**Prothrombin Time**

Prothrombin time (PT) is a blood test that measures how long it takes blood to clot. A prothrombin time test can be used to check for bleeding problems. PT is also used to check whether medicine to prevent blood clots is working.

About 12 blood clotting factors are needed for blood to clot (coagulation). Prothrombin, or factor II, is one of the clotting factors made by the liver. Vitamin K is needed to make prothrombin and other clotting factors. Prothrombin time is an important test because it checks to see if five different blood clotting factors (factors I, II, V, VII, and X) are present. The prothrombin time is made longer by:

- Blood-thinning medicine, such as heparin. Another test, the activated partial thromboplastin time (APTT) test, is a better test to find out if the right dose of heparin is being used.
- Low levels of blood clotting factors.
- A change in the activity of any of the clotting factors.
- The absence of any of the clotting factors.
- Other substances, called inhibitors that affect the clotting factors.
- An increase in the use of the clotting factors.

An abnormal prothrombin time is often caused by liver disease or injury or by treatment with blood thinners.

Another blood clotting test, called partial thromboplastin time (PTT), measures other clotting factors. Partial thromboplastin time and prothrombin time are often done at the same time to check for bleeding problems or the chance for too much bleeding in surgery.

The prothrombin time (PT) and its derived measures of prothrombin ratio (PR) and international normalized ratio (INR) are measures of the *extrinsic pathway* of coagulation. They are used to determine the clotting tendency of blood, in the measure of warfarin dosage, liver damage and vitamin K status. The reference range for prothrombin
time is usually around 12-15 seconds; the normal range for the INR is 0.8-1.2. PT measures factors II, V, VII, X and fibrinogen. It is used in conjunction with the activated partial thromboplastin time (aPTT) which measures the intrinsic pathway.

Prothrombin time (PT) is measured to:

- Find a cause for abnormal bleeding or bruising.
- Check to see if blood-thinning medicine, such as warfarin (Coumadin), is working. If the test is done for this purpose, a PT may be done every day at first. When the correct dose of medicine is found, you will not need so many tests.
- Check for low levels of blood clotting factors. The lack of some clotting factors can cause bleeding disorders such as hemophilia, which is passed in families (inherited).
- Check for a low level of vitamin K. Vitamin K is needed to make prothrombin and other clotting factors.
- Check how well the liver is working. Prothrombin levels are checked along with other liver tests, such as aspartate aminotransferase and alanine aminotransferase.
- Check to see if the body is using up its clotting factors so quickly that the blood cannot clot and bleeding does not stop. This may mean the person has disseminated intravascular coagulation (DIC).

The prothrombin time can be measured roughly on whole blood (which is done in newborns), but is more commonly measured from blood plasma. Blood is drawn into a test tube containing liquid citrate. Citrate acts as an anticoagulant by binding the calcium in a sample. The blood is mixed, and then centrifuged to separate blood cells from plasma.

The plasma is analyzed by a medical technologist on an automated instrument at 37°C, which takes a sample of the plasma. An excess of calcium is added (thereby reversing the effects of citrate), which enables the blood to clot again. For an accurate measurement the
proportion of blood to citrate needs to be fixed; many laboratories will not perform the assay if the tube is underfilled and contains a relatively high concentration of citrate. This is because Vacutainer test tubes generally contain a powdered anticoagulant to prevent blood from clotting. For the prothrombin time test the appropriate sample is the blue top tube, or citrate tube, which is a liquid anticoagulant. Just as adding solvent to any solution will dilute it, adding liquid anticoagulant to blood will dilute it. This dilution will cause a falsely long prothrombin time. So, all analysis takes this dilution into account by multiplying the result by 1.1 to account for the dilution. If a tube is underfilled or overfilled with blood, the standardized dilution of 1.1 is no longer valid.

Tissue factor (also known as factor III or thromboplastin) is added, and the time the sample takes to clot is measured optically. Some laboratories use a mechanical measurement, which eliminates interferences from lipemic and icteric samples.

The prothrombin ratio is the prothrombin time for a patient, divided by the result for control plasma.

**International normalized ratio**

Because of differences between different batches and manufacturers of tissue factor (it is a biologically obtained product), the INR was devised to standardise the results.

Each manufacturer gives an ISI (International Sensitivity Index) for any tissue factor they make. The ISI value indicates how the particular batch of tissue factor compares to an internationally standardized sample. The ISI is usually between 1.0 and 1.4.

The INR is the ratio of a patient’s prothrombin time to a normal (control) sample, raised to the power of the ISI value for the control sample used.

*Interpretation*
The prothrombin time is the time it takes plasma to clot after addition of tissue factor (obtained from animals). This measures the quality of the extrinsic pathway (as well as the common pathway) of coagulation.

The speed of the extrinsic pathway is greatly affected by levels of factor VII in the body. Factor VII has a short half-life and its synthesis requires vitamin K. The prothrombin time can be prolonged as a result of deficiencies in vitamin K, which can be caused by warfarin, malabsorption or lack of intestinal colonization by bacteria (such as in newborns). In addition, poor factor VII synthesis (due to liver disease) or increased consumption (in disseminated intravascular coagulation) may prolong the PT.

Factors determining accuracy

Lupus anticoagulant, a circulating inhibitor predisposing for thrombosis, may skew PT results, depending on the assay used. Variations between various thromboplastin preparations have in the past led to decreased accuracy of INR readings, and a 2005 study suggested that despite international calibration efforts (by INR) there were still statistically significant differences between various kits, casting doubt on the long-term tenability of PT/INR as a measure for anticoagulant therapy.

Normal values may vary from lab to lab.

A method of standardizing prothrombin time results, called the international normalized ratio (INR) system, has been developed so the results among labs using different test methods can be understood in the same way. Using the INR system, treatment with blood-thinning medicine (anticoagulant therapy) will be the same. In some labs, only the INR is reported and the PT is not reported.

| Prothrombin time (PT)           |
|-------------------------------|-------------------------|
| Normal:                       | 10–13 seconds           |

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International normalized ratio (INR): 1.0–1.4

The warfarin (Coumadin) dose is changed so that the prothrombin time is longer than normal (by about 1.5 to 2.5 times the normal value or INR values 2 to 3). Prothrombin times are also kept at longer times for people with artificial heart valves, because these valves have a high chance of causing clots to form.

Abnormal values

- A longer-than-normal PT can mean a lack of or low level of one or more blood clotting factors (factors I, II, V, VII, or X). It can also mean a lack of vitamin K; liver disease, such as cirrhosis; or that a liver injury has occurred. A longer-than-normal PT can also mean that you have disseminated intravascular coagulation (DIC), a life-threatening condition in which your body uses up its clotting factors so quickly that the blood cannot clot and bleeding does not stop.
- A longer-than-normal PT can be caused by treatment with blood-thinning medicines, such as warfarin (Coumadin) or, in rare cases, heparin.

Reasons you may not be able to have the test or why the results may not be helpful include:

- Taking medicines that can affect the action of blood thinners (such as warfarin) and vitamin K. These include antibiotics, aspirin, cimetidine (Tagamet), barbiturates, birth control pills, hormone replacement therapy (HRT), and vitamin K supplements.
- Having severe diarrhea or vomiting that causes fluid loss and dehydration. This may make the PT time longer. If diarrhea is caused by poor absorption of nutrients, vitamins, and minerals from the intestinal tract (malabsorption syndrome), the PT may be longer because of a lack of vitamin K.
• Eating foods that have vitamin K, such as beef liver, pork liver, green tea, broccoli, chickpeas, kale, turnip greens, and soyabean products.
• Drinking a lot of alcohol.
• Taking laxatives.
• Taking some herbal products or natural remedies.

Note:

• A PT is done at the same time of day each time so test results can check whether the right dose of medicine is being used to prevent blood clots.
• Another blood clotting test, called partial thromboplastin time (PTT), measures other clotting factors. Partial thromboplastin time and prothrombin time are often done at the same time to check for bleeding problems. For more information, see the medical test Partial Thromboplastin Time.
• Prothrombin levels are checked along with other liver tests, such as aspartate aminotransferase and alanine aminotransferase to check how the liver is working. For more information, see the medical tests Aspartate Aminotransferase (AST) and Alanine Aminotransferase (ALT).

The test result for PT depends on the method used, with results measured in seconds and compared to the average value in healthy people. Most laboratories report PT results that have been adjusted to the International Normalized Ratio (INR). Patients on anti-coagulant drugs should have an INR of 2.0 to 3.0 for basic “blood-thinning” needs. For some patients who have a high risk of clot formation, the INR needs to be higher - about 2.5 to 3.5. Your doctor will use the INR to adjust your drug to get the PT into the range that is right for you. A prolonged, or increased, prothrombin time means that your blood is taking too long to form a clot. If you are not taking anti-coagulant drugs and your PT is prolonged, additional testing may be necessary to determine the cause.
It is not generally necessary to have your PT/INR measured at a particular time of day. It is, however, important that you take your anti-coagulation medication at the same time each day to maintain a continuous level. If your doctor increases or decreases your dosage, they may want you to have your blood rechecked in a day or so to judge the effect of the dosage change on your PT/INR (it is not an immediate effect).