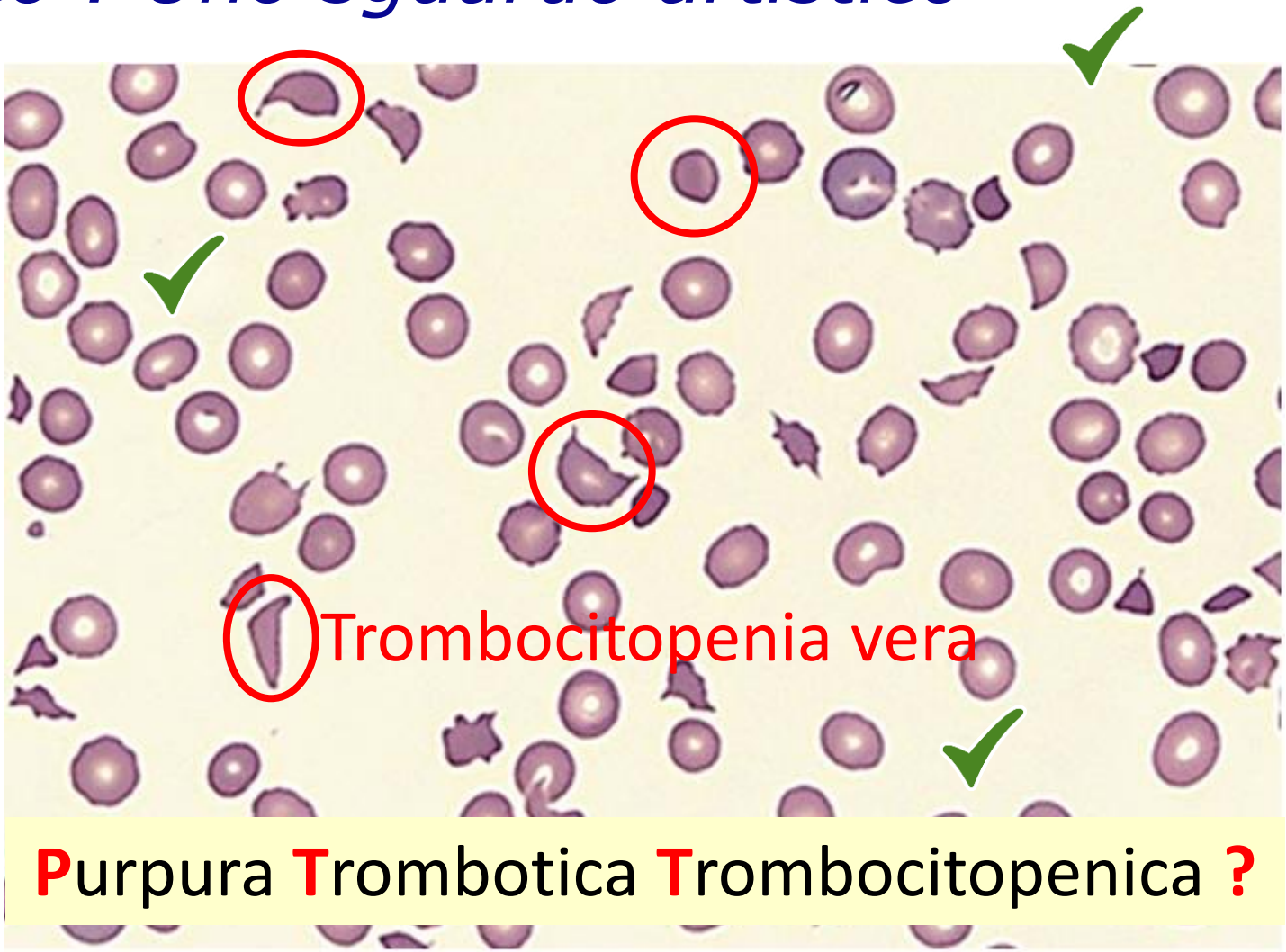
Slight neutrocytosis

DD: normocytic normochromic anaemia

Production ?	Reticulocytes : 133 G/l	hyperregenerative
Destruction ?	LDH : 1031 U/l	haemolytic
Immune ?	DAT : negative !	non-immune
Mechanic ?	Blood film ? (microscope)	

Legend:
DAT, direct antiglobulin test (= Coombs-test) ; LDH, lactate dehydrogenase

Lo striscio ematico : Uno sguardo artistico



Purpura **T**rombotica **T**rombocitopenica **?**

Questa è un'urgenza ematologica

Int J Lab Hematol 2012;34:107

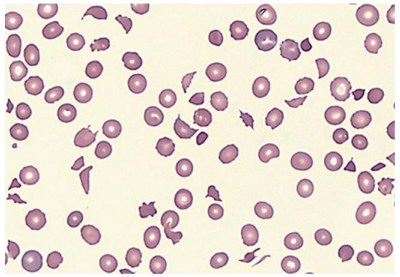
La storia di *Domenica*

Production ?	Reticulocytes: 133 G/l	hyperregenerative
Destruction ?	LDH : 1031 U/l	haemolytic
Immune ?	DAT: negative !	non-immune
Mechanic ?	Fragmentocytes: 9 °/oo	mechanic RBC destruction

Thrombotic Micro-Angiopathy

Legend:
DAT, direct antiglobulin test (= Coombs-test) ; LDH, lactate dehydrogenase ; RBC, red blood cells

Pragmatic approach to TMA treatment



Diagnosis of TMA:

- Low Platelet Count and DAT-negative Anemia
- Increased serum LDH
- Fragmented erythrocytes in the peripheral smear

Draw blood before Plasma Exchange!

TTP mortality:
- 80% without PEX
- 10-20% with PEX

Consider caplacizumab and rituximab

Legend
DAT, direct anti-globulin (Coombs) test
PEX, plasma exchange
TMA, thrombotic microangiopathy
TTP, thrombotic thrombocytopenic purpura

Semin Immunopathol 2014;36:399

Thrombocytopenia + Fragmented RBC

Thrombotic Micro-Angiopathy (TTP)

Legend:
RBC, red blood cells; TTP, thrombotic thrombocytopenic purpura

Alcuni « campanelli d'allarme » ematologici

- *Tommaso: Purpura amiloide secondaria a mieloma multiplo*
  Ematomi periorbitali spontanei → Catene leggere ?

- *Falco: Emofilia acquisita*
  Nuova tendenza a sanguinare → aPTT ? Mix !

- *Giorgio: Leucemia promielocitica*
  Pancitopenia → DIC ?

- *Domenica: Purpura trombotica trombocitopenica*
  Anemia emolitica + trombocitopenia → DAT, frammentociti ?

Legend:
DAT, direct antiglobulin test (= Coombs-test) ; DIC, disseminated intravascular coagulation

Come prevenire il rischio emorragico

Check ALL medications

Table 5. Medications That Cause Bleeding and Bruising

Rare

- Cephalosporins
- Ginkgo biloba
- Gold
- Interferon
- Metaxalone (Skelaxin)
- Penicillins
- Propothiouricil
- Selective serotonin reuptake inhibitors
- Testosterone replacement
- Tricyclic antidepressants

Haghbin H et al.

Risk of **Gastrointestinal** Bleeding with Concurrent Use of NSAID **and** SSRI : A Systematic Review and Network Meta-Analysis.

Dig Dis Sci. 2023;68:1975

Legend:
NSAID, non-steroidal anti-inflammatory drugs

Am Fam Physician 2008;77:1117

Check ALL medications

Table 4. Approximation of overall bleeding risk for each supplement, based on evidence for each

Bleeding risk*	Supplement
High (4)	Garlic; hawthorn; ginkgo biloba; chondroitin-glucosamine
Moderate (25)	a. Cordyceps sinensis; echinacea; aloe vera b. Melatonin; turmeric; bilberry; chamomile; fenugreek; milk thistle; peppermint; cinnamon c. Flaxseed; grape seed extract d. Ashwagandha; black pepper; dandelion; evening primrose; feverfew; honey; lavender; lion's mane e. St. John's wort; ginger; cranberry; spirulina
Low (15)	a. Acidophilus; apple cider vinegar; beet; elderberry; goldenseal; horny goat weed; tea tree oil; valerian b. Black cohosh; chlorella vulgaris; green tea; menthol; propolis; red yeast rice; isoflavones
None (3)	Fish oil; ginseng; saw palmetto

Proc (Bayl Univ Med Cent) 2022;35:802

Check ALL medications

Table 5. Medications That Cause Bleeding and Bruising

Common

Aspirin

Clopidogrel (Plavix)

Heparin

Nonsteroidal anti-inflammatory drugs

Warfarin (Coumadin)

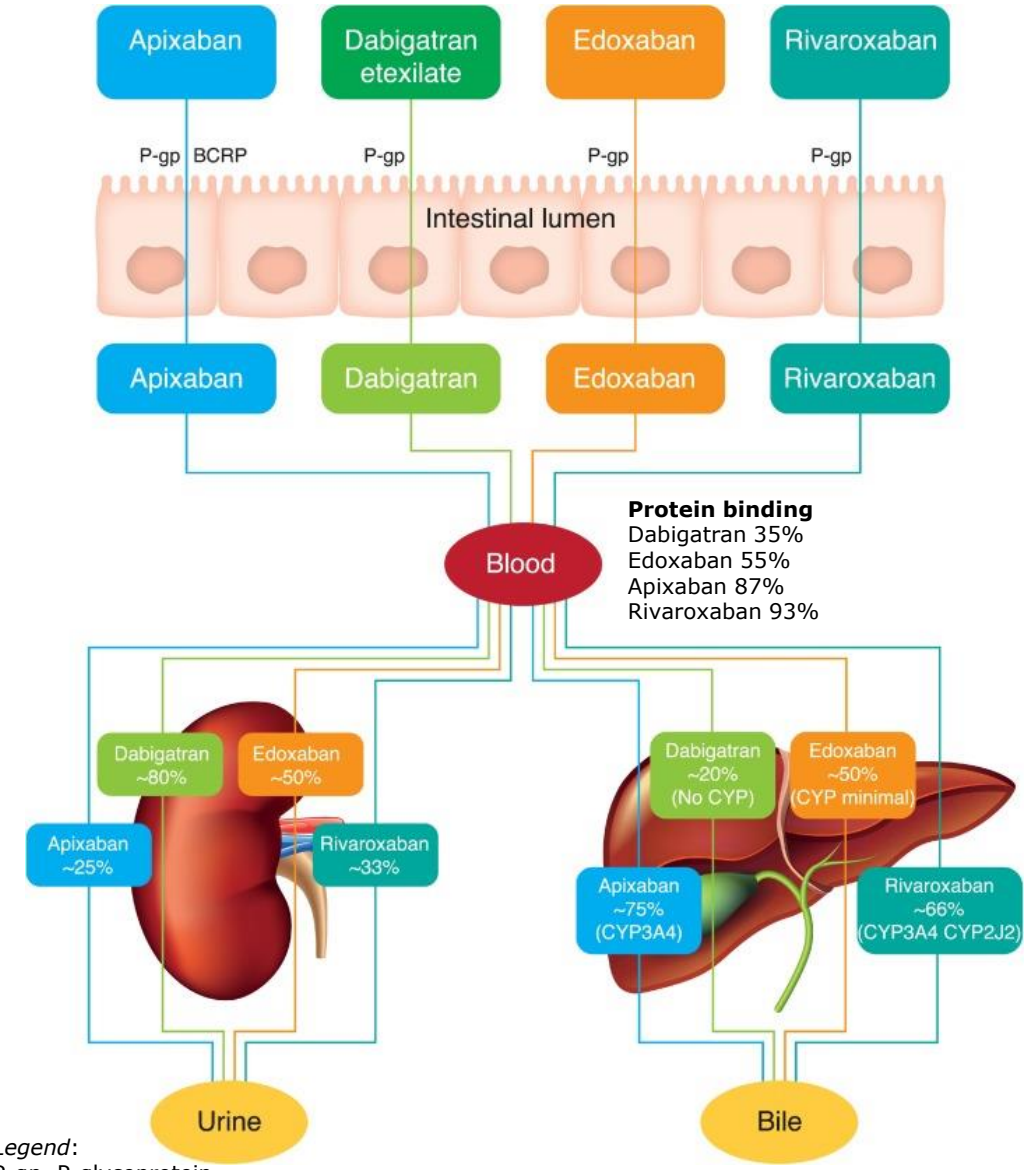
Direct Oral Anticoagulants

Am Fam Physician 2008;77:1117

DOAC in elderly patients

Hämostaseologie 2020;40:292

DOAC in elderly patients



Legend:
P-gp, P-glycoprotein
CYP, cytochrome P450
BCRP, breast cancer resistance protein

Crit Rev Oncol Hematol 2018;132:169

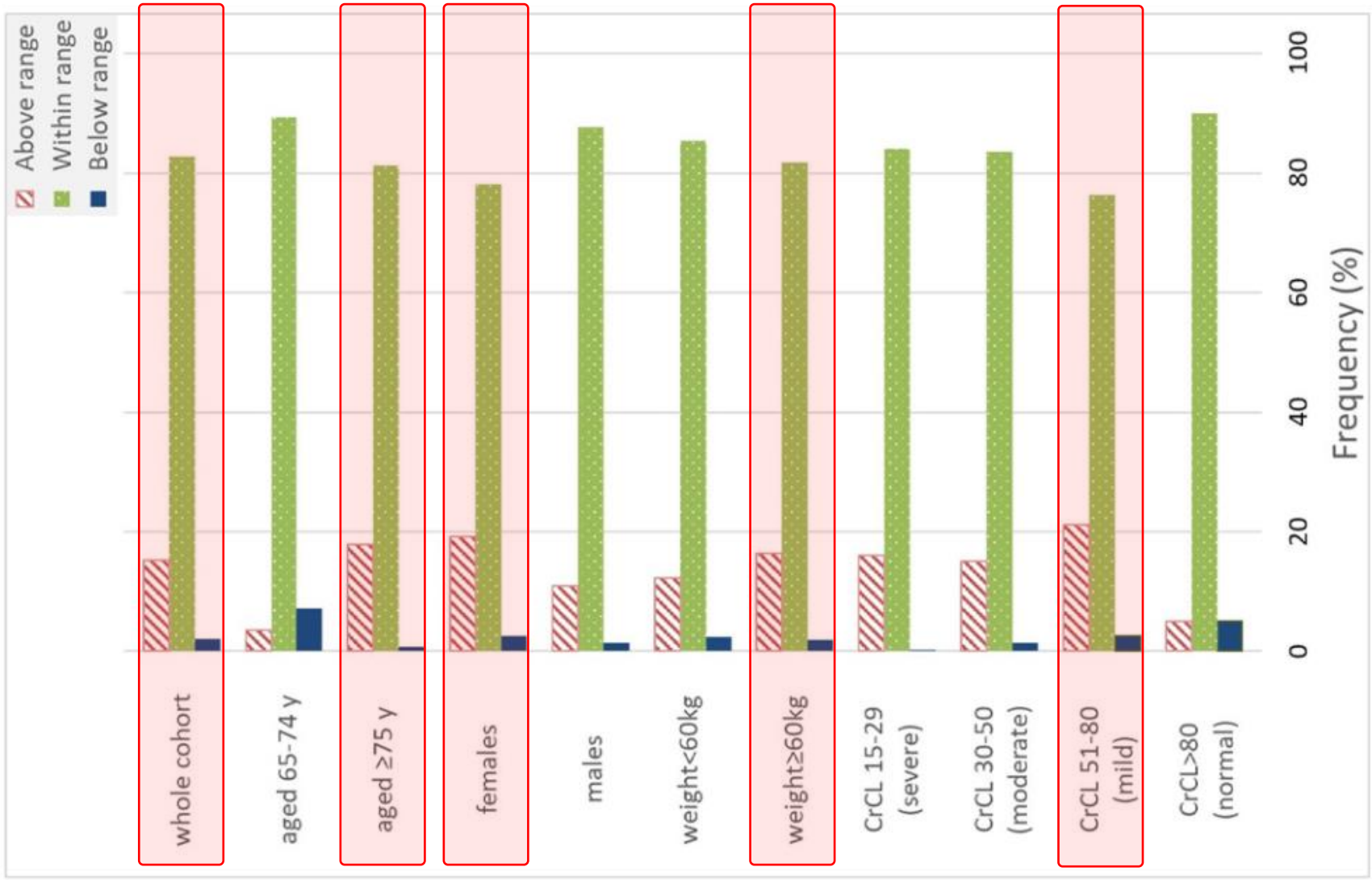
Alteration in organ physiology related to aging	
Physiological changes	**Pharmacokinetic and pharmacodynamic changes**
↑ Gastric pH	Might affect absorption
↓ Gastric emptying	Different bioavailability/solubility of pH-sensitive drugs
Decreased blood flow in organs	
↓ Renal blood flow, ↓ Glomerular filtration rate	Impaired elimination
↓ Liver blood flow	↓ First-pass metabolism
↓ Splanchnic blood flow	
Changes in tissue and body composition	
Changes in renal tissue histology	Impaired elimination
Alterations in liver architecture, ↓ Hepatocyte functional mass	Phase I enzymes affected
↓ Body water, ↓ lean body mass	↑ Plasma concentration of hydrophilic drugs
↑ Body fat	↑ Half-life of lipophilic drugs
↓ Serum albumin	↑ Free fraction in plasma of highly protein-bound acidic drugs

Pol Arch Intern Med 2023;133:16508

DOAC in elderly patients

Are
(very) elderly patients
at risk for
DOAC accumulation ?

DOAC in elderly patients



151 medically stable hospital inpatients
- 76 on apixaban,
- 61 on rivaroxaban,
- 14 on dabigatran,

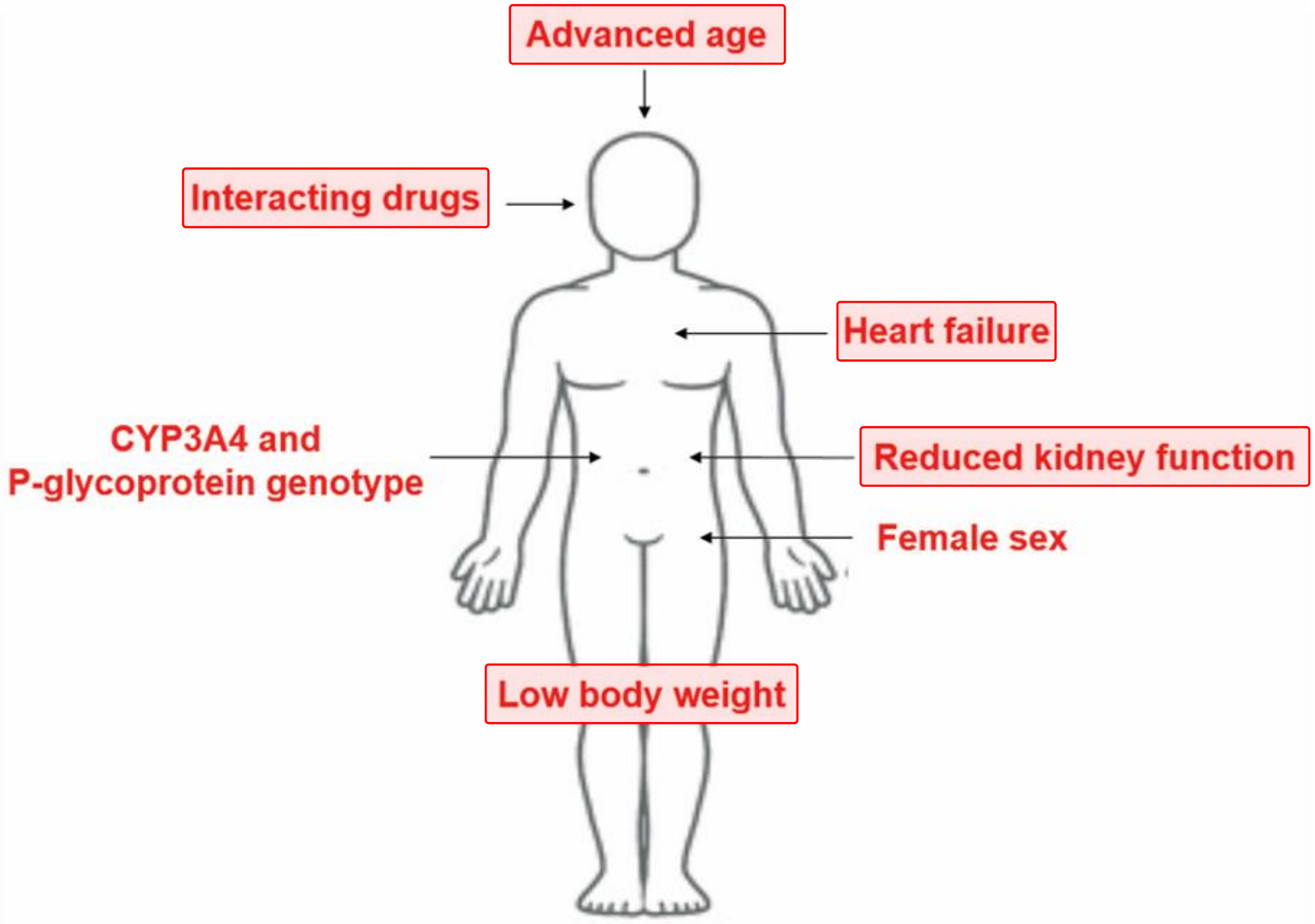
with a median age of 84 years (IQR: 78–89).

There was up to **48-fold** and *13-fold* variation in **trough** and *peak* plasma drug concentrations, respectively.

Br J Haematol 2021;195:790

Frequency of patients with **trough plasma** DOAC concentration below, within and above reported ranges according to *age*, *sex*, *weight,* and *creatinine clearance*.

Independent determinants of DOAC levels



Thromb Haemost 2023;123:377

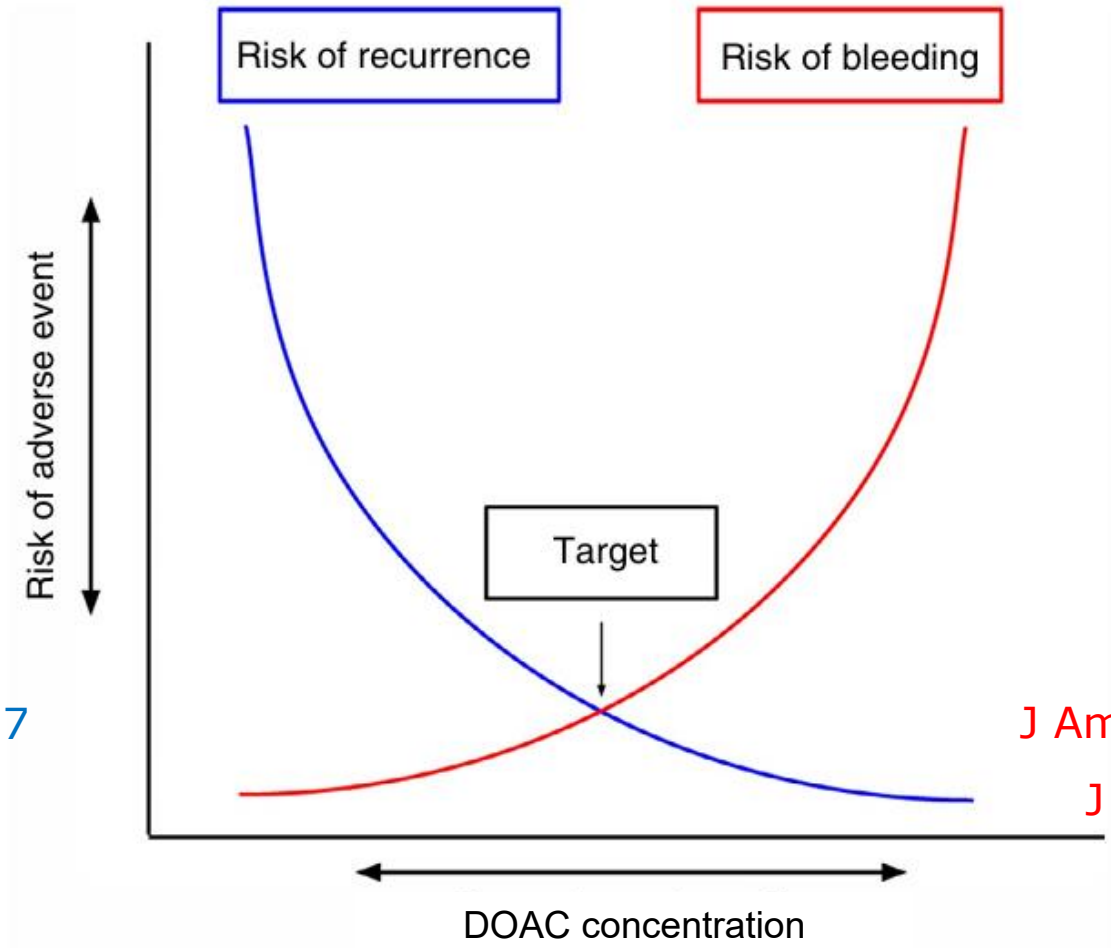
DOAC levels and adverse effects

Int J Cardiol 2024;416:132484

Blood Adv 2024;8:1846

Eur J Clin Pharmacol 2022;78:557

J Thromb Haemost 2018;16:842



Int J Cardiol 2024;416:132484

Blood Adv 2024;8:4913

J Am Heart Assoc. 2023;12:e029865

J Thromb Haemost 2019;17:1064

Hämostaseologie 2020;40:184 | JAMA Cardiology 2017;2:566 | J Thromb Haemost 2020;18:3163

DOAC monitoring ?

PharmacoKinetics

The effect the organism has
on the drug

PharmacoDynamics

The action the drug has
on the organism

Drug monitoring

PK	**PD**
Drug concentration	Drug efficacy

Legend:
PD, pharmacodynamics; PK, pharmacokinetics

DOAC monitoring

PK

Drug concentration

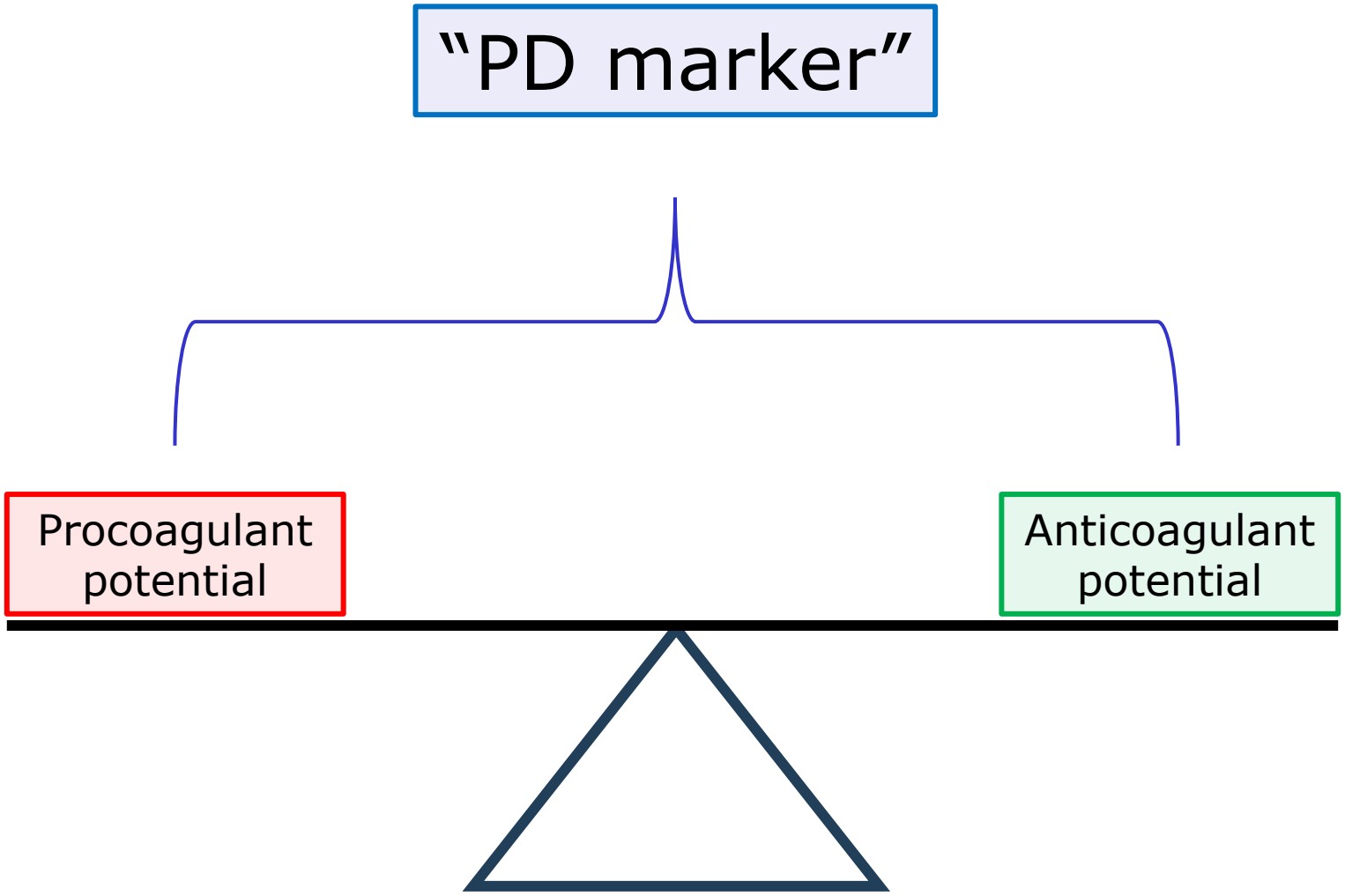
"Anti-Xa-activity" = [DOAC]

PD

Anticoagulant efficacy

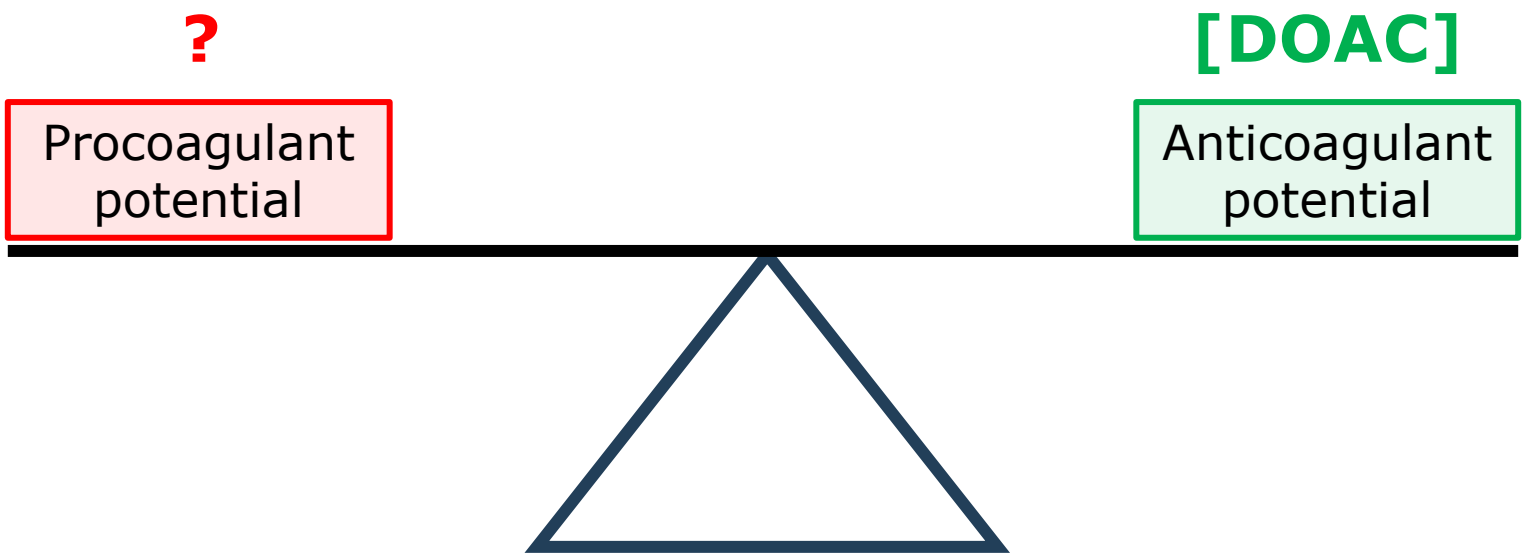
Legend:
PD, pharmacodynamics; PK, pharmacokinetics; [ ], concentration

Anticoagulant efficacy



Legend:
PD, pharmacodynamics

PD : Anticoagulant efficacy

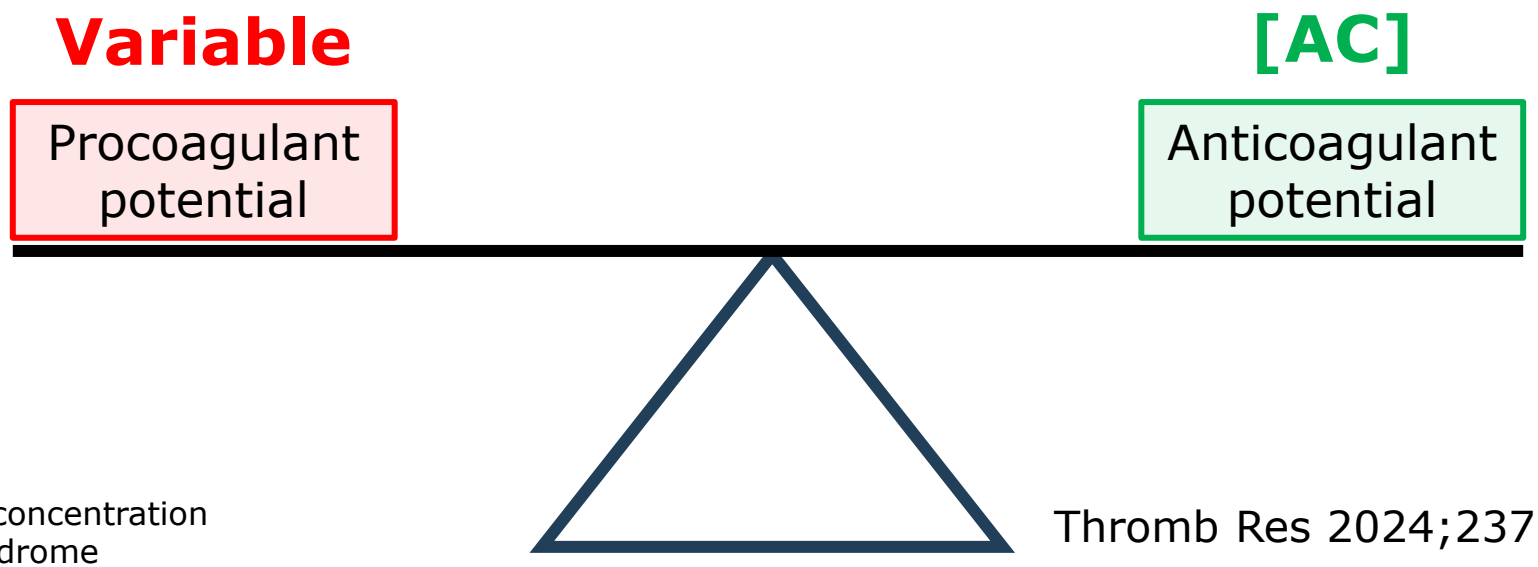


Legend:
[ ], concentration

PD : Anticoagulant efficacy

The anticoagulant efficacy of a given drug concentration varies according to the individual procoagulant potential:

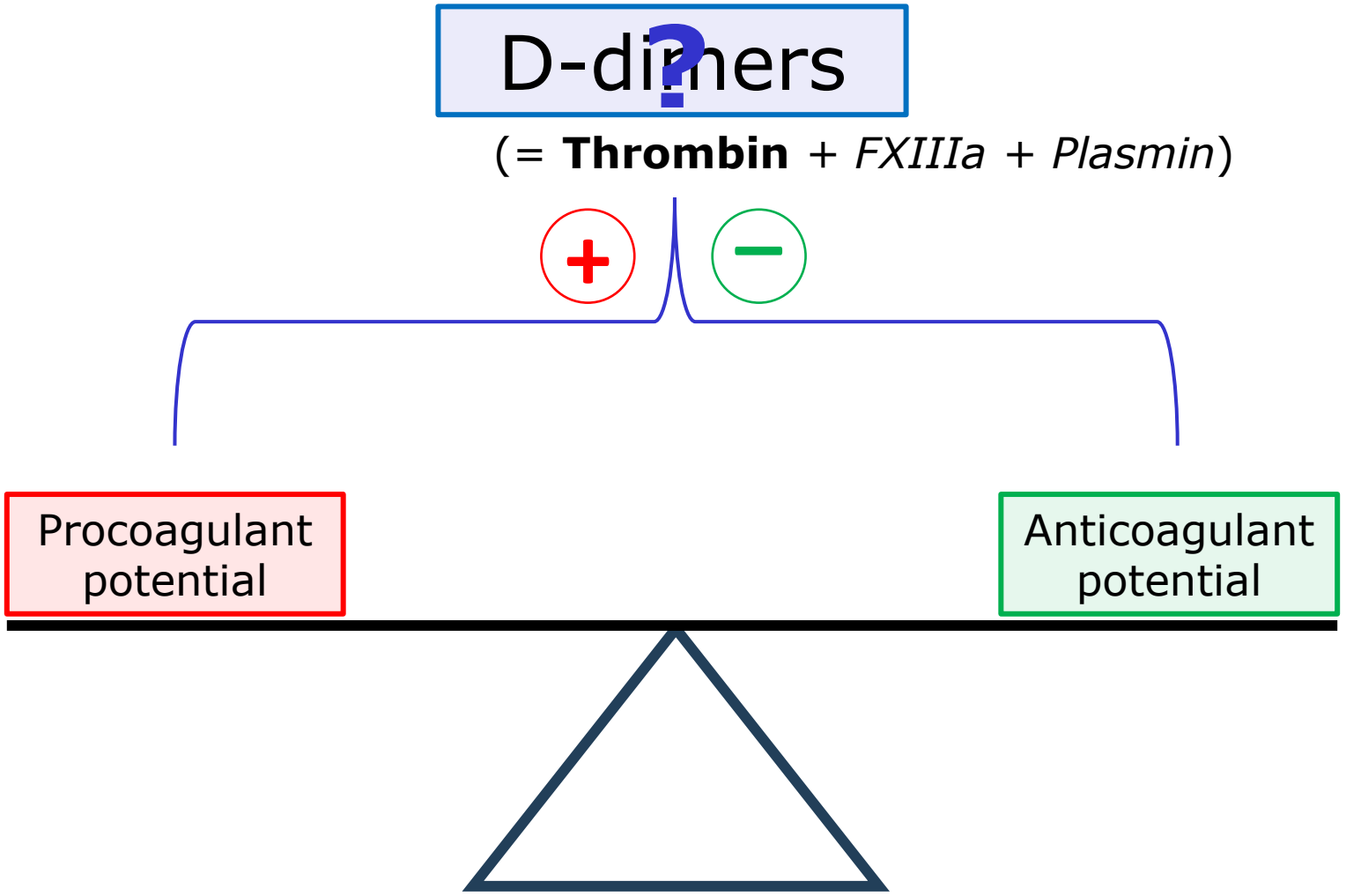
- AVK in **cancer** (Blood 2002;100:3484)
- DOAC in **triple positive APS** (Blood 2018;132:1365)
- DOAC in **advanced cirrhosis** (J Thromb Haemost 2025;23:1938)



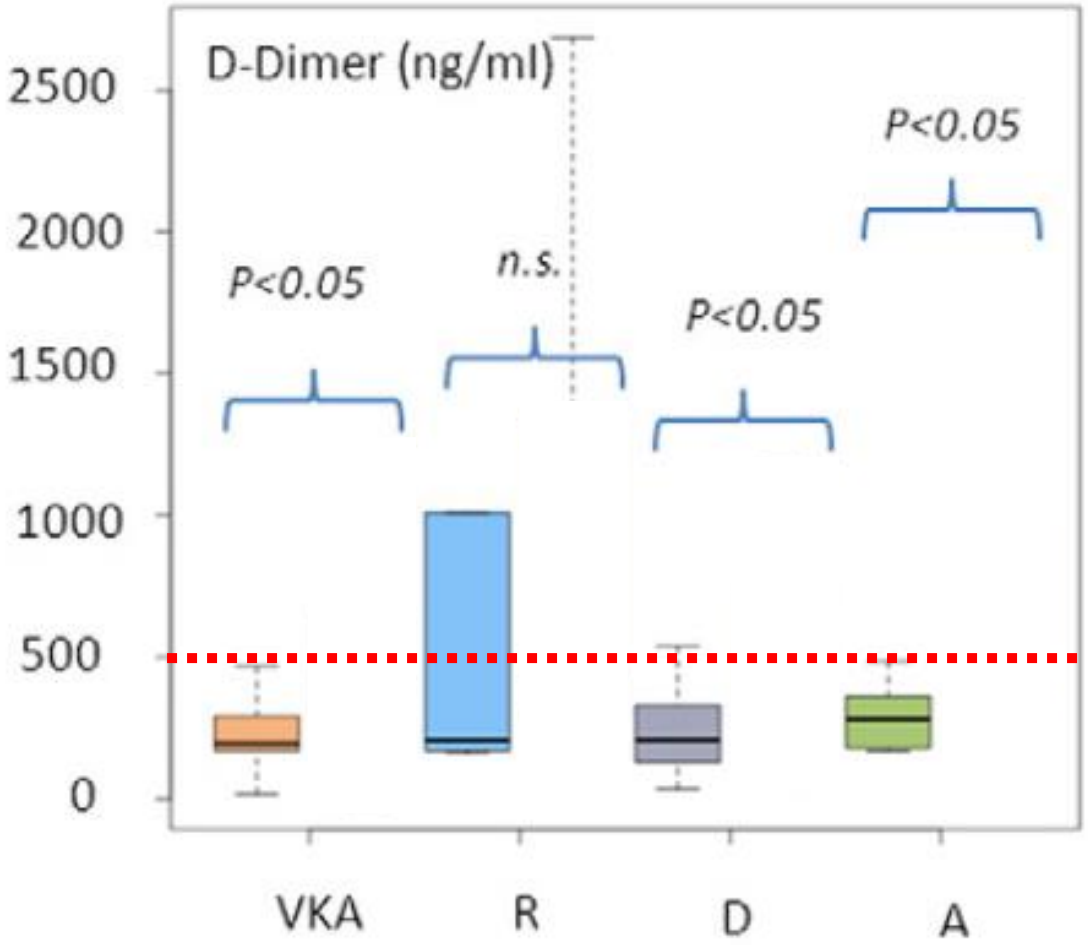
Legend
[AC], anticoagulant drug concentration
APS, antiphospholipid syndrome

Thromb Res 2024;237:34

PD : Anticoagulant efficacy



The effect of anticoagulation on D-dimers



Values at baseline and 4 weeks post treatment

Legend
A, Apixaban (n=37)
D, Dabigatran (n=17)
R, Rivaroxaban (n=9)
VKA, Vitamin K antagonists (n=184)

Thromb Res 2015;136:261

D-dimers in anticoagulated patients

Table 1. Median (IQR) D-dimer levels for patients on VKAs compared with those on DOACs

	D-dimer (µg/L)				
Drugs	**VKAs (n = 33)**	**Apixaban (n = 37)**	**Rivaroxaban (n = 34)**	**Dabigatran (n = 30)**	**Edoxaban (n = 30)**
Trough		219 (174-385)†	290 (163-383)††	201 (98-322)	220 (158-449)†
Peak		225 (158-343)*,†	263 (200-430)††	169 (140-296)	201 (152-445)*,†
VKAs	149 (117-270)				

Blood samples were collected in 1:10 volume of trisodium citrate, centrifuged for 20 minutes at 3000*g* and plasma aliquoted in capped plastic tubes, immediately frozen and stored at −70°C for later testing that was performed within 6 months. To limit methodological variability, the same number of plasma samples from patients on different types of anticoagulants was included in each session. D-dimer was measured with HSD-dimer on ACLTOP (Werfen Bedford, MA).

IQR, interquartile range.

*$P < .05$, trough-vs-peak (paired data [Wilcoxon].

†$P < .05$.

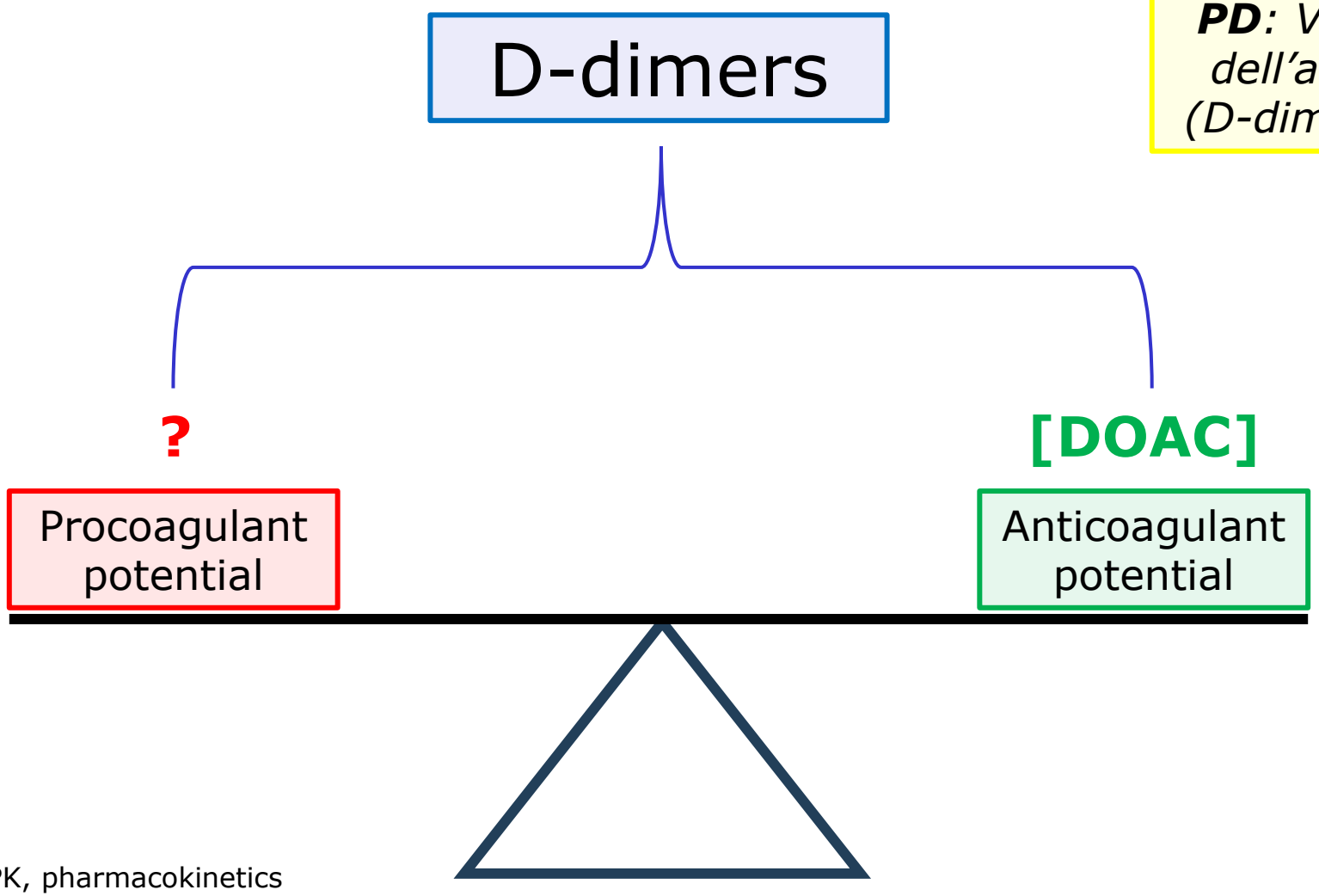
††$P < .01$, trough or peak-vs-VKAs [unpaired data, Mann-Whitney]).

Blood Adv 2024;8:3612

Note

Patients on VKA or DOAC, treated for a first VTE (80%) or atrial fibrillation.

DOAC monitoring



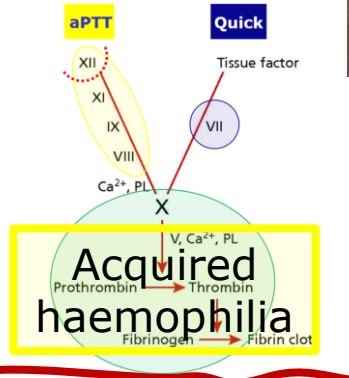
***PD**: Verifica l'efficacia dell'anticoagulazione (D-dimeri <500 ng/ml)*

***PK**: Verifica l'assenza di un accumulo*

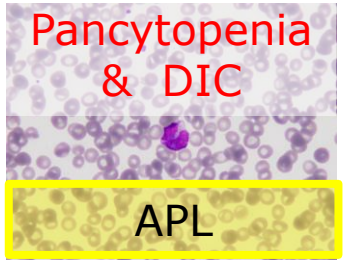
Legend:
PD, pharmacodynamics; PK, pharmacokinetics

Synthesis

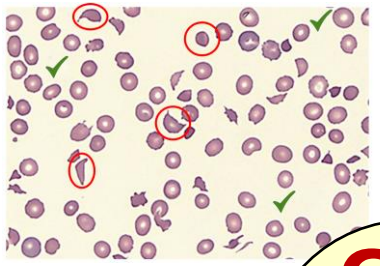
Isolated prolonged aPTT



Acquired haemophilia

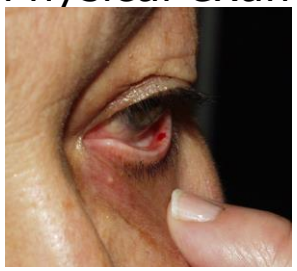


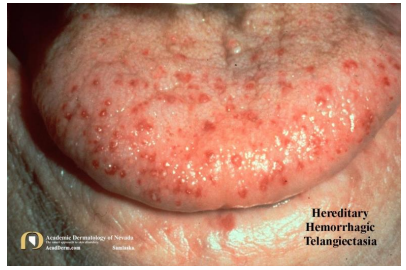
DAT-negative anaemia and thrombocytopenia

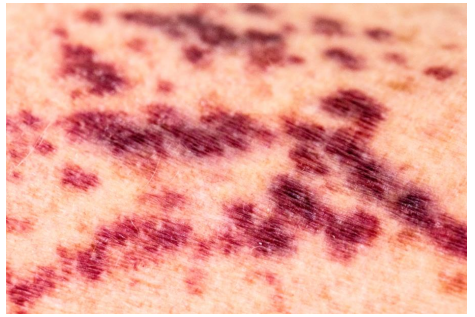


TTP

- History (structured & semi-quantitative)
- Physical examination



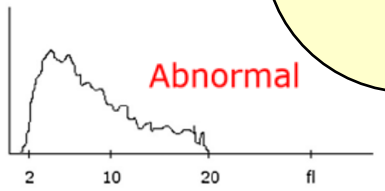




Lab: CBC & differential
basic coagulation tests
renal & liver functions

Gra zie !

- 1st question: Real or pseudo ?
  - → PLT scattergram

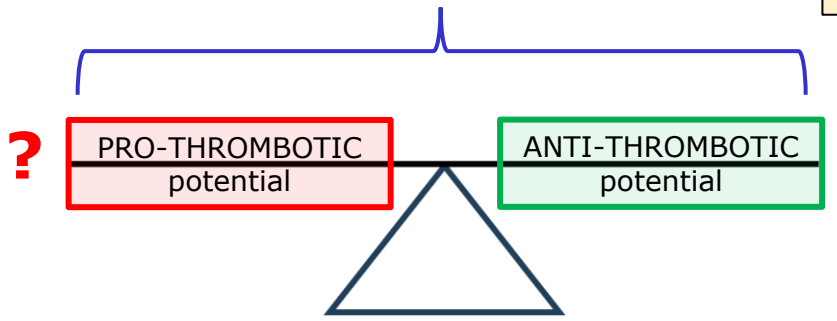


- 2nd question: Cause ?
  - → History
  - → Clinical context
- 3rd question: Urgent treatment needed ?
  - → HIT
  - → Underlying cause / disease
  - → High bleeding risk (Tc <10-20 G/l)

Thrombocytopenia

Primary haemostasis : ▪▪▪

→ Coagulation : D-dimers



AVOID
concurrent use
of
NSAID **and** SSRI

Herbal remedies
Drug interactions
[Drug]
[DOAC]

Legenda: APL, acute promyelocytic leukaemia; CBC, complete blood count; DAT, direct antiglobulin test; DOAC, direct anticoagulant drugs; HIT, heparin-induced thrombocytopenia; NSAID, non-steroidal anti-inflammatory drugs; PLT, platelets; SSRI, selective serotonin-reuptake inhibitors; TTP, thrombotic thrombocytopenic purpura