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BACKGROUND

D-dimer is a small protein fragment in the blood after a clot is degraded by fibrinolysis. It contains two D fragments of the fibrin protein joined by a cross-link. D-dimer levels, measured by a blood test, help diagnose thrombosis and are used to exclude deep vein thrombosis (DVT) or pulmonary embolism (PE). They also guide decisions on anticoagulation in patients with unprovoked venous thromboembolism (VTE). D-dimer assays vary, affecting their performance. This review outlines D-dimer assays, discusses raising the D-dimer threshold for VTE diagnosis based on pretest probability and age, and provides clinical perspectives on D-dimer testing in VTE diagnosis and prognosis.

METHODS

During hemostasis, fibrin clots form in response to vascular injury and are later broken down by the fibrinolytic system. D-dimers are fragments produced when plasmin, an enzyme, cleaves fibrin. These fragments consist of two covalently bound fibrin D domains cross-linked by factor XIII. D-dimer assays use monoclonal antibodies to target these unique epitopes, confirming thrombin generation in the coagulation cascade (Figure 1).

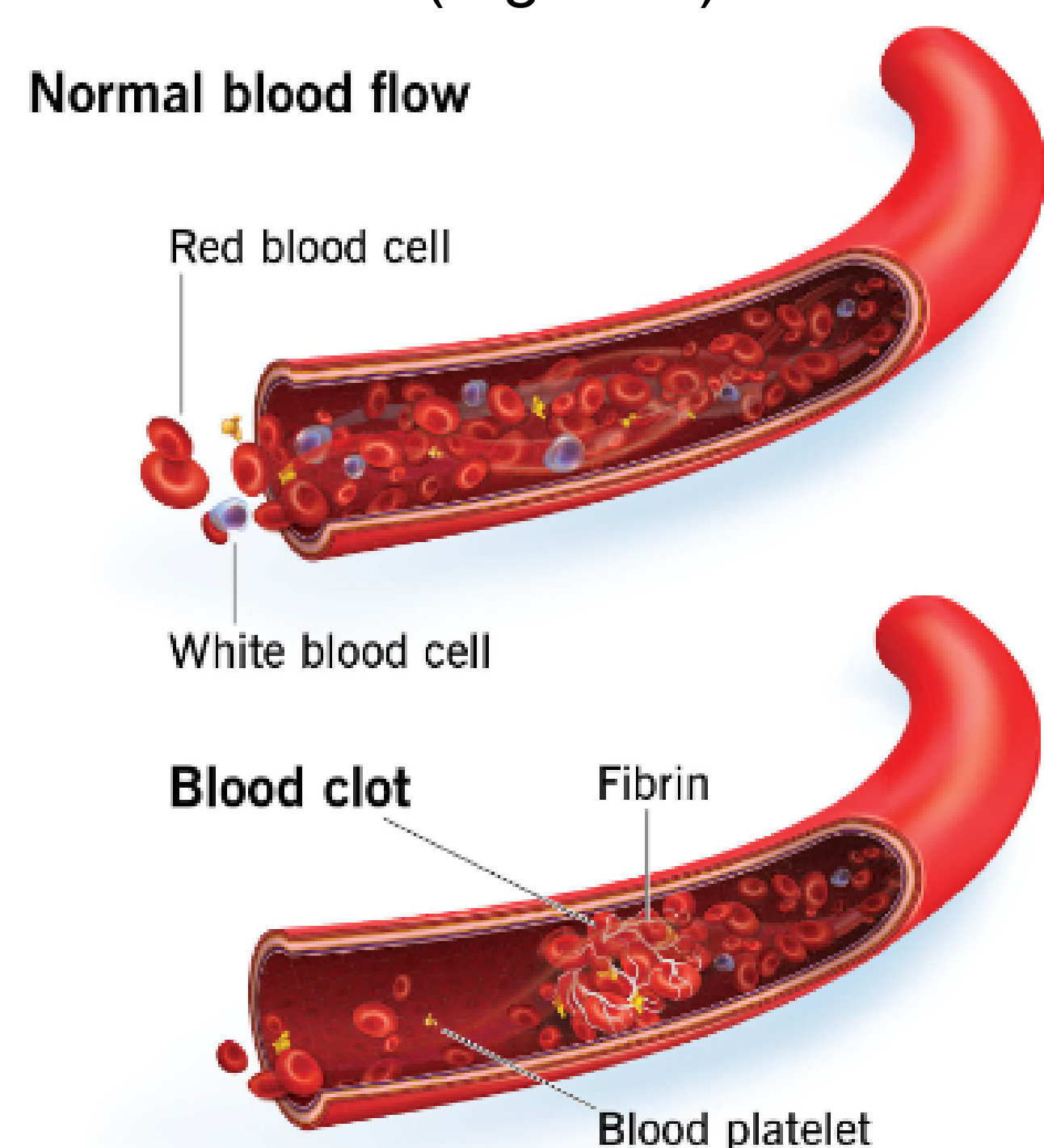


Figure 1: A D-dimer test measures protein fragments that release when a blood clot dissolves.

NORMAL LEVELS FOR D-DIMER

A normal D-dimer is considered less than 0.50 mg/L. A positive D-dimer is 0.50 or greater. False negatives and false positives can occur. D-dimer measurement is a very important step in VTE diagnosis, as it allows clinicians to rule out the disease in around 30% of outpatients with suspected DVT or PE. However, the test is less useful in elderly patients > 50 years.

WHAT IS D-DIMER?

When blood clots break down, they produce fibrin degradation products (FDPs), including D-dimer, a protein fragment. D-dimer levels of 0.50 mg/L or higher may indicate blood clots. A D-dimer test measures these levels to help detect deep vein thrombosis (DVT), pulmonary embolism (PE), and other clots. D-dimer is usually undetectable unless a clot is breaking down. This test can identify increased clotting activity, aiding in diagnosing coagulation disorders. However, D-dimer tests can result in false positives and negatives. Blood clotting is crucial to prevent excessive bleeding after injury, and the body dissolves clots once healing occurs.

With a blood clotting disorder, clots can form when the person doesn't have an obvious injury or does not dissolve when they should. These conditions can be very serious and even life-threatening. A D-dimer test can show if one has one of these conditions (Figure 2 for Coagulation Cascade).

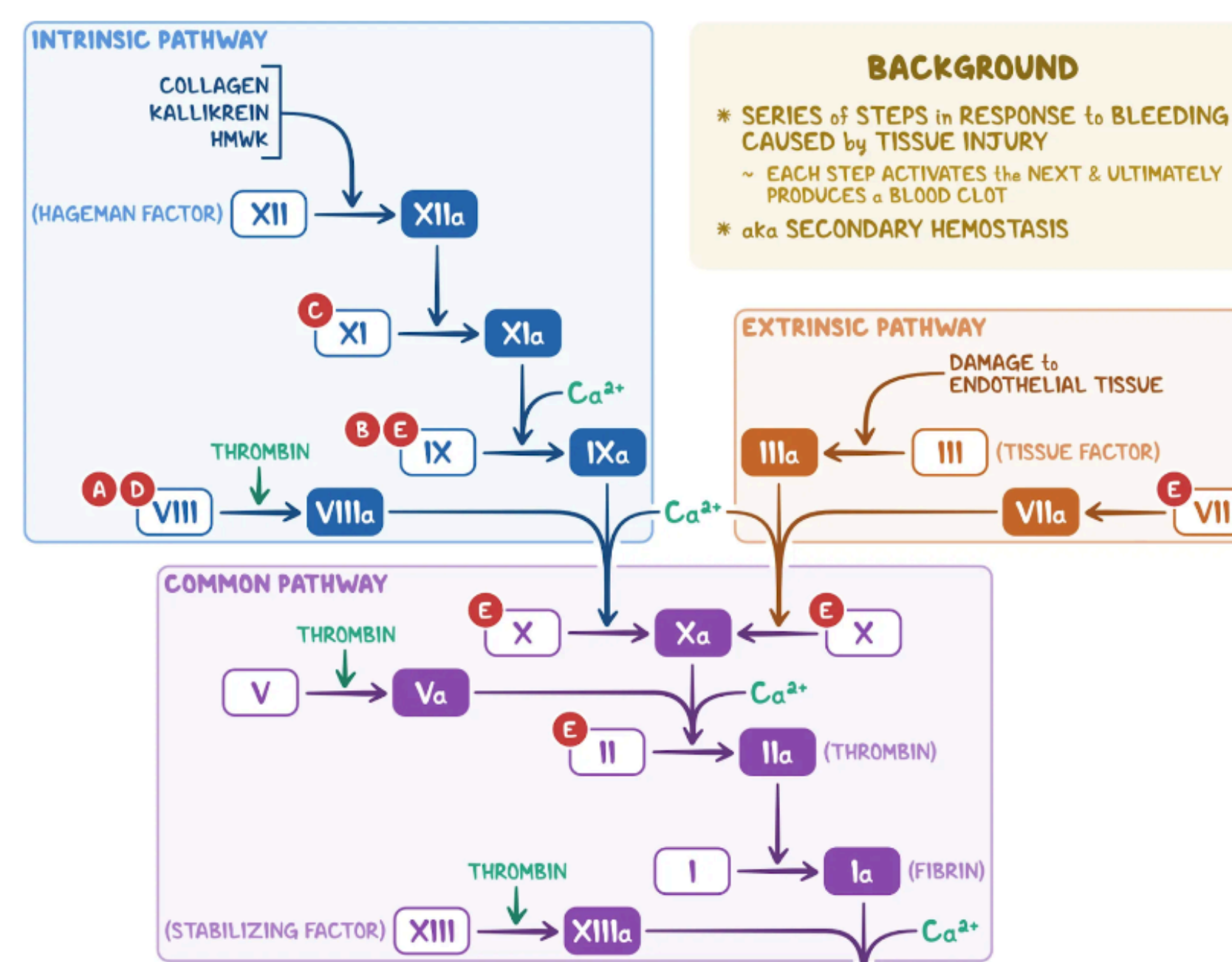


Figure 2: Coagulation Cascade

DISORDERS CAUSED BY ABNORMALITIES IN THE D-DIMER TEST

Deep vein thrombosis (DVT), a blood clot that's deep inside a vein. These clots usually affect the lower legs, but they can also happen in other parts of the body (Figure 3).

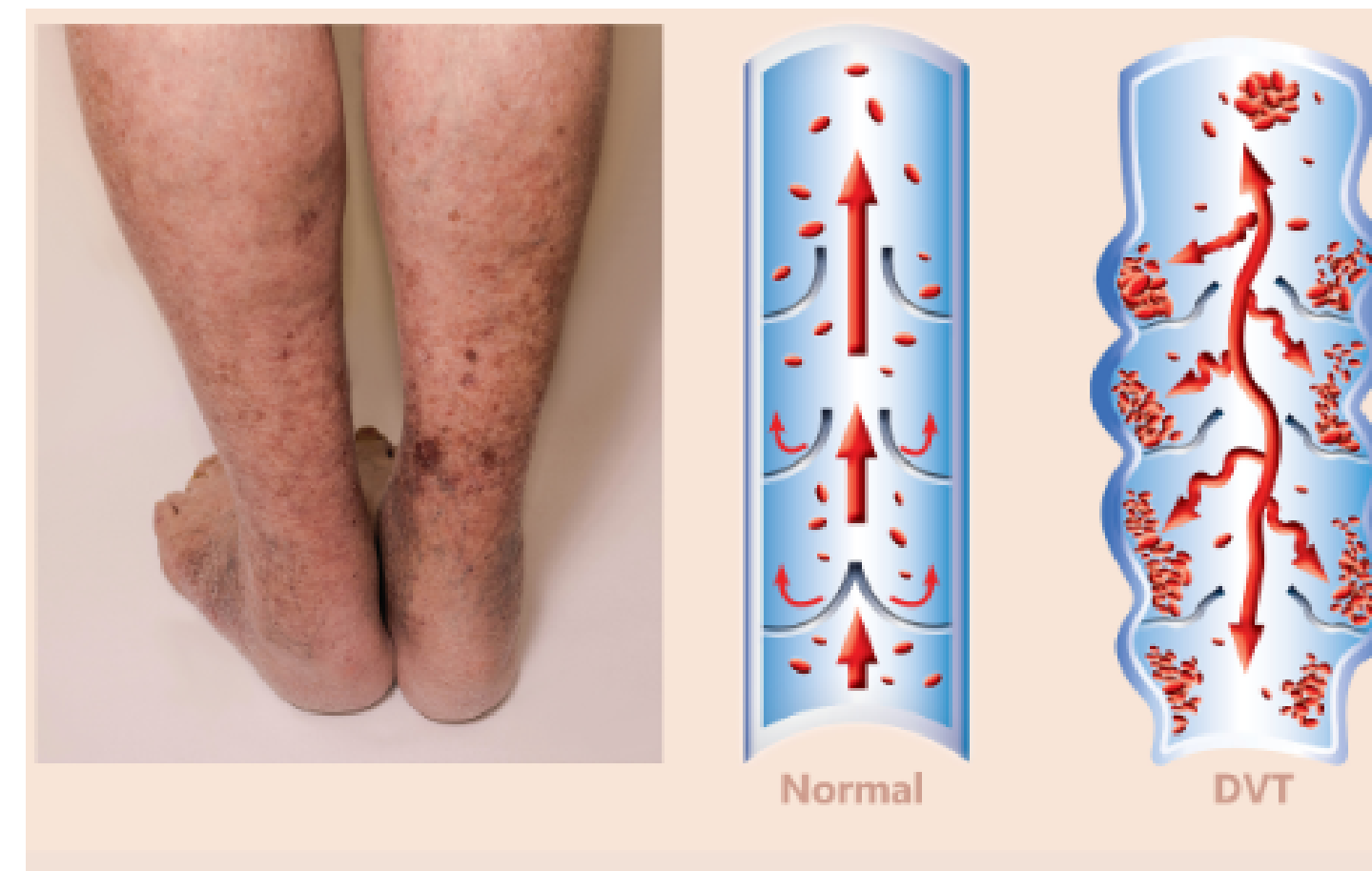


Figure 3: Formation of DVT

SYMPTOMS OF DVT

- Leg pain or tenderness
- Leg swelling
- Redness or red streaks on the legs
- Pulmonary embolism (PE), a blockage in an artery in the lungs. It usually happens when a blood clot in another part of the body breaks loose and travels to the lungs. DVT clots are a common cause of PE (Figure 4).

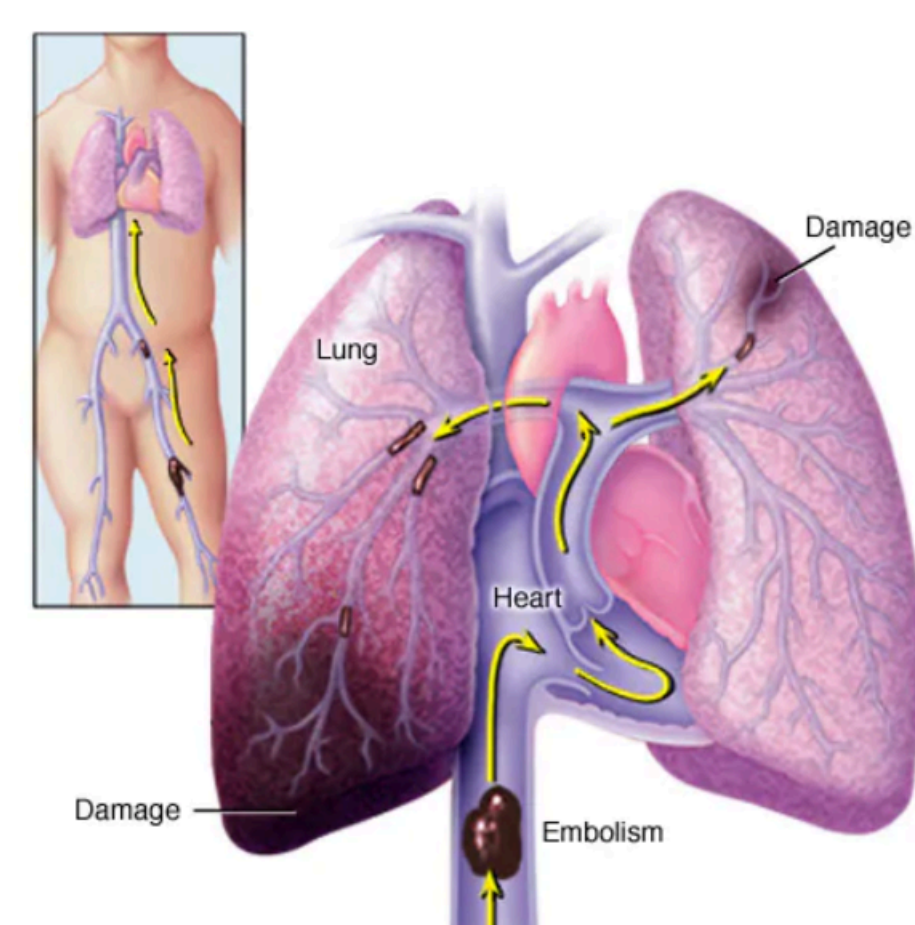


Figure 4: Formation of PE

SYMPTOMS OF PE

- Trouble breathing
- Cough
- Chest pain
- Rapid heartbeat
- Disseminated intravascular coagulation is a condition where excessive blood clots form throughout the body, leading to organ damage and serious complications. It can be triggered by traumatic injuries, infections, or cancer.
- Stroke, a blockage in the blood supply to the brain.

QUESTIONS

Where is the D-dimer test performed?

It is often done in an emergency room or other health care setting.

What happens during a D-dimer test?

A small amount of blood sample from a vein in the arm is obtained

Interpretation of D-dimer results

If results show low or normal D-dimer levels in the blood, it means that the person probably doesn't have a clotting disorder.

- If results show higher than normal levels of D-dimer, it may mean there may be a clotting disorder.
- D-dimer test cannot show where the clot is located or what type of clotting disorder the person has.
- D-dimer levels are not always caused by clotting problems. Other conditions that can cause high D-dimer levels include pregnancy, heart disease, and recent surgery.

REFERENCE RANGE

D-dimer is the degradation product of crosslinked (by factor XIII) fibrin. It reflects ongoing activation of the hemostatic system. The reference concentration of D-dimer is < 250 ng/mL, or < 0.4 µg/mL

WHAT CONDITIONS CAN D-DIMER DIAGNOSE?

D-dimer tests can detect a variety of blood clotting disorders, which can include:

- Pulmonary embolism (PE): A pulmonary embolism is a blockage in the artery that supplies blood to the lungs, caused by a blood clot that travels and becomes lodged in the lung's blood vessels. This can disrupt blood flow and gas exchange, potentially becoming life-threatening.
- Deep vein thrombosis (DVT): Occurs when a blood clot forms in a deep vein. DVT can damage vein valves and may break free, leading to serious complications.
- Disseminated intravascular coagulation: Describes a widespread hypercoagulable state

A positive D-dimer test indicates high levels of proteins related to blood clot formation and breakdown, suggesting a possible clotting condition. A typical result likely means no acute blood clot or abnormal clotting. A wide variety of factors can cause elevated D-dimer levels, including: pregnancy, cigarette smoking, physical trauma, cancer, infections, sepsis, old age, immobility, autoimmune disease.

REFERENCES

1. Cleveland Clinic: [D-Dimer Test: What It Is, What It Is Used For, Risks & Results](#)
2. Webmd: [D-Dimer Test: What It Is and How It Works](#)
3. Osmosis: [D-dimer: What Is It, Testing, and More | Osmosis](#)
4. [Definition of platelet - NCI Dictionary of Cancer Terms - Cancer.gov](#)
5. [What Are Platelets In Blood.](#) - Red Cross Blood
6. [us.com/coag/coagpro.html](#) - RNCenus