

## Overview

### Useful For

Identification of heredity elevation or deficiency of plasminogen activator inhibitor type 1

Determination of risk for veno-occlusive disease associated with bone marrow transplantation

Differential diagnosis of impaired fibrinolysis

Prognostic marker of occurrence or recurrence of thrombosis

### Special Instructions

- [Coagulation Guidelines for Specimen Handling and Processing](#)

### Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

### NY State Available

Yes

## Specimen

### Specimen Type

Plasma Na Cit

### Specimen Required

**Specimen Type:** Platelet-poor plasma

**Collection Container/Tube:** Light-blue top (citrate)

**Submission Container/Tube:** Plastic vial (polypropylene preferred)

**Specimen Volume:** 1 mL

#### Collection Instructions:

1. For complete instructions, see [Coagulation Guidelines for Specimen Handling and Processing](#).
2. Centrifuge, transfer all plasma into a plastic vial, and centrifuge plasma again.
3. Aliquot plasma into a plastic vial leaving 0.25 mL in the bottom of centrifuged vial.
4. Freeze plasma immediately (no longer than 4 hours after collection) at -20 degrees C or, ideally below -40 degrees C.

**Specimen Stability Information:** Frozen 2 years

#### Additional Information:

1. Double-centrifuged specimen is critical for accurate results as platelet contamination may cause spurious results.
2. Each coagulation assay requested should have its own vial.

## Forms

[If not ordering electronically, complete, print, and send a Coagulation Test Request \(T753\)](#) with the specimen.

## Specimen Minimum Volume

0.5 mL

## Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

## Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma Na Cit	Frozen (preferred)		

## Clinical & Interpretive

### Clinical Information

Plasminogen activator inhibitor type 1 (PAI-1) antigen is a single-chain glycoprotein (molecular weight 43 kDa) produced by endothelial cells and hepatocytes and is also present in alpha granules of platelets. PAI-1 is a serine protein inhibitor that is secreted in response to inflammatory reactions. Platelet alpha granules contain large amounts of PAI-1, which is released during vascular injury and assists in fibrin clot stability. PAI-1 is synthesized in the active form but has marked functional instability and a functional half-life of about 2 hours in vivo. Circulating PAI-1 is bound to vitronectin, which protects the inhibitor from inactivation and may assist in targeting the inhibitor to sites of vascular injury. At least 4 different conformations of PAI-1 have been described

- 1) The active form that reacts with plasminogen activator
- 2) A latent form that is nonreactive
- 3) A substrate form that can be cleaved by plasminogen activators but is noninhibitory
- 4) The inert form of PAI-1 generated by the cleavage of the reactive site

PAI-1 is the main inhibitor of tissue-type plasminogen activator (tPA) and urokinase plasminogen activator (uPA) and, as such, plays an important role in the regulation of fibrinolysis. Elevated levels of PAI-1 result in deficient plasminogen activation and are associated with a predisposition to thrombosis, including veno-occlusive disease (VOD) after bone marrow transplantation (BMT).

Primary injury to the hepatic sinusoidal endothelium and hepatocytes induced by high-dose chemoradiotherapy is believed to be the key event in the pathogenesis of VOD. The clinical diagnosis of VOD is complex because the clinical signs and symptoms can occur as a result of other processes that can complicate the posttransplant period such as sepsis, graft-versus-host disease (GVHD), cyclosporine toxicity, other medications, hemolysis, or parenteral nutrition. Liver biopsy, although safer since the widespread introduction of transjugular procedures, remains hazardous in this thrombocytopenic population. A sensitive and specific assay would be invaluable in guiding management and avoiding

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potentially hazardous invasive diagnostic procedures. Along these lines several investigators have studied various markers of hypercoagulability for possible pathogenic and predictive relevance. Aside from serum bilirubin level, no laboratory marker has been standardized as a diagnostic marker of VOD and the severity of VOD remains retrospectively defined. Lee et al analyzed 115 patients after allogeneic BMT in an attempt to identify diagnostic and severity markers of VOD. Of the 115 patients, 50 developed VOD.(1) Multiple logistic regression models were constructed that included recognized relevant clinical and hemostatic variables. Of the hemostatic variables, only PAI-1 antigen was identified as an independent marker for the occurrence of VOD. This confirmed the findings of a previous, smaller study that PAI-1 is a powerful diagnostic marker of VOD during the early period post-BMT and can distinguish VOD from other causes of hyperbilirubinemia post-BMT, such as GVHD and drug toxicity. Furthermore, PAI-1 antigen and bilirubin were independent variables for predicting severe VOD.

Familial thrombosis has been associated with inherited elevation of plasma PAI-1 activity. Increased levels of PAI-1 have also been reported in many conditions including malignancy, liver disease, the postoperative period, septic shock, the second and third trimesters of pregnancy, obesity, and coronary heart disease.

Low plasma levels of the active form of PAI-1 have been associated with abnormal, clinically significant bleeding. Complete deficiency of PAI-1, either congenital or acquired, is associated with bleeding manifestations that include hemarthroses, hematomas, menorrhagia, easy bruising, and postoperative hemorrhage.

**Reference Values**

3.0-72.0 ng/mL

**Interpretation**

Increased levels of plasminogen activator inhibitor type 1 (PAI-1) are associated with a predisposition to thrombosis.

Decreased or absent levels of detectable functional PAI-1 will result in a life-long bleeding diathesis.

**Cautions**

The plasminogen activator inhibitor type 1 (PAI-1) level shows a diurnal variation with the highest levels occurring in the morning.

The PAI-1 level increases during pregnancy and decreases rapidly after delivery.

The extremely rare presence of antimouse antibodies in certain patients may lead to anomalous results.

Inappropriate specimen collection and processing may lead to platelet activation and release of platelet PAI-1. Consequently, care must be taken to remove all platelets and minimize platelet activation during specimen collection and processing.

**Clinical Reference**

1. Lee JH, Lee KH, Lee JH, et al: Plasminogen activator inhibitor-1 is an independent diagnostic marker as well as severity predictor of hepatic veno-occlusive disease after allogeneic bone marrow transplantation in adults conditioned with busulphan and cyclophosphamide. *Br J Haematol.* 2002 Sep;118(4):1087-1094
2. Stiko A, Hervio L, Loskutoff DJ: Plasminogen activator inhibitors. In: Colman RW, Hirsh J, Marder VJ, et al, eds. *Hemostasis and Thrombosis.* Lippincott; 2001:355-365

3. Vaughn DE, Declerck PJ: Regulation of fibrinolysis. In: Loscalzo J, Schager A, eds. Thrombosis and Hemorrhage. Lippincott; 2003:389-396
4. Goodnight SH Jr, Hathaway WE: Fibrinolytic defects and thrombosis. In: Disorders of Hemostasis and Thrombosis: A Clinical Guide. McGraw-Hill Book Company; 2001:389-396
5. Kruihof EK, Gudinchet A, Bachman F: Plasminogen activator inhibitor-1 and plasminogen activator inhibitor-2 in various disease states. Thromb Haemostasis. 1988;59(1):7-12
6. Salat C, Holler E, Kolb HJ, et al: Plasminogen activator inhibitor-1 confirms the diagnosis of hepatic veno-occlusive disease in patients with hyperbilirubinemia after bone marrow transplantation. Blood. 1997;89:2184-2188
7. Fay WP, Shapiro AD, Shih JL, Schleef RR, Ginsburg D: Brief report: complete deficiency of plasminogen-activator inhibitor Type 1 due to a frame-shift mutation. N Engl J Med. 1992 Dec 10;327(24):1729-1733
8. Heiman M, Gupta S, Khan SS, et al: Complete plasminogen activator inhibitor 1 deficiency. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews [Internet]; 2017 Accessed July 7, 2022. Available at [www.ncbi.nlm.nih.gov/books/NBK447152/](http://www.ncbi.nlm.nih.gov/books/NBK447152/)

## Performance

### Method Description

Testing is performed on the Janus G3 liquid handler and BioTek microplate reader with Gen5 software using the Diagnostica Stago, Inc. Asserachrom PAI-1 kit. The method used is an enzyme-linked immunosorbent assay (ELISA). Microtiter plate wells are coated with mouse monoclonal antihuman PAI-1 antibody, which captures the PAI-1 in the sample. Next, a second antibody (mouse monoclonal antihuman PAI-1) coupled with peroxidase binds to another antigenic site distant from the first antibody, forming the "sandwich." The bound enzyme peroxidase is then visualized based on its ability to produce a color reaction when exposed to ortho-phenylenediamine and hydrogen peroxide. The reaction is stopped by the addition of a strong acid (1N HCl). The intensity of the color produced is directly proportional to the PAI-1 concentration in the plasma sample. (Package insert: ASSERACHROM PAI-1. Diagnostica Stago S.A.S; 03/2015)

### PDF Report

No

### Day(s) Performed

Wednesday

### Report Available

7 to 12 days

### Specimen Retention Time

7 days

### Performing Laboratory Location

Rochester

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**Fees & Codes****Fees**

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).

**Test Classification**

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

**CPT Code Information**

85415

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
PAI1	PAI-1 Ag, P	22758-7

Result ID	Test Result Name	Result LOINC® Value
86083	PAI-1 Ag, P	22758-7