Introduction to Bleeding Disorders

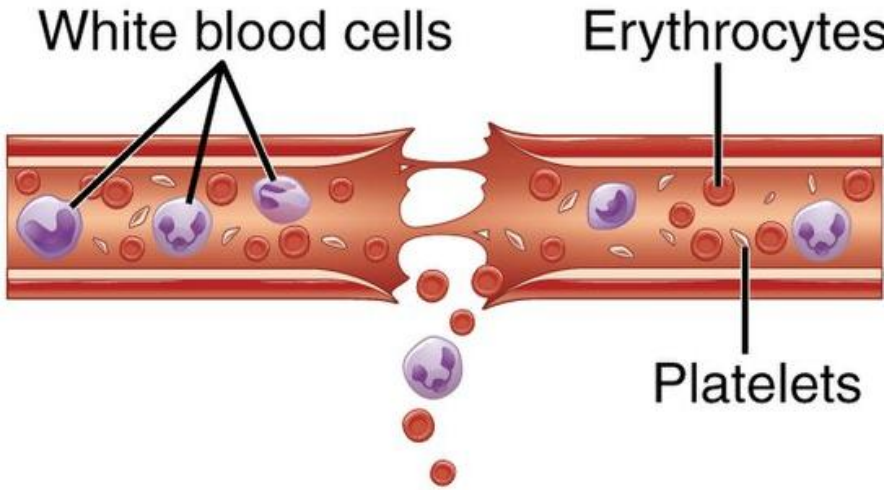
- **Is it a bleeding disorder?**
- **Which step failed?**
- **Born with it, or acquired?**
- **What the first panel says**

Husain Alkhaldy

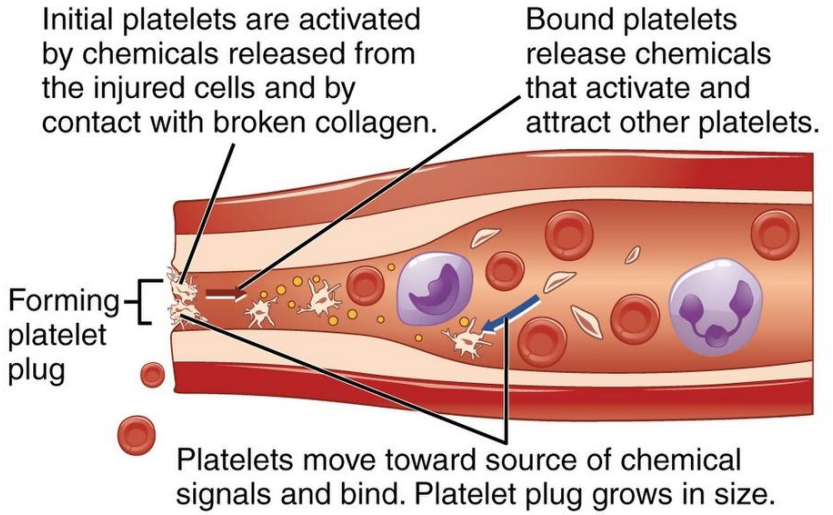
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These slides are an outline only. Read them with the handbook (chapters 20 to 25), the casebook (Case 53) and the question bank.

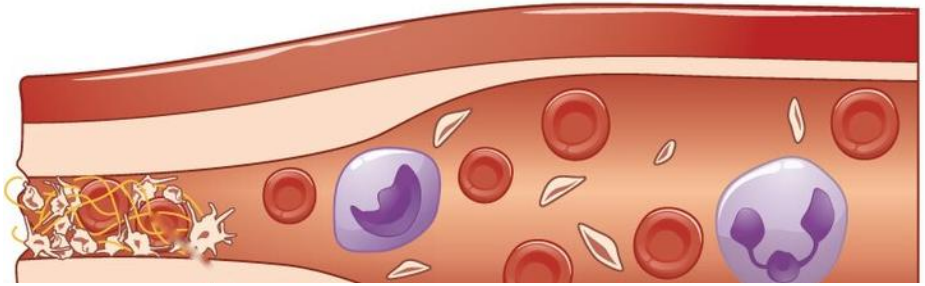
Hemostasis: from injury to clot



1. Injury: the vessel breaks, and its wall constricts to slow the loss



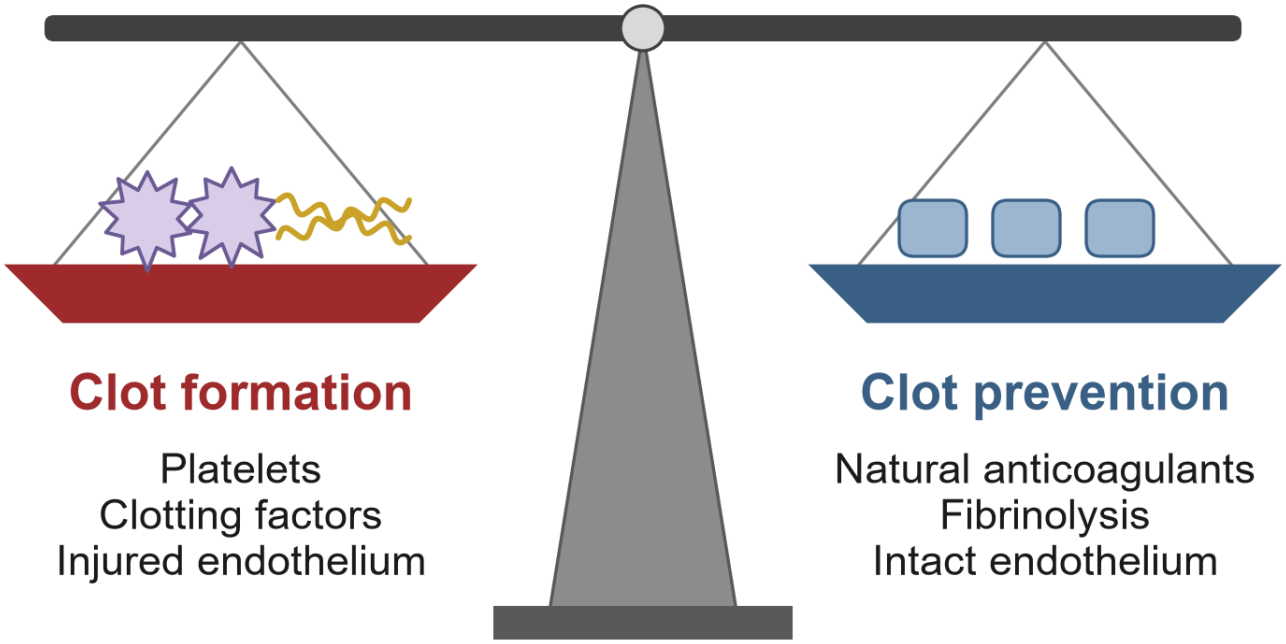
2. Platelet plug: platelets stick at the break and call in more



3. Fibrin clot: fibrin strands bind the plug

OpenStax, Anatomy & Physiology, fig. “1909 Blood Clotting”, CC BY 3.0, via Wikimedia Commons (cropped; leader lines removed from the fibrin-clot panel)

Hemostasis: a balance

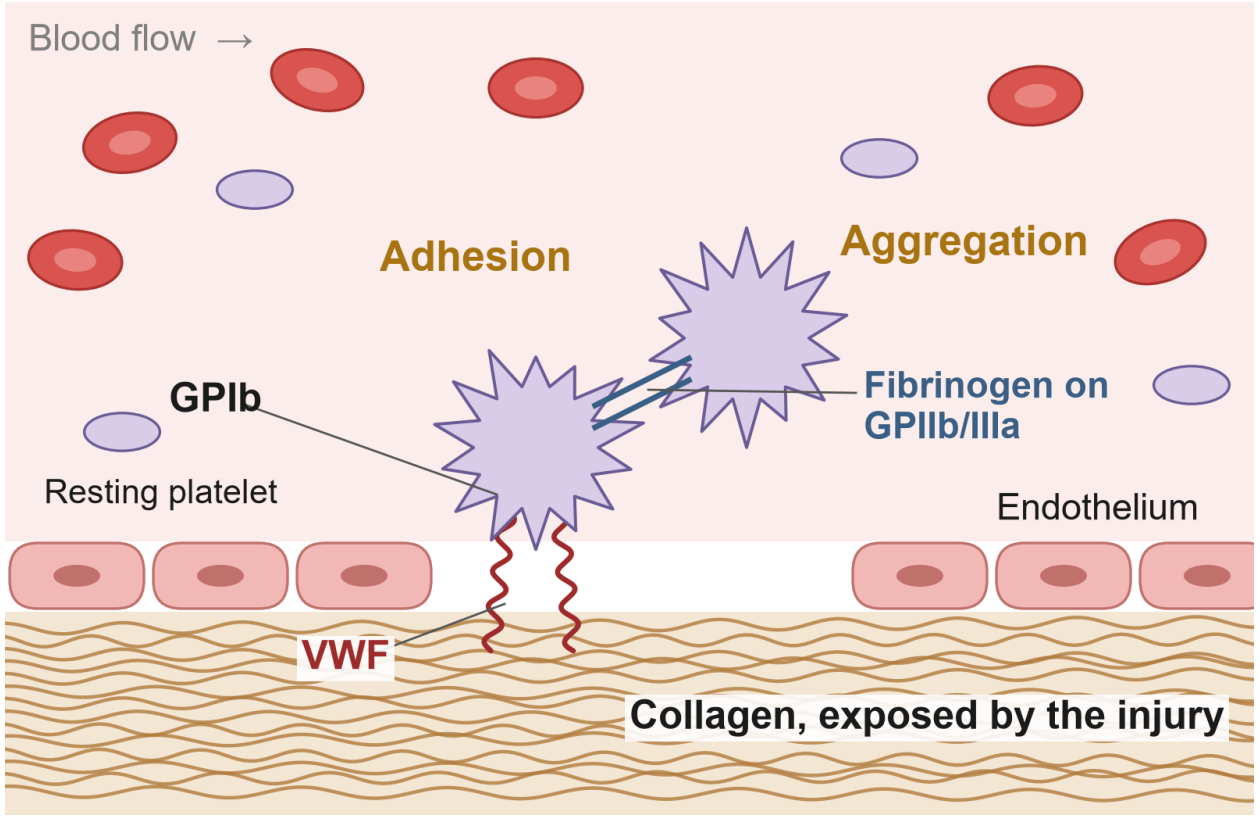


- Bleeding tendency: the balance tips toward prevention
  - Hemophilia is one example. Low platelets, VWD and warfarin are others
- Thrombosis tendency: it tips toward formation (handbook ch 26)
- The endothelium sits on both sides: intact, it prevents clots; injured, it starts them

Four verbs: START, MAKE, STOP, CLEAN

Verb	What happens	Test	Fails in
STOP	At rest, the brakes keep blood liquid		
START	Platelet plug, within seconds	Count, film	ITP, VWD, aspirin
MAKE	Fibrin clot on the plug	PT, aPTT, fibrinogen	Hemophilia, warfarin, liver disease
STOP	The brakes keep the clot at the injury		Too little brake: thrombosis
CLEAN	Plasmin dissolves the clot	D-dimer	Too much: bleeding

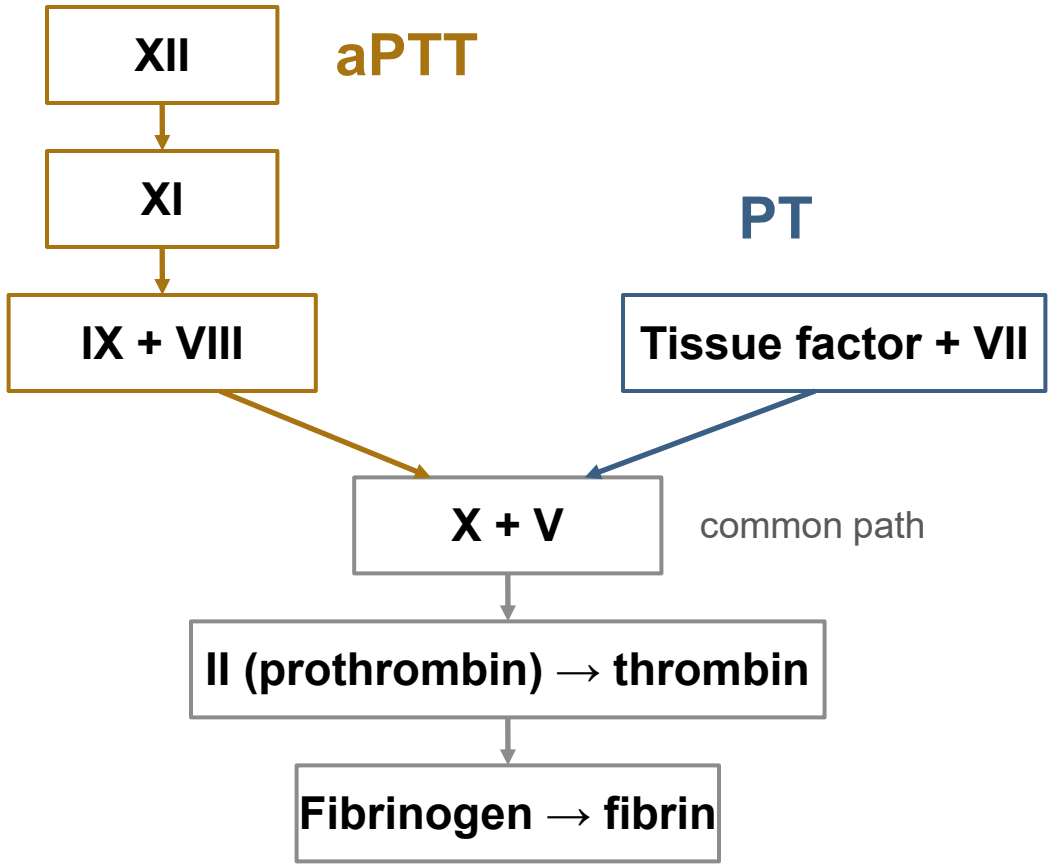
START: the platelet plug



Step	How	Fails in
Adhesion	VWF bridges GPIb to collagen	VWD; Bernard-Soulier (big platelets)
Activation	Granules and thromboxane call in more platelets	Aspirin: COX blocked for the platelet's life
Aggregation	GPIIb/IIIa links platelets through fibrinogen	Glanzmann (normal count)

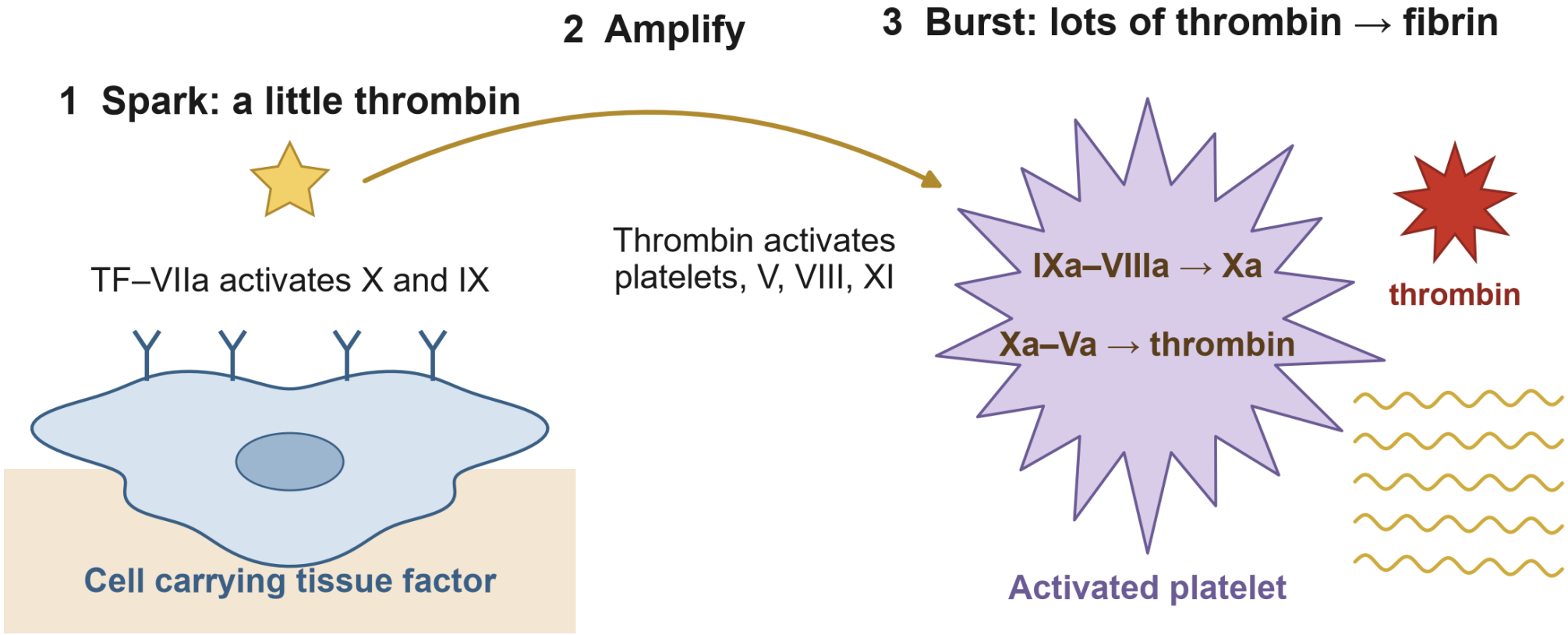
Saudi registry, 2023: Glanzmann thrombasthenia is the largest rare bleeding disorder, 356 patients (WFH Global Survey; registry counts, not prevalence).

MAKE: what the tests measure



- PT = VII + the common path (X, V, II, fibrinogen)
- aPTT = XII, XI, IX, VIII + the common path
- Vitamin K factors: X, IX, VII, II (“1972”), and proteins C and S
- Warfarin lowers all four factors. VII falls first, so the PT moves first

Why hemophilia bleeds



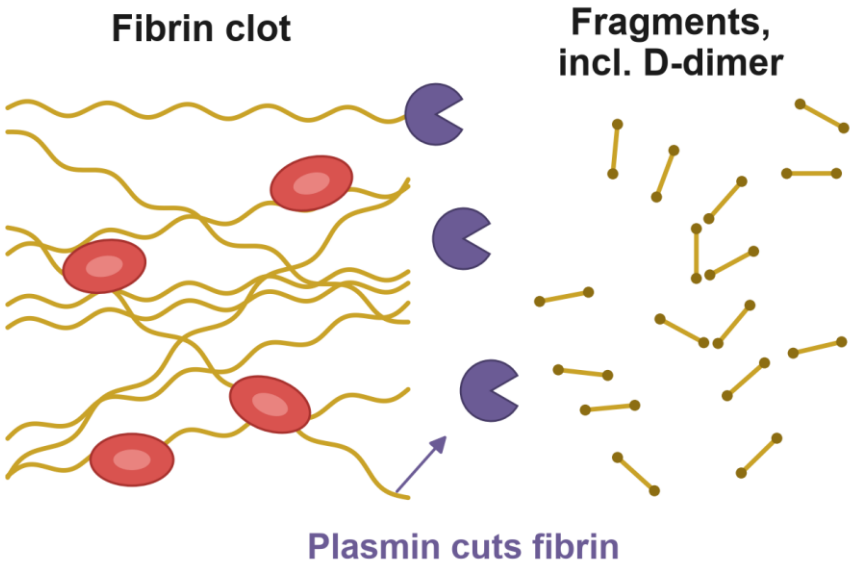
- Hemophilia: no IXa–VIIIa on the platelet, so no burst. The spark still works, but in the wrong place
- Factor XII deficiency: a long aPTT and no bleeding

STOP and CLEAN

STOP: the brakes

- TFPI switches off TF–VIIa and Xa
- Antithrombin blocks thrombin and Xa
- Protein C, with protein S, cuts Va and VIIIa
- Too little brake tips toward thrombosis (handbook ch 26)

CLEAN: fibrinolysis



- tPA turns plasminogen into plasmin; plasmin cuts fibrin
- D-dimer: sensitive, not specific
- Too much fibrinolysis can itself cause bleeding

The patient who bleeds

A. A boy, aged 2

- Painful, swollen knees, again and again
- A large bruise after a small fall

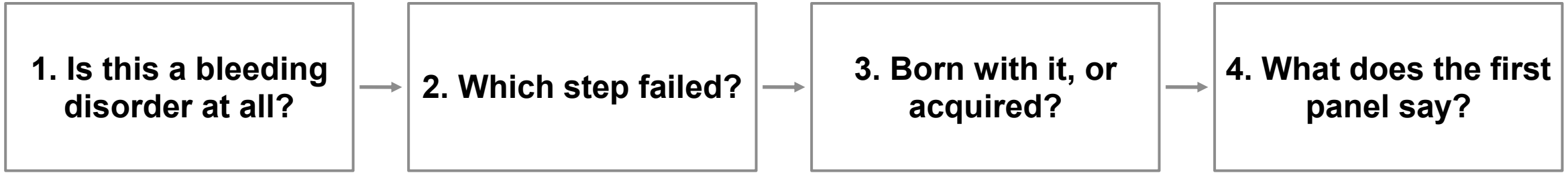
B. A woman, aged 24

- Three weeks of bruising and bleeding gums
- A period much heavier than usual
- A viral illness a month ago

C. An older adult

- Sudden large bruises
- Never bled before: teeth out, surgery, all without trouble

Four questions



- Question 1: the complaint. One site, or a pattern?
- Question 2: the examination. The plug, or the clot?
- Question 3: past challenges, family, drugs, illness
- Question 4: count, film, PT, aPTT, fibrinogen
- **Two cases run the same questions: hemophilia and ITP**

Local bleed or bleeding disorder?

One site: look for the lesion

- A nosebleed on its own
- Blood in the urine
- Vomiting blood
- Coughing blood
- Usually a local cause: a vessel, an ulcer, a tumour, a stone

A pattern: think of a disorder

- More than one site
- Bleeding out of proportion to the injury
- Bleeding after past challenges: teeth, surgery, childbirth, circumcision
- A family history

Plug or clot?

	START failed: the plug	MAKE failed: the clot
Where	Skin and mucosa: petechiae, bruises, gums, nose, heavy periods	Joints and muscles: hemarthrosis, deep hematoma
When	Straight after the injury	Delayed; bleeds again after it seemed to stop
Petechiae	Yes	No
Think of	Low platelets, platelet function, VWD	Hemophilia, other factor lack, anticoagulants, liver disease

Inherited or acquired?

Past challenges

- Circumcision
- Teeth out, tonsils out
- Surgery, childbirth
- Periods since menarche

Family

- X-linked: brothers, the mother's brothers
- Autosomal: both sexes
- Are the parents related?

Drugs and illness

- Antiplatelets, anticoagulants
- Anti-inflammatory and herbal drugs
- Liver, kidney, cancer, infection, pregnancy

- Lifelong points to inherited. New, in an adult, points to acquired
- Saudi Arabia: about 56% of marriages were between relatives in a national survey (2004–05). Recessive bleeding disorders are not rare here

First-panel patterns

Pattern	Think of
Low platelets	Look at the film first. ITP, marrow disease, TTP, DIC, HIT, clumping in the tube
Long PT alone	Factor VII lack, early warfarin, early liver disease, vitamin K lack
Long aPTT alone	Hemophilia A or B, XI or XII lack, VWD, heparin, lupus anticoagulant
Both long	DIC (low fibrinogen), severe liver disease, vitamin K lack, warfarin, massive transfusion
All normal, still bleeding	VWD, platelet function defect, factor XIII lack, a vessel cause

- A long time with no cause: the mixing test. Corrects = a factor is missing; does not correct = an inhibitor (next lecture)

Case 1

- A boy, aged 2
- His knees swell and hurt, again and again
- A large bruise after a small fall
- No petechiae
- Ask: did he bleed at circumcision? Does any man on his mother's side bleed?

Run the questions

1. A disorder? Two sites, again and again: yes
2. Which step? Joints, no petechiae: the clot (MAKE)
3. Born or acquired? A toddler, a boy: inherited, X-linked
4. First panel: next slide

Case 1: first panel

Test	Result
Platelet count	Normal
PT	Normal
aPTT	**Long**
Mixing test	**Corrects**
Factor VIII	**Below 1%**

- **Diagnosis: severe hemophilia A**
- Pattern 3: a long aPTT alone
- The mix corrects, so a factor is missing, not blocked
- The factor assay names it: VIII, not IX
- Below 1% means severe

Hemophilia

Severity	Factor level	Bleeds with
Severe	Below 1%	No injury: joints and muscles
Moderate	1–5%	Minor injury
Mild	5–40%	Surgery or major injury

Saudi registry, 2023: 1,595 people with hemophilia (A 1,281, B 306). Registry counts, not prevalence (WFH Global Survey 2023).

- X-linked. Mostly males; carrier women can bleed if their level is low
- A (VIII) is far more common than B (IX). They look the same
- Target joints, then lasting joint damage. Fear head and retroperitoneal bleeds
- Treatment: replace the missing factor
- No intramuscular injections. No anti-inflammatory drugs

Case 2

- A woman, aged 24
- Three weeks of bruising on her legs. Gums bleed when she brushes
- Two long nosebleeds. A period far heavier than usual
- A viral illness a month ago. Otherwise well. No medicines
- Petechiae on shins and forearms. Blood blisters in the mouth. No nodes, no big spleen, no bone tenderness

Run the questions

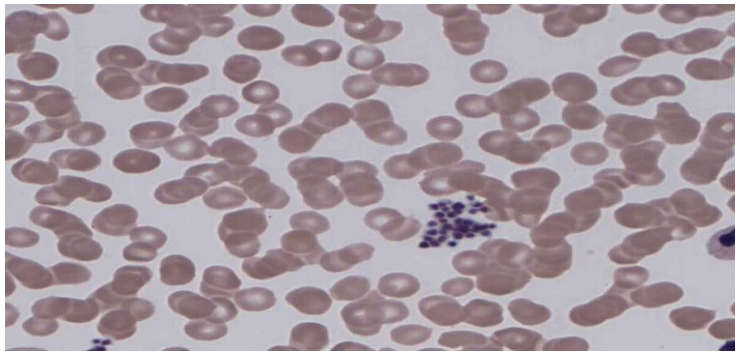
1. A disorder? Many sites at once: yes
2. Which step? Skin and mucosa, petechiae: the plug (START)
3. Born or acquired? Three weeks, no past bleeding: acquired
4. First panel: the count and the film

Case 2: first panel and film

Test	Result
Platelets	**8 ×10⁹/L**
Hemoglobin	118 g/L
White cells	Normal
PT and aPTT	Normal
Film	Few platelets, some large. No clumps, blasts or fragments

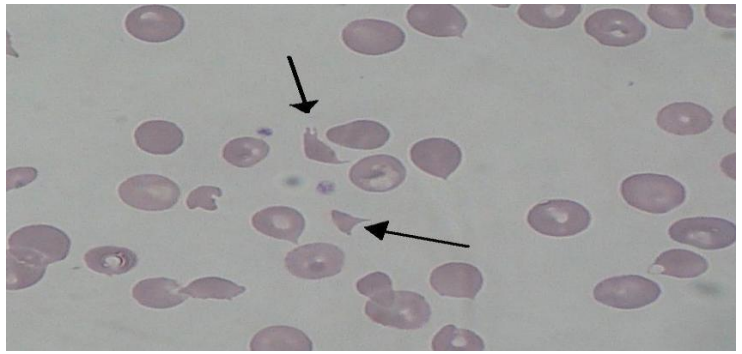
Low platelets: three causes

- Too few made
- Too many destroyed
- Held in a big spleen



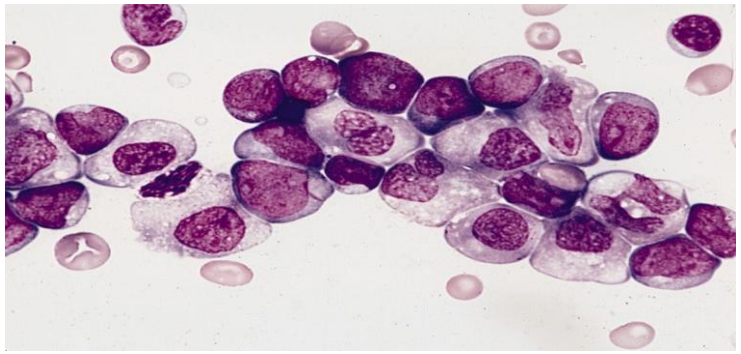
Clumps: the count is false

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Fragments: think TTP or DIC

Paulo Henrique Orlandi Mourao, CC BY-SA 3.0, via Wikimedia Commons



Blasts: marrow disease

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ITP: diagnosis

Exclude first

- Clumping: the film shows none
- Marrow disease: no nodes, spleen or bone pain; no other low counts
- TTP: no fragments on the film
- DIC: PT and aPTT normal
- HIT: no heparin

Then

- ITP: a well patient with a low platelet count and nothing else. No test proves it
- Send: HIV, hepatitis C, H. pylori, ANA, immunoglobulins, thyroid tests, pregnancy test
- Marrow only if something does not fit: older age, systemic symptoms, other low counts, abnormal film, no response
- Blood blisters in the mouth (wet purpura) raise the urgency
- Treatment is decided by bleeding, not the count; managed by hematology

Acquired hemophilia

- An older adult, or a woman after childbirth
- Sudden, severe bleeding. Never bled before
- Long aPTT alone; PT and platelets normal
- An autoantibody against factor VIII. Not inherited; both sexes

The mixing trap

- The antibody works slowly, so an immediate mix can correct
- Compare the aPTT straight after mixing and after 2 hours at 37 °C

What to do

- Call hematology the same day

Acquired causes in adults

Cause	First panel
Antiplatelets, anti-inflammatories	Count and screen normal
Warfarin	PT (INR) long first; lowers II, VII, IX, X
Heparin	aPTT long
Direct oral anticoagulants	No routine monitoring test
Liver disease	PT long, then both
Vitamin K lack	PT long, then both
DIC	Both long, low fibrinogen, falling platelets, fragments
Kidney failure (uremia)	Count and screen normal; platelets work poorly

Regional points

Ask about	Where	What we know
Snakebite	Asir	Some venoms cause a coagulopathy. Ask about a bite in anyone who bleeds without a clear cause
Alkhurma fever	Najran	28 cases, 2006–2009: nosebleeds in 8, gum bleeding in 5, no deaths (Alzahrani 2010)
Dengue	Red Sea coast: Jeddah, Makkah	Ask about fever and travel. No regional bleeding rates found

- Good Saudi data are few, and most come from Riyadh, Madinah and the Eastern Province. These are reasons to ask, not local rates

The three patients, and a fourth

Patient	Findings	Diagnosis
A. Boy, 2	Joints, delayed. Long aPTT, low VIII	Hemophilia A
B. Woman, 24	Skin and mucosa, new. Platelets 8, clean film	ITP
C. Older adult	New and severe. Long aPTT. Never bled before	Acquired hemophilia
D. Woman, 19	Heavy periods and bruising since her teens. Bled after wisdom teeth. Platelets, PT and aPTT normal	**? Next lecture**

Read next

- Handbook chapters 20 to 25
- Casebook Case 53, The Bleeding Patient: Case 2 in full
- Hematology question bank, items 46 to 59
- Next lecture: Disorders of Hemostasis — the full history, the tests in depth, and patient D

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