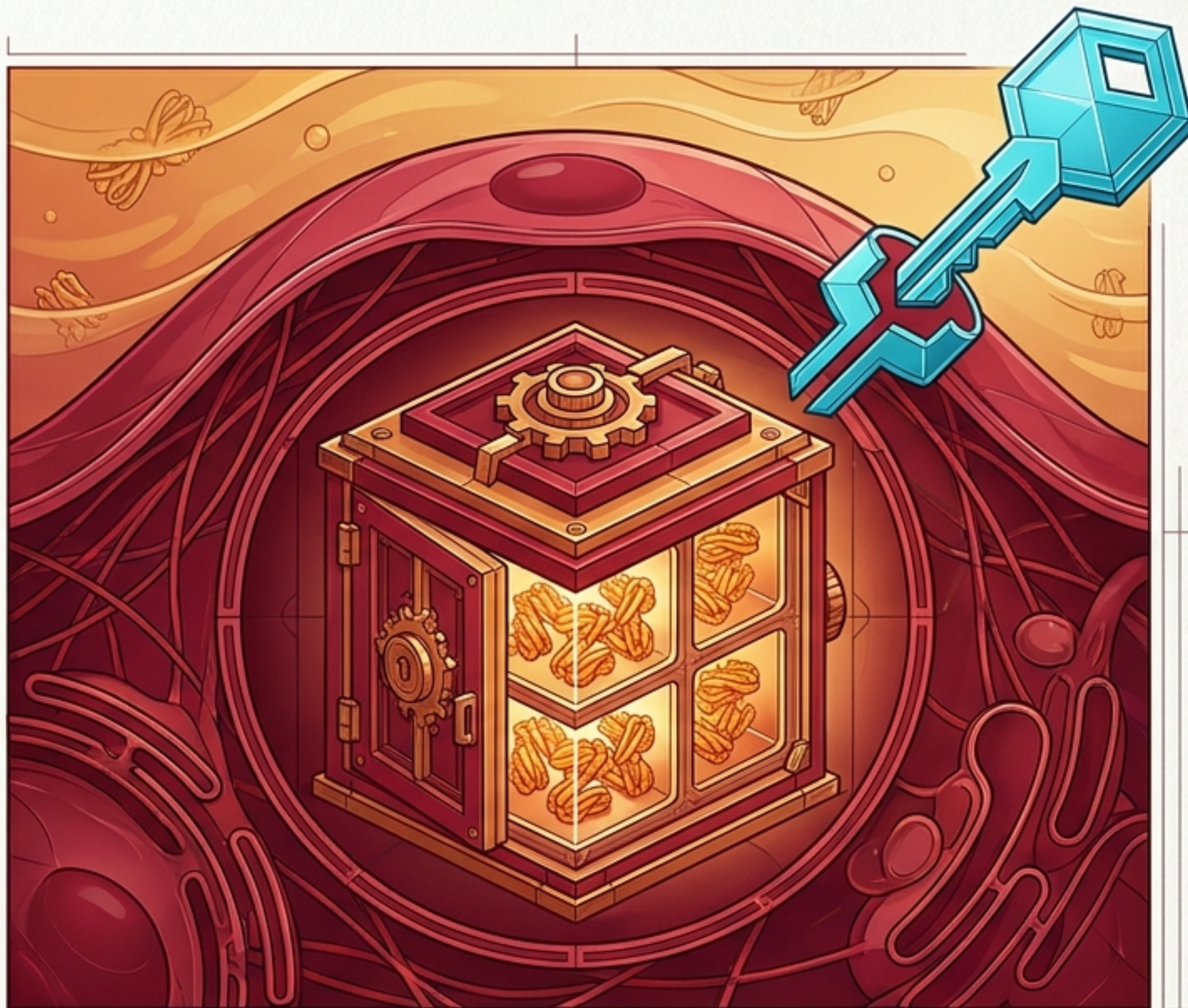


Mobilizing Endogenous Reserve

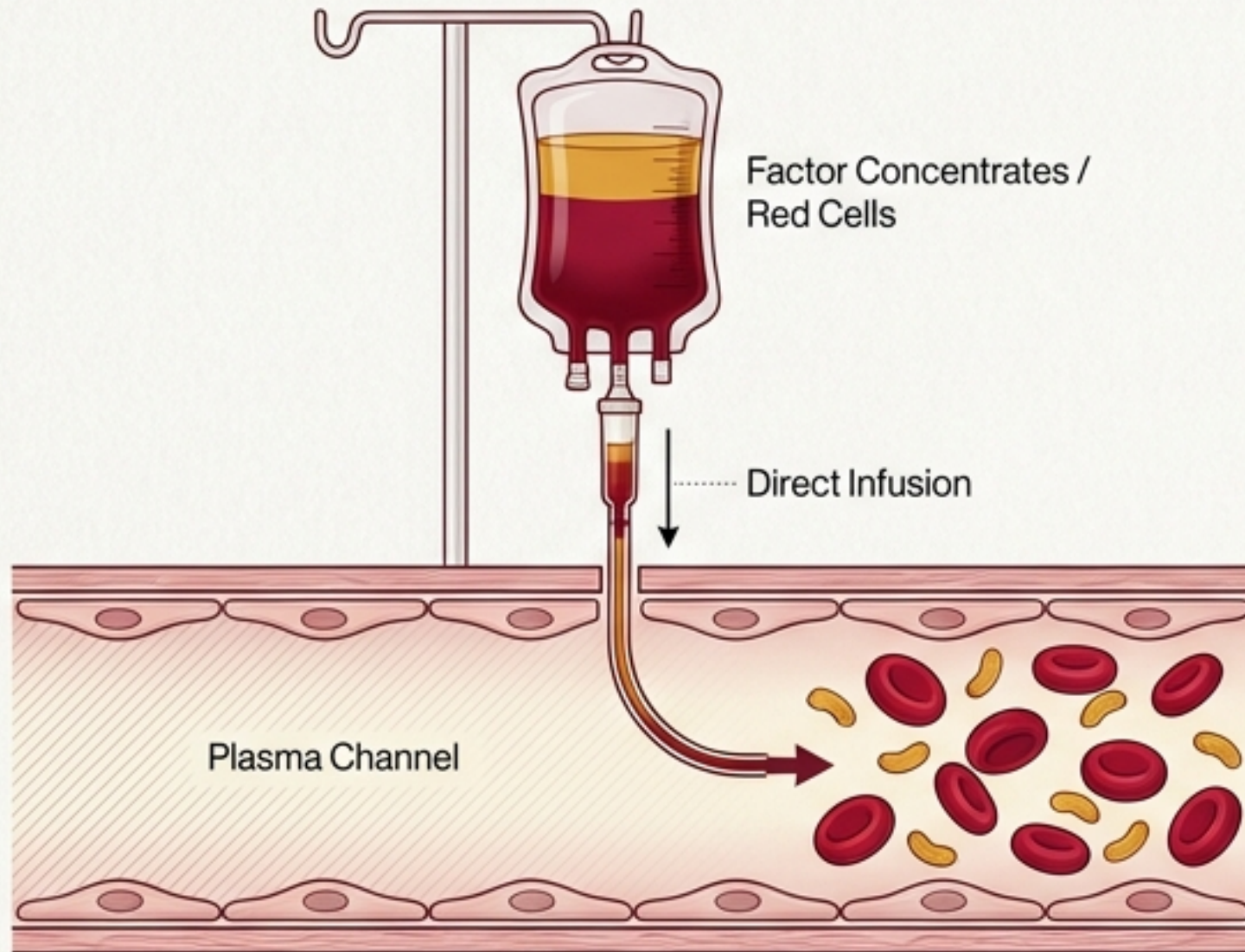
A clinical framework for
desmopressin and the endothelium
in von Willebrand Disease.

Based on the clinical insights
of William Aird.



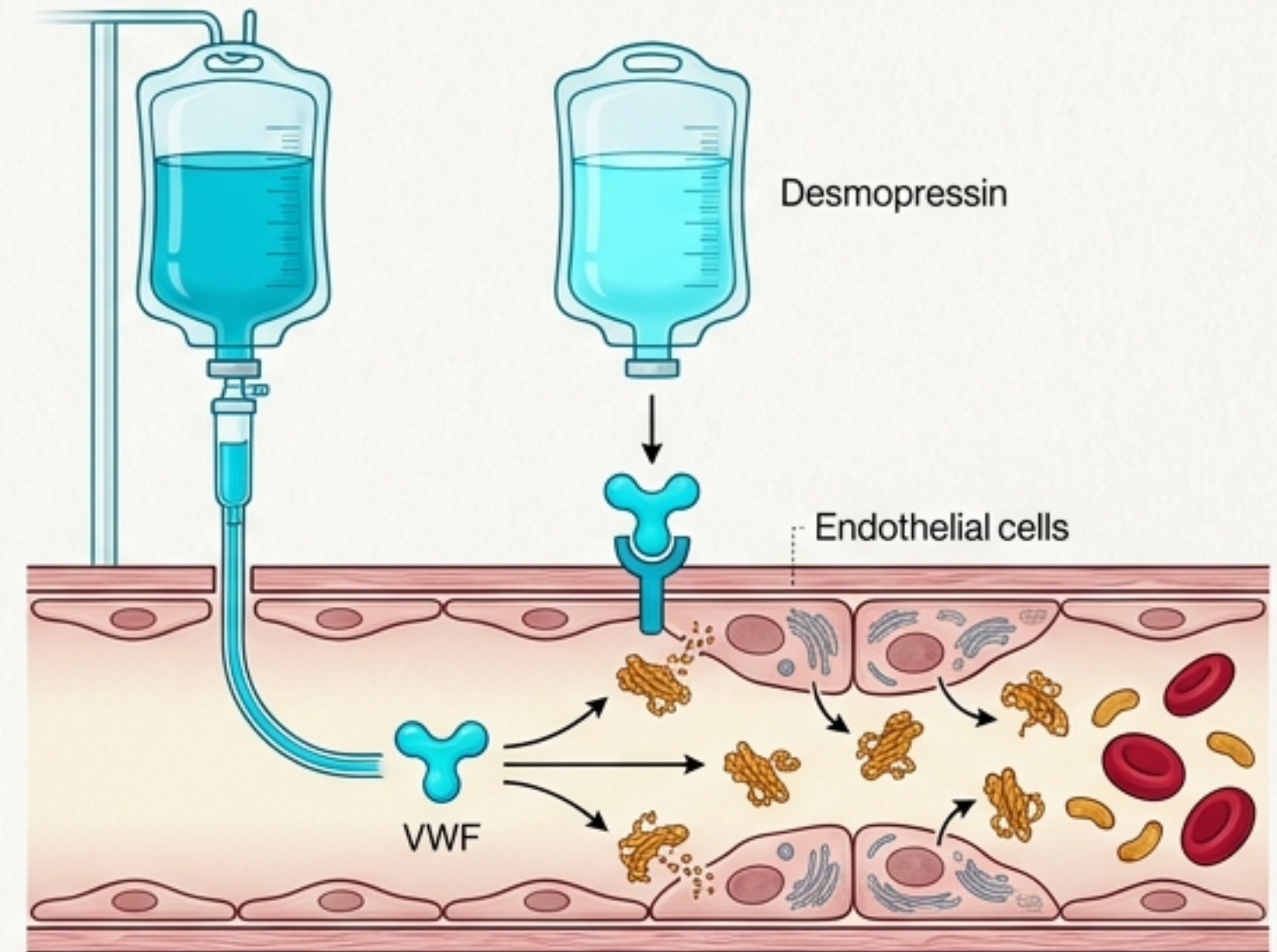
Borrowing from the Endothelium, Not Replacing It

Replacement Therapies



Supplies exogenous product (Factor concentrates, Red cells).

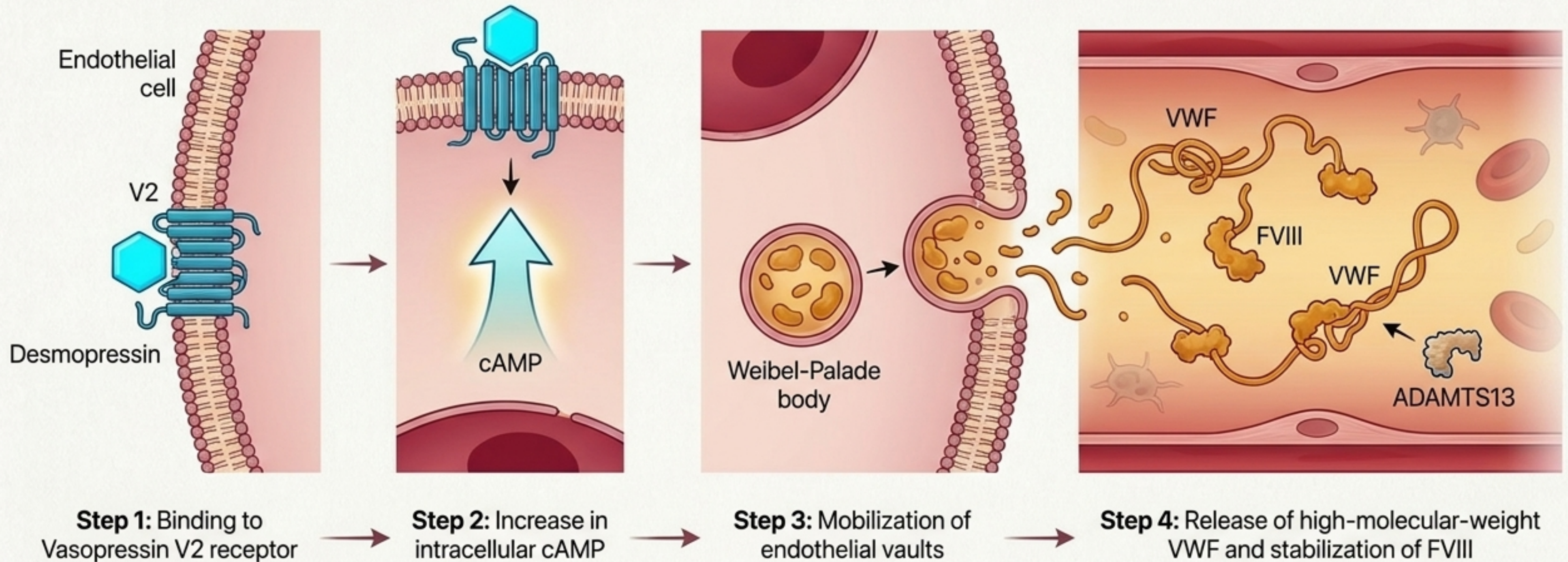
Mobilization Therapies



Asks the endothelium to release what is already stored (Desmopressin).

Desmopressin does not create von Willebrand factor. It is a way of temporarily mobilizing the body's own finite hemostatic reserve.

The Pharmacological Key to the Endothelial Vault



Desmopressin is not isolated pharmacology. It is a temporary activation of an existing, regulated-release hemostatic pathway.

Therapy Only Works if it Matches the Mechanism

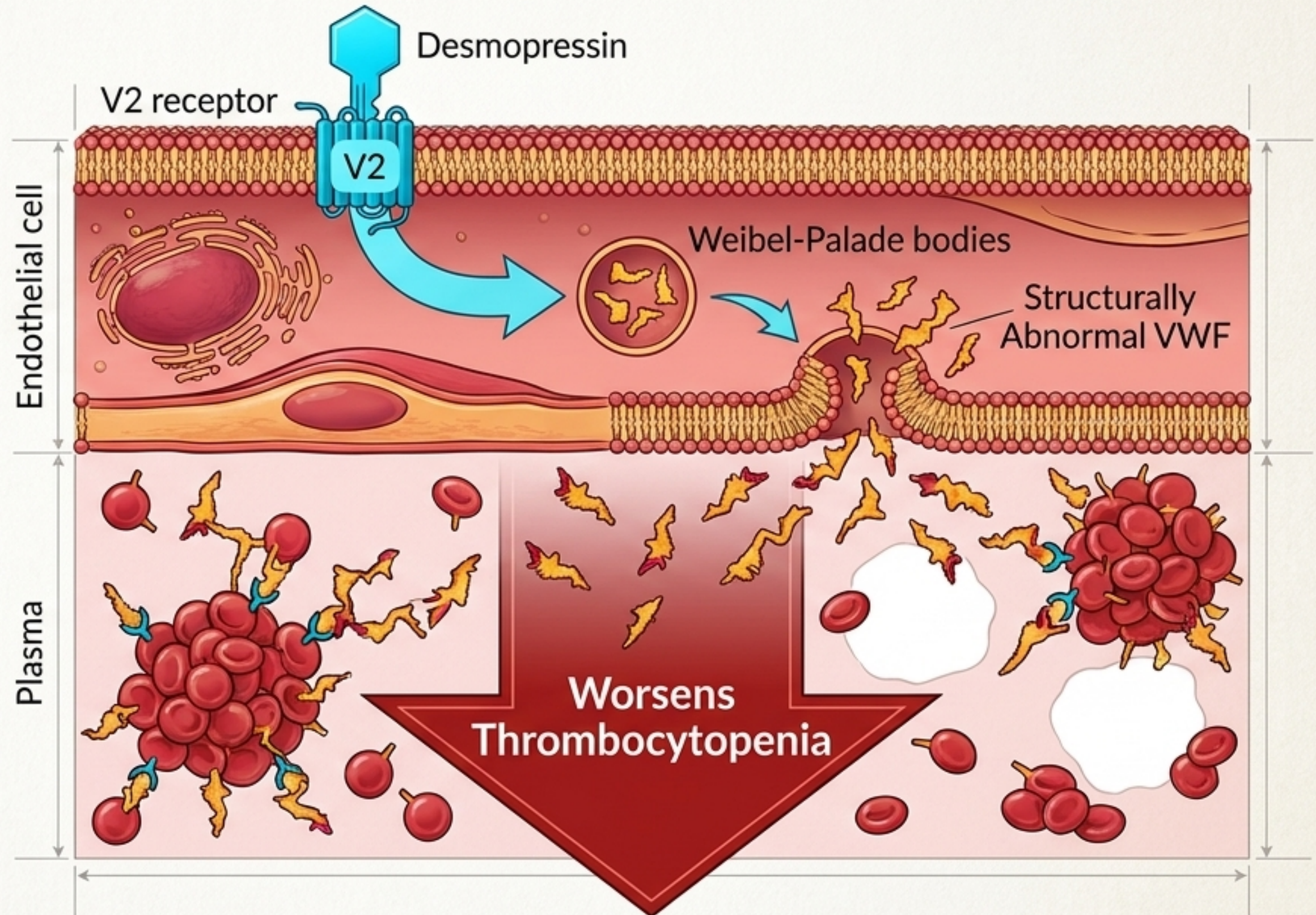
Diagnostic Subtype Matrix			
VWD Subtype	Vault Status	Expected Response	Clinical Action
Type 1	Intact but low capacity 	↑ Often highly responsive; predictable	✓ Prime candidate
Type 2A / 2M / 2N	Contains functionally abnormal VWF 	↘ Variable laboratory rise; function may remain impaired	🔍 Requires mechanistic interpretation
Type 3	Empty vault 	— Ineffective (no VWF to release) ✗	⊘ Avoid
Type 2B	Contains dangerous contents 	↓ Worsens thrombocytopenia	The principle is simple: no releasable reserve, no meaningful response.

The Type 2B Danger Zone: Releasing Harmful Contents

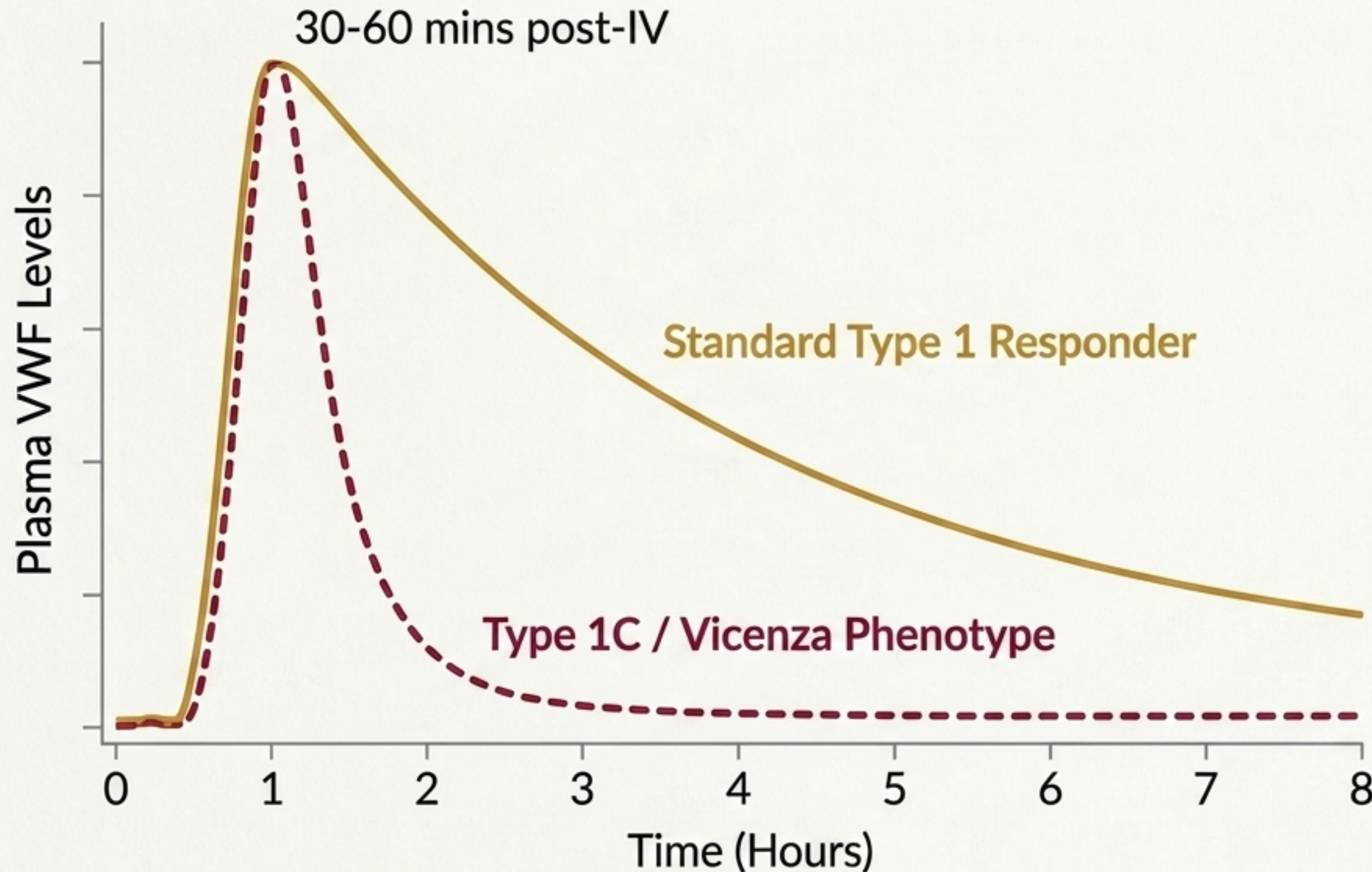
Releasing more VWF is not always helpful.

In Type 2B, mobilizing the reserve worsens abnormal VWF-platelet interaction and preferentially depletes high-molecular-weight multimers.

Desmopressin is strictly contraindicated.



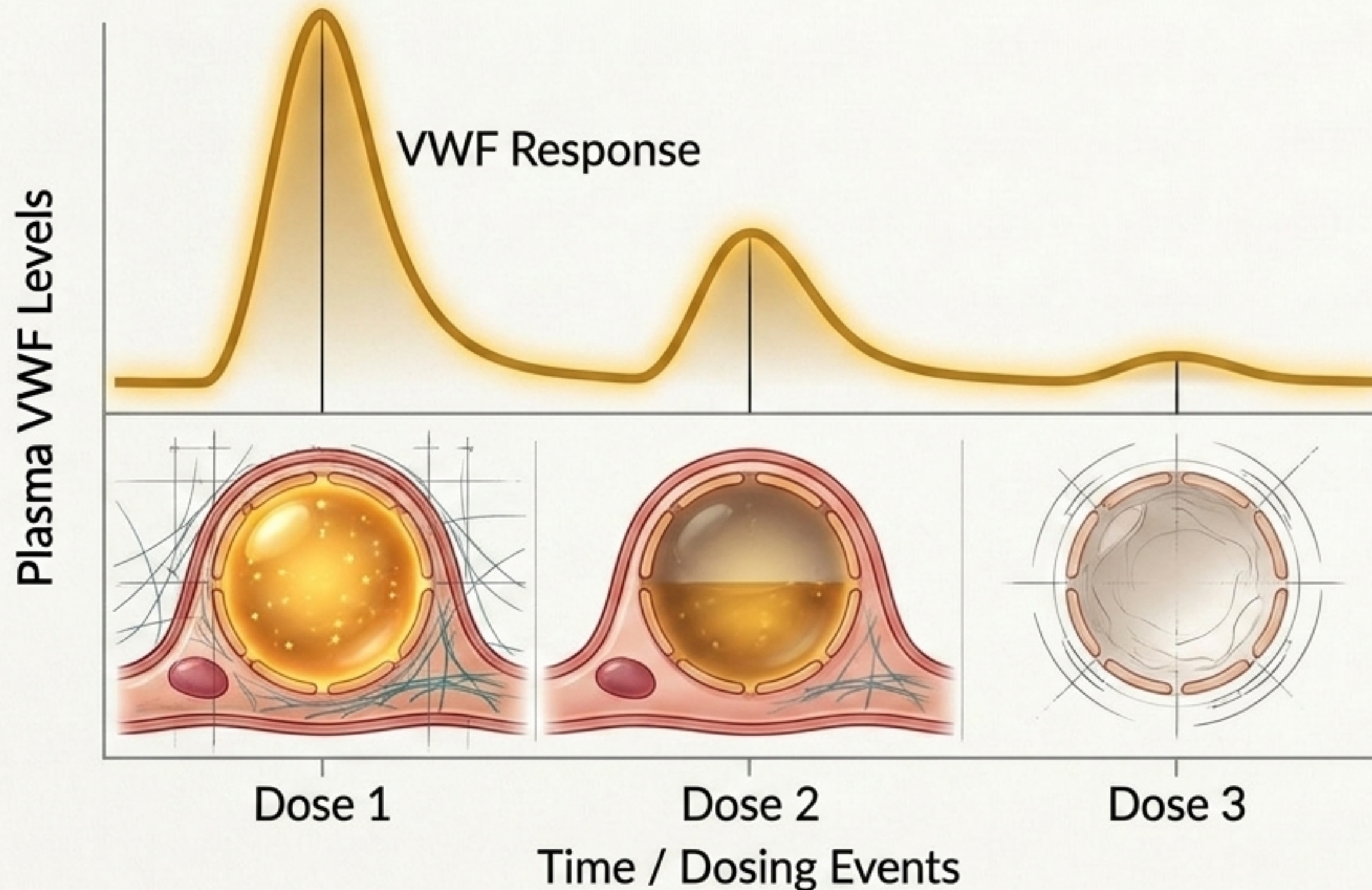
Temporary Correction Does Not Mean Permanent Normalization



A normal peak value (usually 30-60 mins post-IV) does not guarantee sustained hemostatic protection.

In accelerated clearance phenotypes (like Type 1C), the rapid fall rapid fall leaves the patient vulnerable during prolonged postoperative periods.

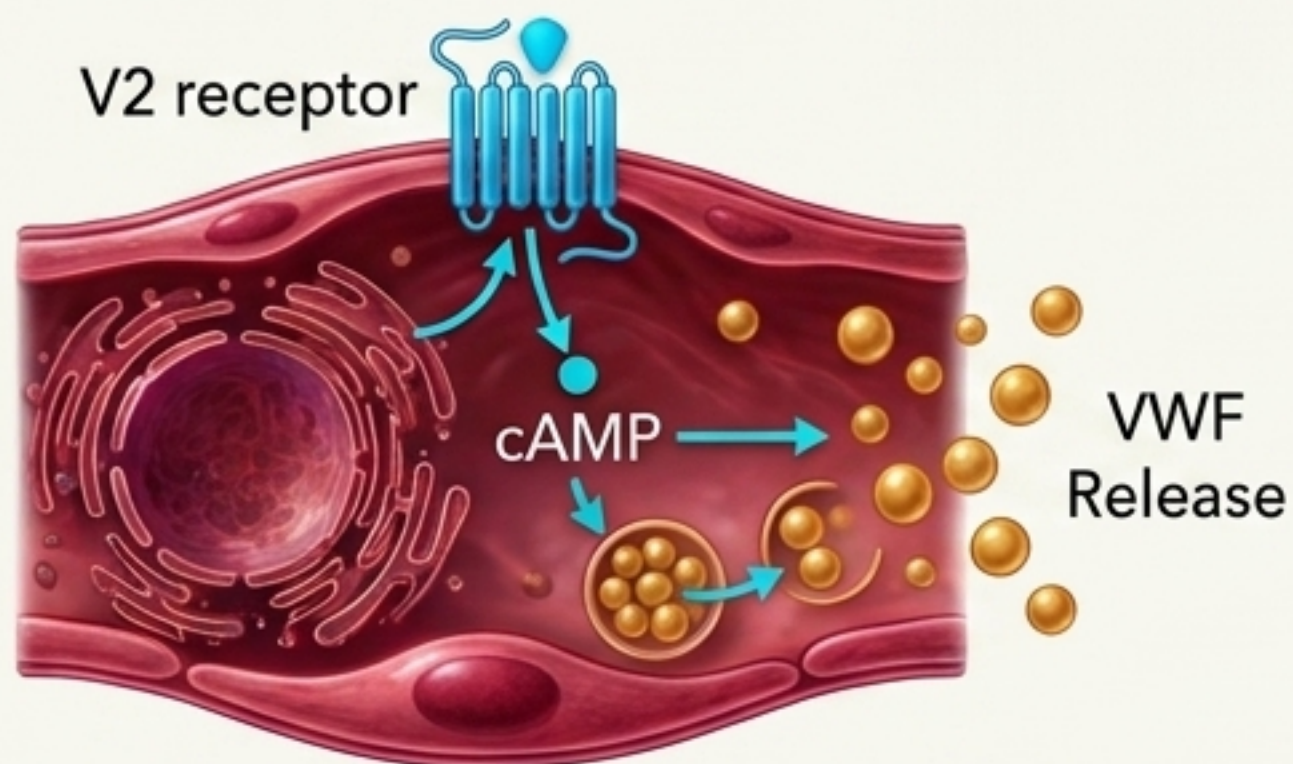
The Endothelium is Not an Infinite Reservoir



- ➡ Tachyphylaxis occurs because desmopressin does not stimulate immediate new synthesis—it only accelerates the release of what is already available.
- ➡ This limits its use to short hemostatic challenges rather than prolonged major surgical coverage.

The Duality of V2 Activation: Efficacy and Risk

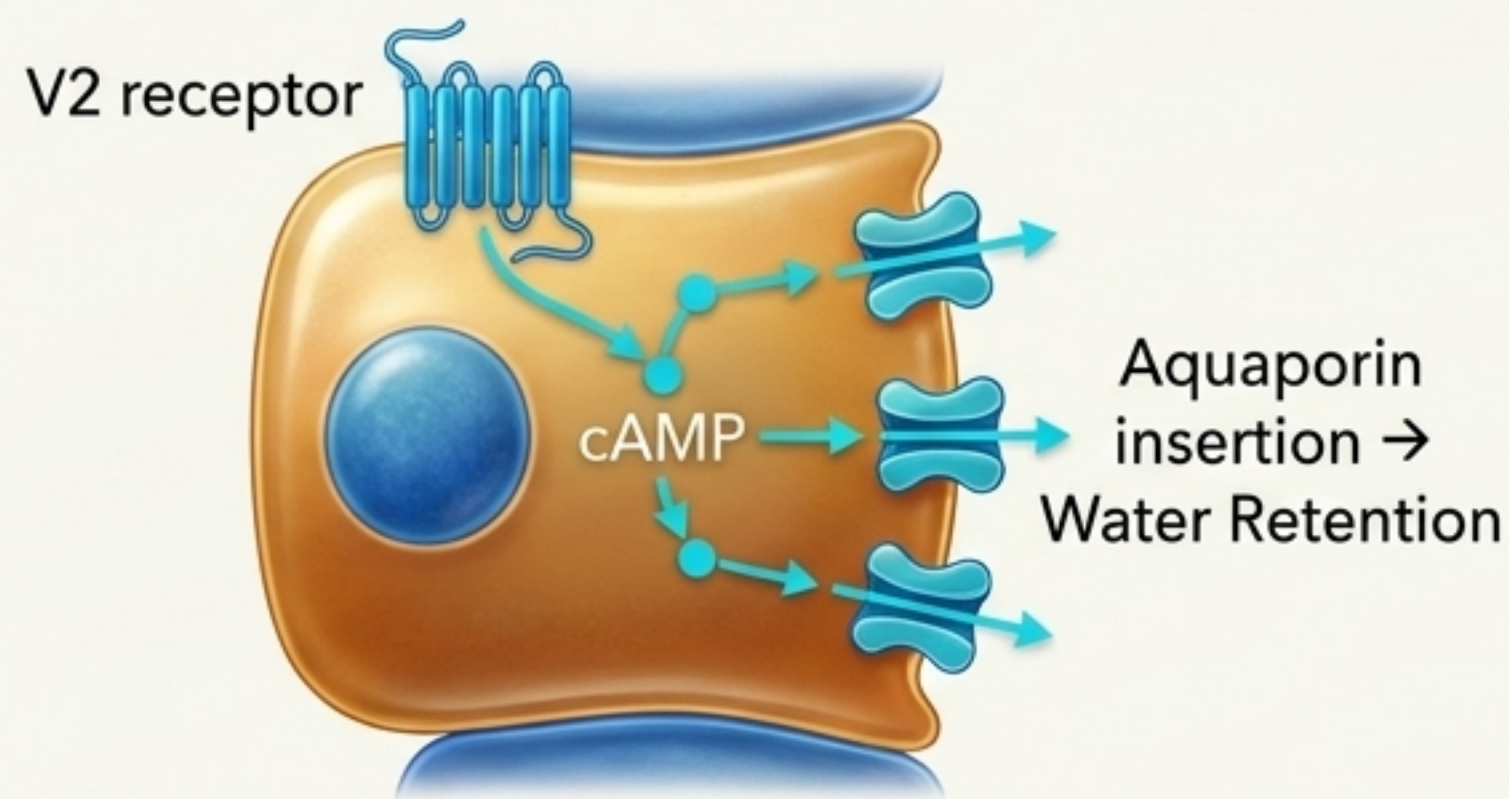
The Target



Benefit: Hemostasis

Requires strict fluid restriction and patient counseling. A prescription without a water plan is incomplete.

The Bystander



Risk: Hyponatremia

Contraindicated in high hyponatremia risk or uncontrolled hypertension.

Use caution in high thrombotic risk, severe cardiovascular disease, and very young age.

The Desmopressin Trial: Turning Uncertainty into a Plan

Valid candidate identified (e.g., Type 1) with anticipated future hemostatic challenge.

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graph TD; A[Valid candidate identified (e.g., Type 1) with anticipated future hemostatic challenge.] --> B[Guideline Focus: Trial strongly recommended if baseline VWF is < 0.30 IU/mL.]; B --> C[Do not empirically treat without prior trial results in this group.];
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Guideline Focus:
Trial strongly recommended if
baseline VWF is < 0.30 IU/mL.

Do not empirically treat without prior trial results in this group.

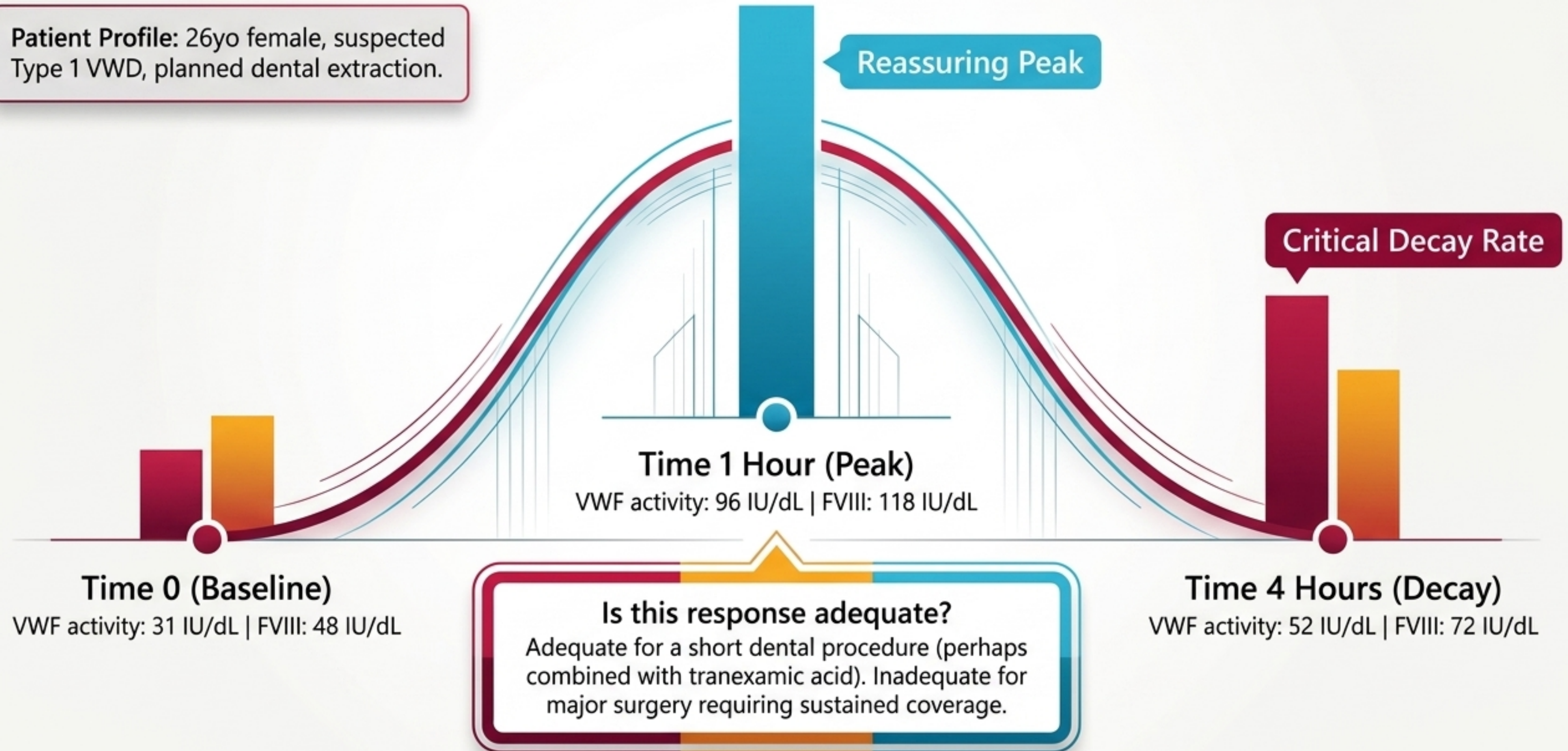
The trial asks a practical question:

Can this patient safely rely on their own endothelium?

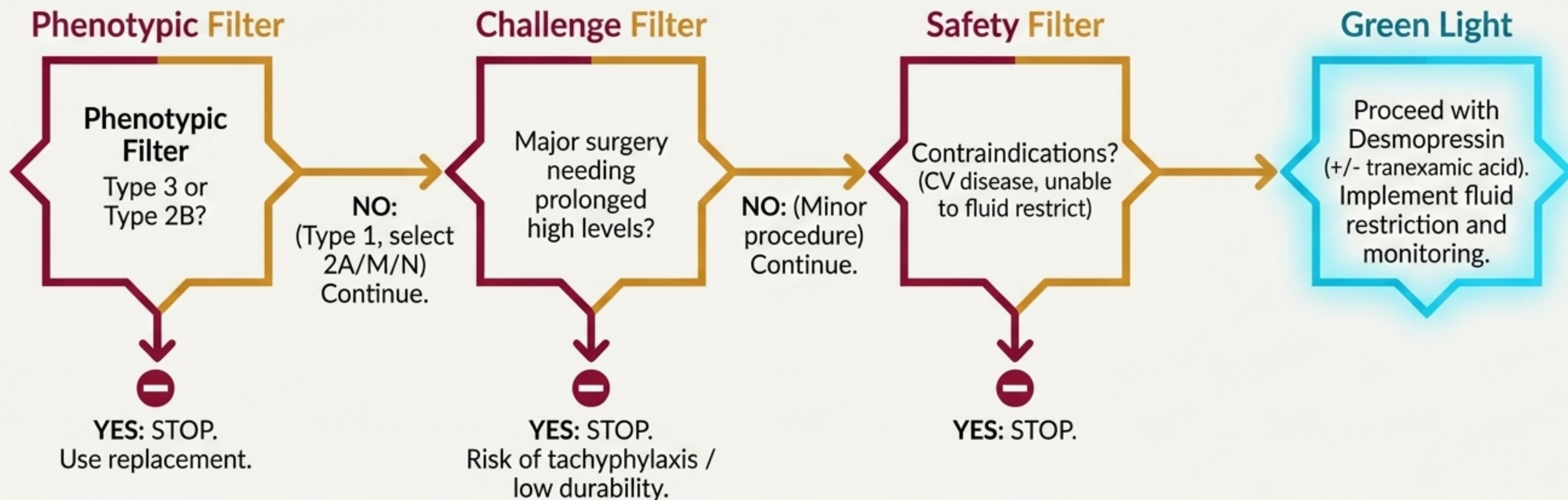
It tests for meaningful rise, sufficient durability, and clinical fit before the actual procedure.

Case Timeline: Why the 4-Hour Mark Matters

Patient Profile: 26yo female, suspected Type 1 VWD, planned dental extraction.

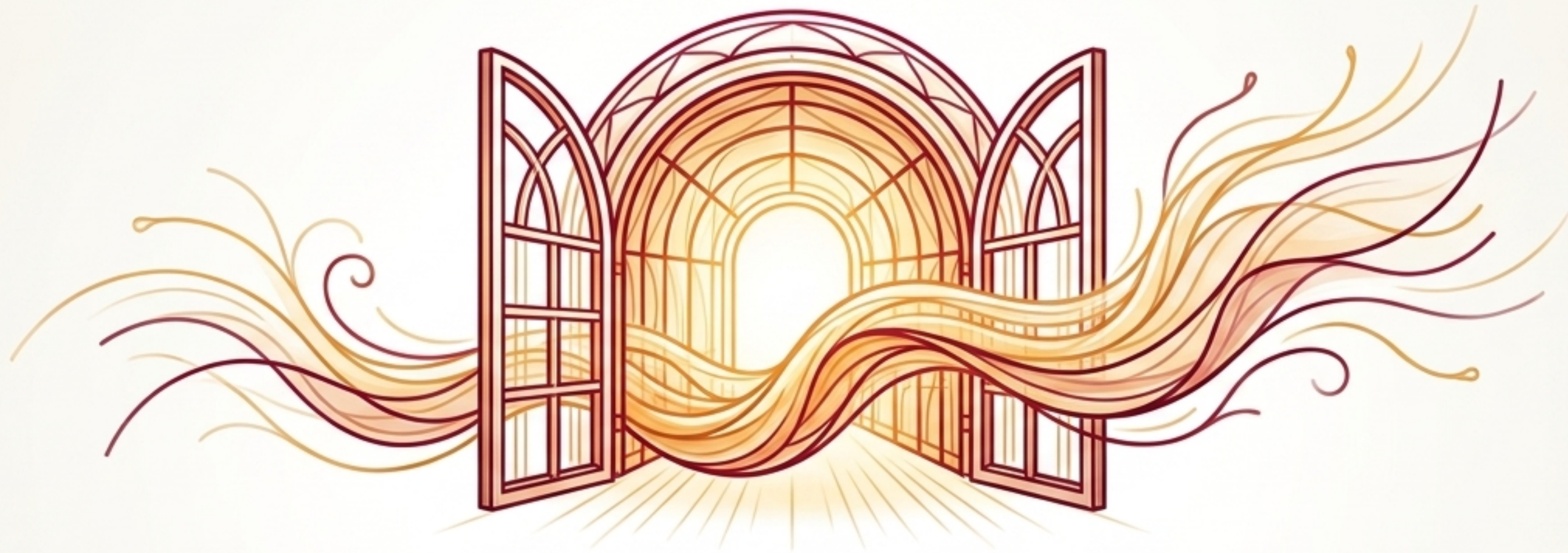


The Clinical Decision Framework



The choice is not always “replace the missing factor.”
Sometimes the better question is: Can we safely mobilize what is already there?

The Endothelium as an Active Hemostatic Organ



Therapy Reveals Biology

Desmopressin is not just a drug; it is a precise question asked of the endothelium's functional reserve.

Pattern Over Peak

A good peak value is meaningless without the durability to match the specific clinical challenge.

Mechanism Over Rote Rules

Understanding that you are mobilizing a finite vault makes tachyphylaxis and contraindications intuitive.

If the endothelium can answer, the drug may be elegant. If it cannot, replacement strategies are needed.