Partial Thromboplastin Time, Activated

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Reference Range

Partial thromboplastin time (PTT) and activated partial thromboplastin time (aPTT) are used to test for the same functions; however, in aPTT, an activator is added that speeds up the clotting time and results in a narrower reference range. The aPTT is considered a more sensitive version of the PTT and is used to monitor the patient's response to heparin therapy.

The reference range of the aPTT is 30-40 seconds.

The reference range of the PTT is 60-70 seconds.

Critical values that should prompt a clinical alert are as follows:

- aPTT: More than 70 seconds (signifies spontaneous bleeding)
- PTT: More than 100 seconds (signifies spontaneous bleeding) [1, 2]

Interpretation

A prolonged aPTT result may indicate the following[1, 2] :

- Congenital deficiencies of intrinsic system clotting factors such as factors VIII, IX, XI, and XII, including hemophilia A (Christmas disease) and hemophilia B (two inherited bleeding disorders resulting from a deficiency in factors VIII and IX, respectively)
- Congenital deficiency of Fitzgerald factor (prekallikrein)
- Von Willebrand disease, which is the most common inherited bleeding disorder, affecting platelet function owing to decreased von Willebrand factor activity
- Hypofibrinogenemia
- Liver cirrhosis (the liver makes most of the clotting factors, including those that are vitamin K-dependent ones); diseases of the liver may result in an inadequate quantity of clotting factors, prolonging the aPTT
- Vitamin K deficiency: The synthesis of some clotting factors requires vitamin K, so vitamin K deficiency results in an inadequate quantity of intrinsic system and common pathways clotting factors, as a result the aPTT is prolonged
- Disseminated intravascular coagulation (DIC): The clotting factors involved in the intrinsic pathway are consumed, prolonging the aPTT
- Heparin therapy, which inhibits the intrinsic pathway at several points (eg, prothrombin II), prolonging the aPTT [3]
- Coumarin therapy, which inhibits the function of factors I, IX and X, prolonging the aPTT
- Nonspecific inhibitors, such as lupus anticoagulant and anticardiolipin antibodies, which bind to phospholipids on the surface of platelets
- Specific circulating anticoagulants, inhibitor antibodies that specifically target certain coagulation factor, such as in individuals with hemophilia after many plasma transfusions, systemic lupus erythematosus, rheumatoid arthritis, tuberculosis, and chronic glomerulonephritis

A shortened aPTT result may indicate the following[1, 2] :

- Early stages of DIC: circulating procoagulants exist in the early stages of DIC, shortening the aPTT
- Extensive cancer (eg, ovarian cancer, pancreatic cancer, colon cancer)
- Immediately after acute hemorrhage
- An acute-phase response leading to high factor VIII levels

Collection and Panels

Many drugs can change the results of the activated partial thromboplastin time (aPTT), including nonprescription drugs.[1]

No specific preparation is required. However, since lipemia may interfere with photoelectric measurements of clot formation, specimens should not be obtained after a meal.[4]

If the patient is receiving heparin by intermittent injection, the sample should be drawn 30-60 minutes before the next dose, while, if the patient is receiving a continuous heparin infusion, the sample can be drawn at any time.[1]

Factors that interfere with the aPTT test are include the following[1, 2] :

1. **The reference range of the aPTT is 30-40 seconds.**
Anchor Name: Ref range of the aPPT is 30-40 seconds
[Agency UK becky.stirk@hansonzandi.co.uk]

2. **The reference range of the aPTT is 30-40 seconds.**
Anchor Name: aPTT
[Agency W2O - Claudia Alves]

- Drugs that may prolong the test values, including antihistamines, ascorbic acid, chlorpromazine, heparin, and salicylates
- Incorrect blood-to-citrate ratio
- Hematocrit that is highly increased or decreased
- Blood samples drawn from heparin lock or a heparinized catheter

Specimen preparation [4, 5]

Usually, 5 mL of citrated, platelet-poor plasma is prepared from 4.5 mL of peripheral venous blood collected via venipuncture and drawn directly into a blue-top tube that contains 0.5 mL of the anticoagulate sodium citrate at a ratio of 9:1.

Invert the tubegently several times to mix the anticoagulant, but do not agitate it.

After collection, the whole blood sample is centrifuged, and the plasma is removed and placed in another blue-top tube.

The plasma should be stored covered at 4°C. The test should be run within 4 hours of collection.

Keep the specimen cool because a high temperature alters the results.

Related tests

Related tests include the following[1, 5] :

- Prothrombin time (PT)
- Coagulation factor concentration
- Fibrinogen testing
- Thrombin time testing
- Platelet counts

Background

Description

Partial thromboplastin time (PTT) and activated partial thromboplastin time (aPTT) are used to test for the same functions; however, in aPTT, an activator is added that speeds up the clotting time and results in a narrower reference range. The aPTT is considered a more sensitive version of the PTT and is used to monitor the patient's response to heparin therapy.

The aPTT test is used to measure and evaluate all the clotting factors of the intrinsic and common pathways of the clotting cascade by measuring the time (in seconds) it takes a clot to form after adding calcium and phospholipid emulsion to a plasma sample. The result is always compared to a control sample of normal blood.

The aPTT evaluates factors I (fibrinogen), II (prothrombin), V, VIII, IX, X, XI and XII.

When the aPTT test is performed in conjunction with prothrombin time (PT) test, which is used to evaluate the extrinsic and common pathways of the coagulation cascade, a further clarification of coagulation defects is possible. If, for example, both the PT and aPTT are prolonged, the defect is probably in the common clotting pathway, and a deficiency of factor I, II, V, or X is suggested. A normal PT with an abnormal aPTT means that the defect lies within the intrinsic pathway, and a deficiency of factor VIII, IX, X, or XIII is suggested. A normal aPTT with an abnormal PT means that the defect lies within the extrinsic pathway and suggests a possible factor VII deficiency.[1, 2, 5, 6]

Normal hemostasis

Normal hemostasis is achieved when there is a balance between factors that encourages clotting and factors that encourages clot dissolution. Following damage to a blood vessel, the first reaction of the body is vascular constriction to reduce blood loss. In small-vessel injury, this may be enough to stop bleeding. However, for large blood vessels, hemostasis is required.

Primary hemostasis occurs within seconds and results in platelet plug formation at sites of injury.Next, secondary hemostasis occurs, which consists of the reactions of the plasma coagulation system that result in fibrin formation. It requires several minutes for completion. The fibrin strands that are produced strengthen the primary hemostatic plug.

In the first phase of reactions, called the intrinsic system, 3 plasma proteins, Hageman factor (factor XII), high-molecular-weight kininogen, and prekallikrein, form a complex on vascular subendothelial collagen, and, through a series of reactions, activated factor XI (XIa) is formed and activates factor IX (IXa). Then, a calcium- and lipid-dependent complex is formed between factors VIII, IX, and X, and activated X (Xa) is formed.

At the same time, the extrinsic system is activated and provides a second pathway to initiate coagulation by activating factor VII (VIIa). In this pathway, a complex formed between factor VII, calcium, and tissue factor results in activation of factor VII (VIIa). VIIa can directly activate factor X and activated X (Xa) is formed. Alternatively, both factors IX and X can be activated more directly by factor VIIa, generated via the extrinsic pathway. Activation of factors IX and X provides a link between the intrinsic and extrinsic coagulation pathways.

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The final step, the common pathway, converts prothrombin II to thrombin (IIa) in the presence of activated V (Va), activated X (Xa), calcium, and phospholipid. The main purpose of thrombin (IIa) is the conversion of fibrinogen to fibrin, which is then polymerized into an insoluble gel. The fibrin polymer is then stabilized by the cross-linking of fibrin polymers by factor XIII.

Clot lysis and vessel repair begin immediately after the formation of the definitive hemostatic plug. Three potential activators of the fibrinolytic system, Hageman factor fragments, urinary plasminogen activator, and tissue plasminogen activator, diffuse from endothelial cells and convert plasminogen, which had previously been adsorbed to the fibrin clot, into plasmin. Plasmin then degrades fibrin polymer into small fragments, which are cleared by the macrophages.[7]

Indications/Applications

aPTT is indicated for the following[1, 2, 5] :

- Unexplained bleeding or bruising
- Thrombotic episode or recurrent miscarriages
- To evaluate the effectiveness of drug therapy (eg, unfractionated heparin therapy)
- To assess the integrity of the intrinsic and final common pathways
- As part of a presurgical screen (if the patient has a history of bleeding or easy bruising)
- As part of an evaluation for lupus anticoagulant or anticardiolipin antibodies
- As part of coagulation panel workup

Considerations

Because factors II, IX, and X are vitamin K–dependent, biliary obstruction, which precludes gastrointestinal absorption of fat and fat-soluble vitamins (including vitamin K), can reduce their concentrations and thus prolong the aPTT.[1]

aPTT is used to monitor heparin anticoagulant therapy; however, it cannot be used to monitor therapy with newer low-molecular-weight heparin.[1, 2]

Prolonged aPTT is usually followed by mixing studies (when the cause is not obvious, eg, due to heparin contamination or to other preanalytical problems such as an insufficient or clotted blood sample) to evaluate for deficient coagulation factor(s) or a coagulation inhibitor(s).

In mixing studies, the patient's plasma is mixed with normal plasma. If mixing the two plasma samples corrects the aPTT result, there is clotting factor deficiency, and specific coagulation factor testing is performed to determine which factor(s) is deficient. If the mixing fails to correct the aPTT results within 3-4 seconds, it strongly suggests (1) a coagulation factor inhibitor (eg, an acquired factor VIII antibody) or (2) an antiphospholipid antibody or lupus anticoagulant (a nonspecific inhibitor). In this case, the aPTT result will not correct with normal plasma mixing but it will usually correct if an excess of phospholipid is added to the sample. If lupus anticoagulant is suspected, a more sensitive test, lupus anticoagulant–sensitive aPTT or Dilute Russell Viper Venom Test, should be performed.[2]

Contributor Information and Disclosures

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References

1. Pagana KD, Pagana TJ, eds. (2010). *Mosby's Manual of Diagnostic and Laboratory Tests*. 4th ed. St. Louis: Mosby Elsevier; Chap 2. Blood Studies.
2. Fischbach FT, Dunning MB III, eds. (2009). *Manual of Laboratory and Diagnostic Tests*. 8th ed. Philadelphia: Lippincott Williams and Wilkins; chap 6. Overview of Chemistry Studies.
3. Yie K, Chon SD, Na CY. Activated clotting time test alone is inadequate to optimize therapeutic heparin dosage adjustment during post-cardiopulmonary resuscitational extracorporeal membrane oxygenation (e-CPR). *Perfusion*. 2015 Sep 9. [Medline].
4. Estridge B .H, Reynolds A.P, Walters N.G eds.(2000). *Basic Medical Laboratory Techniques*. 4th ed. Delmar: Cengage Learning; unit 3.Basic hemostatsis.
5. Daniels R, ed. (2009). *Delmar's Guide to Laboratory and Diagnostic Tests*. 2nd ed. Delmar: Cengage

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Learning;

6. Tripodi A, Lippi G, Plebani M. How to report results of prothrombin and activated partial thromboplastin times. *Clin Chem Lab Med*. 2015 Aug 6. [Medline].
7. Kasper D L, Braunwald E, Fauci A S, Hauser S L, Longo D L, Jameson J. L, et al. *Harrison's of Internal Medicine*. 16th ed. United States of America: McGraw-Hill; part two: Cardinal Manifestation And Presentation Of Diseases, section 10:Hematology Alteration, Bleeding And Thrombosis, p.373.

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