MFDS · HUMAN DISEASE · LECTURE 1 (PART 2)

Bleeding disorders in dental practice

Dr Mohamed J. Abuasi · coNNct International Academy · 9 May 2025 · source deck slides 40–62

EXAM-DAY SUMMARY

everything on this page → detail in §§ overleaf

HAEMOSTASIS IN 5 STAGES → §1

- Vasoconstriction → primary → secondary → fibrinolysis → regeneration
- Primary = platelets, soft plug; secondary = factors, fibrin mesh
- Antiplatelets hit primary · anticoagulants hit secondary

PRIMARY HAEMOSTASIS & CASCADE → §1

- Adhesion (vWF→collagen) → shape change → granule release ADP + TXA_2 → recruitment → aggregation
- Intrinsic XII→XI→IX (+VIII); extrinsic TF (III) + VII
- Converge on Xa → prothrombin (II) → thrombin → fibrin
- Thrombin → XIII → XIIIa + Ca^{2+} → cross-linked fibrin

INVESTIGATIONS → §2

- PT 12–15 sec · extrinsic
- INR 0.8–1.2 · extrinsic (warfarin)
- APTT 25 sec · intrinsic (heparin)
- TT 10–15 sec · heparin
- Bleeding time 2–9 MINUTES · primary haemostasis

THROMBOCYTOPENIA → §3

- ↓production (marrow failure/infiltration/HIV) · ↑consumption (DIC, heparin-induced) · sequestration (splenomegaly) · dilution · ↑destruction (SLE, **aspirin**) · ITP
- Prolonged bleeding, petechiae, ecchymosis, nose + gum bleeding
- Mx: platelets within normal average · atraumatic · local measures

THROMBOCYTHAEMIA → §3

- High count of **immature** platelets → bleeding signs as thrombocytopenia
- Splenomegaly
- Plugs everywhere: head (headache, dizziness); hands/feet (numbness, burning)

HAEMOPHILIA A VS B → §4

- A = factor VIII · B = factor IX (Christmas disease); clinically identical
- Males predominantly; specialist centre only, keep phone number
- IV factor before surgery — factor VIII lifetime only 8 hrs, may repeat
- Desmopressin: works in A (releases VIII from endothelium); **no role in B**
- Suspect HBV / HCV / HIV

VON WILLEBRAND → §4

- Platelet + factor VIII deficiency → neither primary nor secondary haemostasis
- Inherited **AD** → males *and* females
- Desmopressin and IV factor VIII both effective

ANTIPLATELETS → §5

- Aspirin (COX) · clopidogrel/Plavix (ADP receptor) · dipyridamole · prasugrel · ticagrelor
- Affect primary haemostasis
- Deck error: TXA_2 inhibition is **aspirin**, not dipyridamole

ANTIPLATELET EXTRACTIONS → §5

- Single drug: up to 3 teeth, no drug alteration + local measures
- Aspirin + clopidogrel: no alteration + local measures
- Aspirin + dipyridamole: no alteration + local measures

WARFARIN → §6

- Vit K antagonist → factors II, VII, IX, X in hepatocyte · oral · effect lasts 3 days
- Test INR (valid 72 hrs if stable) — extract up to INR 4
- Antidote vit K (8 hrs to work); emergency = fresh frozen plasma
- Heparin bridge before surgery · single tooth extraction per visit

HEPARIN → §6

- Antithrombin III activator → inactivates factor Xa · IV or SC · effect 8 hrs
- Test APTT (25 sec) · antidote protamine sulphate, works immediately
- Common in renal dialysis → extract the **day after** dialysis

INR: STABLE VS UNSTABLE → §6

- Stable: no weekly monitoring; no reading >4 in last 2 months; INR valid 72 hrs
- Unstable: weekly monitoring; reading >4 in last 2 months; INR within 24 hrs

NOACS → §7

- Apixaban, rivaroxaban = Xa · dabigatran = IIa (thrombin)
- Max effect 2 hrs · half-life 12 hrs · no test · no antagonist (per deck; reversal agents now exist)
- Don't stop for ≤4 simple extractions, 1–2 quadrants max, or abscess incision/simple surgery
- >4 teeth/difficult: AF (permanent) → delay morning dose; post-knee/hip (2–6 wks) → delay till course ends

LOCAL HAEMOSTATIC MEASURES → §8

- Tight suture · saline-soaked gauze · tranexamic acid mouthwash 4 days
- Resorbable gelatin · oxidised cellulose · collagen sponges
- Plus: work atraumatically, check the number before you start

WHERE THE DECK DIFFERS → §4 §5 §7

- Haemophilia A/B: deck says AR — standard is X-linked recessive (explains "males predominantly")
- TXA_2 inhibition = aspirin; dipyridamole raises platelet cAMP
- NOACs: reversal agents now exist (idarucizumab, andexanet alfa)

§1 Normal haemostasis

Haemostasis is the physiological sequence that arrests bleeding from a damaged vessel and then restores the vessel wall. Every bleeding disorder and every antithrombotic drug in this lecture is best understood as a failure or a deliberate blockade of one specific step in that sequence, so the sequence comes first.

A note on terminology: the deck writes *homeostasis* throughout. The correct term for clot formation is **haemostasis** (Greek *haima*, blood + *stasis*, halting); *homeostasis* is the unrelated concept of maintaining a stable internal environment. The notes use *haemostasis* from here on.

KEY POINTS

Haemostasis proceeds in five stages: **vasoconstriction → primary haemostasis → secondary haemostasis → fibrinolysis → regeneration**. Primary haemostasis is a *platelet* event producing a soft plug; secondary haemostasis is a *clotting-factor* event that reinforces that plug with cross-linked fibrin.

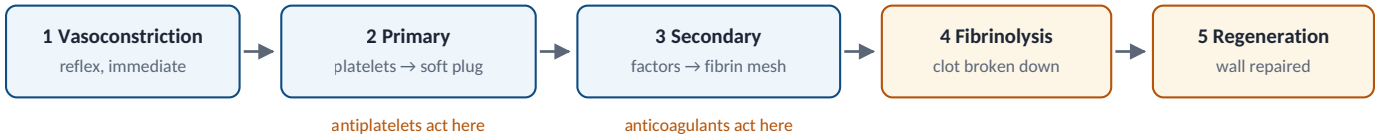

Diagram 1 — The five stages of haemostasis, and the two stages targeted by antithrombotic drugs.

1.1 Primary haemostasis — the soft platelet plug

Injury strips away the endothelium and exposes the basement membrane and subendothelial collagen. Five events follow in order:

1. **Platelet adhesion** — platelets bind the exposed collagen, bridged by **von Willebrand factor (vWF)**.
2. **Shape change** — adherent platelets flatten and spread over the defect.
3. **Granule release** — the activated platelet degranulates, releasing ★**adenosine diphosphate (ADP) and thromboxane A_2 (TXA_2)**.
4. **Recruitment** — those mediators attract and activate further circulating platelets.
5. **Aggregation** — recruited platelets bind to one another, forming the soft **haemostatic plug**.

This stage is entirely platelet-dependent. It is the step abolished by thrombocytopenia, by von Willebrand disease and by every antiplatelet drug — and the step measured by the bleeding time.

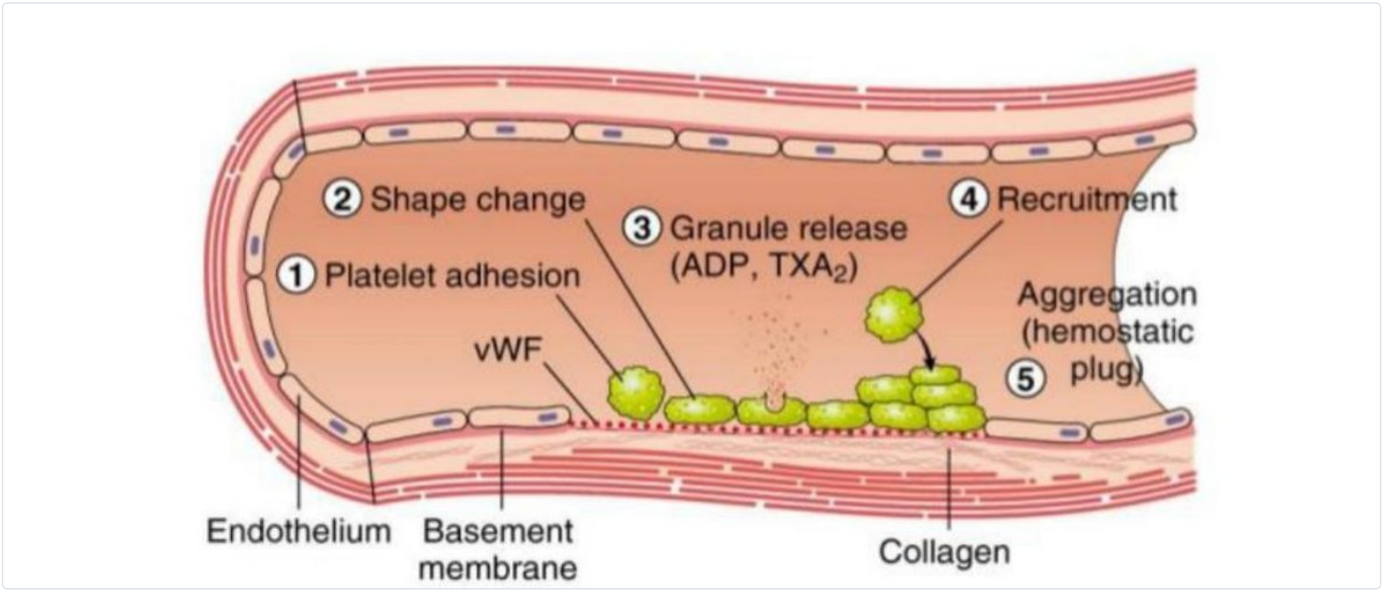

Fig. 1 — Primary haemostasis. Platelets adhere to exposed collagen via vWF (1), change shape (2), release ADP and TXA_2 (3), recruit further platelets (4) and aggregate into the soft haemostatic plug (5). Note the exposed basement membrane and collagen beneath the breached endothelium.

1.2 Secondary haemostasis — the coagulation cascade

The soft plug is mechanically weak and must be reinforced by fibrin. The clotting factors form an amplifying enzyme cascade with two entry points that converge on factor X.

- **Intrinsic pathway** — triggered by contact with collagen or other activators. XII → active XII; XI → active XI (calcium-dependent); IX → active IX (calcium-dependent), with factor VIII acting as cofactor; then X → active X, requiring ★**calcium (Ca^{2+}) and phospholipids (PL)**.
- **Extrinsic pathway** — tissue damage exposes **tissue factor (factor III)**, which with factor VII forms the tissue factor/active VII complex; this activates both factor IX and factor X directly.
- **Common pathway** — active X, with calcium, factor V and phospholipid, converts prothrombin (factor II) to **thrombin**. Thrombin cleaves fibrinogen to fibrin, and also activates factor XIII; active XIII, with calcium, cross-links fibrin into the definitive clot.
- **Positive feedback** — thrombin feeds back onto factor VII and onto factor XI, accelerating its own generation once the cascade has started.

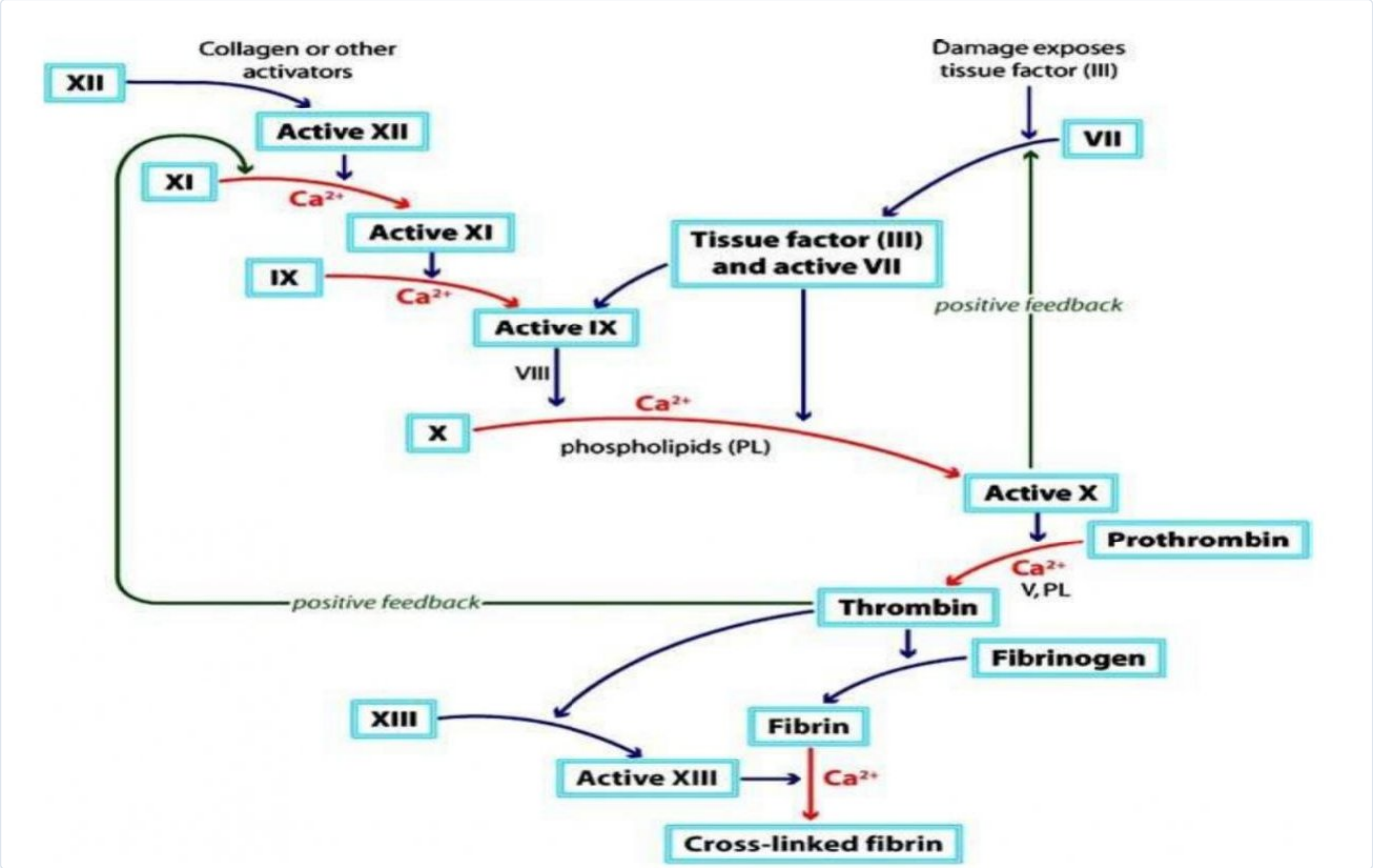

Fig. 2 — The coagulation cascade. Intrinsic limb (left) and extrinsic limb (right) converge on active factor X; thrombin then converts fibrinogen to fibrin and activates factor XIII to cross-link it. Two thrombin positive-feedback loops (green) run back to factors VII and XI.

1.3 Fibrinolysis and regeneration

Once the vessel is sealed, the clot is progressively lysed and the vessel wall regenerates. These final two stages are why a healthy socket stops bleeding permanently rather than simply being plugged, and why clot-stabilising agents such as tranexamic acid — which slow fibrinolysis — are useful adjuncts after extraction in an at-risk patient.

> ★ EXAM PEARL
>
> The commonest single-best-answer trap in this topic is **which limb a test interrogates**. Factor VIII and IX sit in the **intrinsic** limb, so haemophilia A and B prolong the **APTT**. Warfarin's most sensitive target is factor VII, the **extrinsic** limb, so warfarin prolongs the **PT/INR**. Platelet problems disturb neither — they prolong the **bleeding time**.

§2 Laboratory investigations

Four coagulation tests plus the bleeding time cover the whole of this lecture. Learn each one as a pair: *the number* and *the limb of haemostasis it reports on.*

Table 1 — Haemostatic investigations, reference values and what each tests

Test	Normal value	Reports on
PT (prothrombin time)	12–15 sec	Extrinsic pathway
INR	0.8–1.2	Extrinsic pathway — used to monitor warfarin
APTT	25 sec	Intrinsic pathway — used to monitor heparin
TT (thrombin time)	10–15 sec	Heparin effect
Bleeding time	2–9 **minutes**	Primary haemostasis (platelets)

KEY POINTS

Every value above is in **seconds** except the ★**bleeding time, which is 2–9 minutes**, and the INR, which is a ratio with no units. The INR is the internationally standardised expression of the PT, which is why both report the extrinsic pathway.

§3 Platelet disorders

Platelet disorders disturb primary haemostasis. Whether the count is too low (thrombocytopenia) or too high but dysfunctional (thrombocythaemia), the clinical picture the dentist meets is the same pattern of mucocutaneous bleeding.

3.1 Thrombocytopenia

Thrombocytopenia is a reduced circulating platelet count. The causes group into five mechanisms, plus one idiopathic entity:

Decreased production
: Marrow failure, marrow infiltration, HIV infection and similar marrow insults.

Increased consumption
: Disseminated intravascular coagulopathy (DIC), or heparin-induced thrombocytopenia.

Platelet sequestration
: Splenomegaly — platelets are pooled and trapped in the enlarged spleen.

Dilution
: Dilution of circulating platelets, as after large-volume fluid or red-cell replacement.

Increased platelet destruction
: Systemic lupus erythematosus (SLE), and **aspirin**.

Idiopathic thrombocytopenic purpura (ITP)
: Thrombocytopenia with no identified underlying cause.

The deck lists aspirin under increased destruction. In practice aspirin's dominant effect is irreversible *impairment of platelet function* rather than destruction of platelets — the count is usually normal and the bleeding time prolonged. Either way, the practical consequence for the dentist is the same: defective primary haemostasis.

Signs and symptoms. Prolonged bleeding; **petechiae** (pinpoint capillary haemorrhages); **ecchymosis** (bruising); and ★**nose and gum bleeding** — often the presenting complaint in the dental chair.

Dental management. Three principles:

1. Ensure the platelet level is within the normal average before proceeding — liaise with the haematologist and obtain a recent full blood count.
2. Work **atraumatically**: minimal flap reflection, minimal bone removal, no unnecessary soft-tissue trauma.
3. Apply **local haemostatic measures** (§8) at the end of every procedure rather than as a rescue when bleeding fails to stop.

3.2 Thrombocythaemia

Thrombocythaemia is the mirror image: a **high count of immature platelets**. Because those platelets are immature and functionally defective, the patient paradoxically shows **the same bleeding signs as thrombocytopenia** — prolonged bleeding, petechiae, ecchymosis, nose and gum bleeding. Additional features are:

- **Splenomegaly.**
- **Platelet plugs forming everywhere**, producing symptoms wherever microvascular occlusion occurs — classically in the ★**head (headache, dizziness) and the hands and feet (numbness, burning)**.

★ EXAM PEARL

A high platelet count is **not** reassuring. Thrombocythaemia is the counter-intuitive disorder that bleeds *and* clots at the same time: the platelets are too numerous to keep the microcirculation clear, yet too immature to form a competent plug where you need one.

§4 Coagulation factor disorders

Three inherited disorders account for almost all factor-related bleeding seen in dentistry. Haemophilia A and B are clinically indistinguishable and differ only in the missing factor; von Willebrand disease straddles both halves of haemostasis.

4.1 Haemophilia A

- Defect of **factor VIII**.
- Inherited; affects **males predominantly**.
- **Treatment at a specialist centre only** — the general dental practitioner does not manage surgical haemostasis in these patients alone. Keep the centre's contact telephone number available.
- **Intravenous factor VIII** is given before surgery and ★**may need to be repeated, as its lifetime is only 8 hours**.
- **Desmopressin** nasal spray helps by releasing stored factor VIII from the endothelium.
- Suspect **HBV, HCV or HIV** co-infection — a legacy of pooled factor concentrate given before viral inactivation and recombinant products became standard.

4.2 Haemophilia B

- Also called **Christmas disease**.
- Defect of **factor IX**.
- **Clinically identical to haemophilia A** — the two cannot be separated at the chairside.
- Managed by **intravenous factor IX**.
- ★**Desmopressin has no role** — it releases factor VIII, not factor IX.

4.3 Von Willebrand disease

- Deficiency affecting **platelet function and factor VIII** — vWF both bridges platelets to collagen and carries factor VIII in the plasma.
- Consequently **neither primary nor secondary haemostasis works properly**: the patient shows the manifestations of *both* haemophilia and thrombocytopenia.
- Inherited **autosomal dominant**, and therefore **affects both males and females**.
- **Desmopressin and intravenous factor VIII are both effective.**

Table 2 — The three inherited factor disorders compared

	Haemophilia A	Haemophilia B	Von Willebrand disease
Defect	Factor VIII	Factor IX	vWF → platelet function *and* factor VIII
Other name	—	Christmas disease	—
Inheritance (per lecture)	Recessive; males predominantly	As haemophilia A	Autosomal dominant
Sexes affected	Males predominantly	Males predominantly	Males and females
Haemostasis affected	Secondary	Secondary	Primary *and* secondary
Replacement	IV factor VIII	IV factor IX	IV factor VIII
Desmopressin	Effective	**No role**	Effective

★ EXAM PEARL

The deck records haemophilia A as inherited **autosomal recessive**. The standard description is **X-linked recessive**, which is what actually explains the "affects males predominantly" line on the same slide — an autosomal recessive condition would affect the sexes equally. Haemophilia B is likewise X-linked recessive. Von Willebrand disease genuinely is autosomal dominant, which is why it affects both sexes. Answer *X-linked recessive* for the haemophilias in an examination, but be aware of what your deck says.

CAUTION

Do not undertake surgery on a haemophiliac in general practice. Factor cover must be arranged and timed by the haemophilia centre, and because intravenous factor VIII lasts only 8 hours, re-dosing may be required before the socket is secure.

§5 Antiplatelet drugs ("blood thinners")

Antiplatelet agents impair **primary haemostasis** — they act on the platelet, not on the clotting factors. This is the key division to hold in mind: antiplatelets attack the soft plug, anticoagulants (§6–§7) attack the fibrin mesh.

5.1 The agents and how they work

1. **Aspirin** — cyclo-oxygenase (COX) inhibitor.
2. **Clopidogrel (Plavix)** — binds covalently and irreversibly at the platelet ADP ($P2Y_{12}$) receptor.
3. **Dipyridamole** — given in the deck as inhibiting thromboxane A_2 formation.
4. **Prasugrel.**
5. **Ticagrelor.**

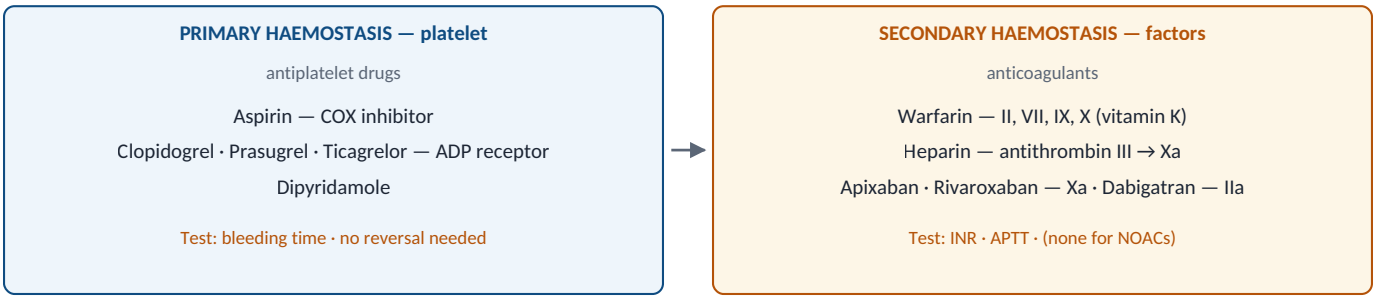

Diagram 2 — Where each antithrombotic class acts, and which test monitors it.

★ EXAM PEARL

The deck attributes thromboxane A_2 inhibition to **dipyridamole**. That mechanism belongs to **aspirin**, whose COX blockade is precisely what stops TXA_2 synthesis. Dipyridamole is a phosphodiesterase and adenosine-reuptake inhibitor that raises platelet cyclic AMP. Note also that clopidogrel binds the platelet *ADP receptor*, not ADP itself. If the examination asks "which drug inhibits thromboxane A_2 formation", the answer is aspirin.

5.2 Dental management of the antiplatelet patient

The governing principle is that antiplatelet drugs are **not stopped or altered** for routine dental extractions — the thrombotic risk of interrupting them outweighs the bleeding risk of proceeding. Local measures do the work instead.

Table 3 — Extraction rules by antiplatelet regimen

Regimen	Drug alteration	Extraction limit
Single drug	None	Up to **3 teeth**, with local measures
Aspirin + clopidogrel	None	Extraction with local measures
Aspirin + dipyridamole	None	Extraction with local measures

KEY POINTS

For every antiplatelet regimen in this lecture — single agent or dual — there is ★**no alteration of the drug**. Extract and apply local haemostatic measures. The only numerical limit given is **up to 3 teeth** on a single agent.

§6 Anticoagulants: warfarin and heparin

Anticoagulants affect **secondary haemostasis**: they interfere with the production or the activation of clotting factors, so the fibrin mesh cannot be laid down normally.

6.1 Mechanisms

Warfarin

Inhibits the **vitamin K-dependent factors II (prothrombin), VII, IX and X** within the hepatocyte — it blocks their *production*, which is why its onset and offset are slow.

Heparin

Inactivates **activated factor X (factor Xa)**, acting as an **antithrombin III activator** — it blocks factor *activity*, which is why it works and wears off quickly.

6.2 Warfarin versus heparin

Table 4 — Warfarin and heparin compared

	Warfarin	Heparin
Mechanism	Vitamin K antagonist (factors II, VII, IX, X)	Antithrombin III activator → inactivates factor Xa
Route	Orally	Intravenous or subcutaneous
Duration of effect	Up to **3 days**	**8 hours**
Monitoring test	**INR** — valid within 72 hrs only for stable patients	**APTT** (25 sec)
Antidote	**Vitamin K** — takes 8 hrs to work	**Protamine sulphate** — works immediately
Emergency reversal	Fresh frozen plasma	Protamine sulphate
Dental threshold	Extract up to **INR 4**; single tooth extraction per visit	Extract the **day after** dialysis
Other notes	Heparin bridge before surgeries	Commonly used in renal dialysis

KEY POINTS

Three numbers carry this section: warfarin's effect persists **up to 3 days**; heparin's for **8 hours**; and you may ★**extract up to an INR of 4**. Vitamin K takes 8 hours to reverse warfarin — useless in an emergency, which is why fresh frozen plasma is the emergency antidote. Protamine sulphate reverses heparin immediately.

6.3 Stable versus unstable INR patients

How recent an INR must be before extraction depends on whether the patient's anticoagulation is stable. The definition is not a matter of clinical impression — it rests on two objective criteria.

Table 5 — INR patients: stable versus unstable

	Stable	Unstable
Weekly INR monitoring	Not required	Required
INR above 4 in the last 2 months	None	Yes
INR valid for how long before extraction	Up to **72 hours**	No more than **24 hours**

★ EXAM PEARL

★**72 hours for stable, 24 hours for unstable** — and a patient is *unstable* if they need weekly monitoring **or** have had any reading above 4 in the last two months. Both the definition and the two time windows are examinable; candidates who learn only "check the INR first" lose the mark.

§7 Novel oral anticoagulants (NOACs)

7.1 The agents and their pharmacology

1. **Apixaban** — factor Xa inhibitor.
2. **Rivaroxaban** — factor Xa inhibitor.
3. **Dabigatran** — factor IIa (thrombin) inhibitor.

- Takes **2 hours** to reach maximum effect.
- Half-life ★**12 hours**.
- **No monitoring test** — unlike warfarin, there is no INR equivalent to check before you operate.
- **No antagonist** (as taught in this deck — see the caution below).

> **CAUTION**
> The "no test, no antagonist" teaching is now out of date and worth verifying against your current textbook. **Idarucizumab** reverses dabigatran and **andexanet alfa** reverses the factor Xa inhibitors; specific anti-Xa assays and the dilute thrombin time can quantify drug effect where a laboratory offers them. The practical point the deck is making still holds for the dental chair: you cannot obtain a bedside number equivalent to an INR, so you manage these patients on timing and local measures rather than on a test result.

7.2 Dental management of the NOAC patient

Management is stratified by how extensive the procedure is, and — for the more extensive cases — by why the patient is taking the drug at all.

- **Do not stop the drug** for up to ★**4 simple extractions in one or two quadrants maximum**.
- **Do not stop the drug** for abscess incision or simple surgery.
- For **difficult surgery or extraction of more than 4 teeth**:
  - **Permanent use for atrial fibrillation** — **delay the morning dose** on the day of extraction, and treat later in the day.
  - **Temporary use**, typically the 2–6 weeks following knee or hip replacement surgery — **delay non-urgent procedures** until the drug course is complete.

> **KEY POINTS**
> The NOAC decision reduces to one question: **is this within the "up to 4 simple extractions in one or two quadrants" ceiling?** If yes, carry on and use local measures. If no, ask why the patient is anticoagulated — **permanent** (atrial fibrillation) means delay the morning dose; **temporary** (post-joint-replacement, 2–6 weeks) means delay the procedure.

§8 Local haemostatic measures and atraumatic practice

Local measures are the common thread through every section of this lecture: they are the reason antiplatelets and NOACs need not be stopped, and the safety net for the thrombocytopenic, the warfarinised and the haemophiliac patient alike. They should be applied routinely and prophylactically in any at-risk patient, not reserved as a rescue.

> **KEY POINTS**
> Six local haemostatic measures: **tight suture**; **saline-soaked gauze**; ★**tranexamic acid mouthwash for 4 days**; **resorbable gelatin material**; **oxidised cellulose**; and **collagen sponges**.

Tight suture
: Approximates the socket margins and holds the packing material in place; the first mechanical measure after any extraction in a bleeding-risk patient.

Saline-soaked gauze
: Pressure pack bitten onto the socket — simple, immediate and effective for primary bleeding.

Tranexamic acid mouthwash, 4 days
: An antifibrinolytic: it slows the fibrinolysis stage of haemostasis (§1) so the clot formed is not prematurely broken down over the following days.

Resorbable gelatin material
: Sponge packed into the socket; provides a physical scaffold for clot formation and resorbs without removal.

Oxidised cellulose
: Socket dressing that promotes clotting on contact with blood.

Collagen sponges
: Socket dressing that directly triggers platelet adhesion and aggregation — collagen is the natural stimulus for primary haemostasis.

Alongside these, the general principle from the thrombocytopenia slides applies to every patient in this lecture: **work atraumatically**, and confirm the relevant number — platelet count, INR, or the time since the last dialysis — before you start rather than after the socket begins to ooze.

> **★ EXAM PEARL**
> The tranexamic acid duration is the number most often dropped: the mouthwash runs for **4 days**, not a single application, because it is fibrinolysis over the following days — not the initial clot formation — that it exists to suppress.