

Factor V Leiden

Factor V Leiden is the most common inherited clotting disorder in people of European ancestry. A single gene change makes one clotting protein last too long in the blood, raising the risk of abnormal blood clots in veins.

THE ONE-LINE TRUTH

Factor V Leiden is a genetic mutation that makes factor V resistant to protein C degradation, shifting the coagulation balance toward clot formation.

The chain — how it unfolds

1. Factor Va persists on platelet surfaces and continues generating thrombin — why: Without effective protein C cleavage, the prothrombinase complex (factor Va-Xa) remains active and produces excess thrombin in areas of sluggish blood flow
2. Excess thrombin converts more fibrinogen to fibrin and activates more platelets — why: High thrombin levels accelerate clot growth beyond what is needed for hemostasis, especially in veins where flow is slow and clotting factors accumulate
3. Fibrin meshwork forms in deep veins of legs or pelvis without clear injury — why: Prolonged sitting, dehydration, or minor endothelial damage provides enough trigger for unchecked thrombin generation to produce an inappropriate clot
4. A clot in a deep leg vein (Deep vein thrombosis) (DVT) obstructs venous return and causes leg swelling — why: Clot fills the vein lumen, blocking blood from draining back to the heart and causing blood and fluid to back up into leg tissues
5. Clot fragment breaks off and travels through right heart to pulmonary arteries — why: Muscle contraction or sudden movement dislodges part of the DVT, creating a pulmonary embolism (a clot lodging in a lung artery) (PE) that lodges in lung blood vessels
6. Pulmonary embolism (a clot lodging in a lung artery) blocks blood flow to lung segments, impairing gas exchange — why: Obstructed pulmonary arteries prevent blood from reaching alveoli (air sacs) for oxygen pickup, creating ventilation-blood flow (perfusion) mismatch and low oxygen in the blood (hypoxemia) (low blood oxygen)
7. Right ventricle strains against increased pressure from blocked lung vessels — why: Pulmonary artery obstruction raises afterload (resistance) on the right heart, which is thin-walled and not designed to pump against high pressure

- 8.** Massive PE causes right heart failure, cardiovascular collapse, and death — why: Right ventricle cannot maintain cardiac output against sudden severe pulmonary high blood pressure (hypertension), leading to shock, loss of blood pressure, and cardiac arrest if clot burden is large

Spot it — what you see, and why

- Leg swelling (unilateral): A clot in a deep leg vein (Deep vein thrombosis) (clot in deep leg veins) blocks blood return, causing fluid buildup in tissues downstream
- Leg pain or tenderness: A blood clot (Thrombus) (blood clot) stretches vein wall and triggers inflammation in surrounding tissue
- Sudden shortness of breath: Pulmonary embolism (a clot lodging in a lung artery) (clot travels to lung arteries) blocks oxygen exchange in alveoli (air sacs)
- Chest pain with deep breathing: Pulmonary embolism (a clot lodging in a lung artery) irritates pleura (lung lining), which has pain nerves that fire with lung expansion
- No symptoms at baseline: Factor V Leiden creates hypercoagulable state (increased clotting tendency) but requires trigger like surgery or pregnancy to form clots
- Recurrent miscarriages: Microthrombi (tiny clots) form in placental vessels, reducing oxygen delivery to developing fetus

Red flags — act now

- Sudden shortness of breath with chest pain suggests pulmonary embolism (a clot lodging in a lung artery) requiring emergent CT angiography
- Leg swelling with warmth and cord-like vein needs urgent ultrasound for a clot in a deep leg vein (deep vein thrombosis)
- Family history of multiple clots before age 50 indicates high-risk thrombophilia requiring testing
- Clot in unusual site (hepatic vein, cerebral sinus) suggests severe combined thrombophilia needing hematology consultation

Treat it — in this order

- 1.** Anticoagulation for acute VTE → Prevents clot propagation (growth) by blocking thrombin generation, allowing endogenous fibrinolysis (natural clot breakdown) to dissolve existing a blood clot (thrombus) over weeks
- 2.** Avoid estrogen-containing contraceptives → Eliminates 30-fold VTE risk increase from estrogen-induced changes in clotting factor production and natural anticoagulant reduction

3. Thromboprophylaxis during high-risk periods → Temporary anticoagulation during surgery, pregnancy, or immobility prevents stasis-triggered clot formation (thrombosis) when baseline hypercoagulability meets environmental risk
4. Extended anticoagulation after unprovoked VTE → Reduces recurrent VTE rate from 10% per year to 1% per year by maintaining therapeutic anticoagulation in patients with permanent thrombophilia
5. Compression stockings for post-thrombotic syndrome → Graduated compression (20-30 mmHg) reduces venous high blood pressure (hypertension) (high pressure) from damaged valves, decreasing leg swelling and pain

Your top priorities at the bedside

1. Monitor for signs of a clot in a deep leg vein (deep vein thrombosis) (DVT) and pulmonary embolism (a clot lodging in a lung artery) (PE) — why: Factor V Leiden increases clot risk by making blood resistant to protein C (a natural anticoagulant). DVT causes leg swelling and pain; PE causes sudden shortness of breath and chest pain and can be fatal.
2. Educate patient about when to seek emergency care for clot symptoms — why: Early recognition saves lives. Teach patients to call 911 for sudden chest pain, trouble breathing, coughing up blood, severe leg swelling, or leg pain that worsens with walking.
3. Review all medications and supplements that increase clot risk — why: Birth control pills and hormone therapy containing estrogen dramatically raise clot risk in Factor V Leiden patients. Smoking also multiplies risk. These must be avoided or alternatives found.