1. Ingestion of drugs that either promote or interfere with the absorption or action of warfarin
2. Marked changes in dietary ingestion of vitamin K
3. Exacerbation of underlying hepatic disease
4. Biliary obstruction
5. Profuse diarrhea or vomiting

F. A prothrombin time >40 seconds (with a mean of normal range of approximately 10 seconds) resulting from warfarin overdose may be critical enough to warrant immediate treatment with fresh frozen plasma or vitamin K. (See section on warfarin therapy.)

REFERENCES

1. Quick AJ, Stanley-Brown M, Bancroft FW: A study of the coagulation defect in hemophilia and in jaundice. Am J Med Sci 190:501-511, 1935.
2. Koepke JA, Gilmer PR, Triplett DA, O'Sullivan MB: The prediction of prothrombin time system performance using secondary standards. Am J Clin Pathol 68:191-194, 1977.

Partial Thromboplastin Time (PTT)

I. USEFUL IN:

A. Screening for the diagnosis of congenital or acquired deficiencies of coagulation proteins of the intrinsic pathway (Factors VIII, IX, XI, XII, prekallikrein, and high molecular weight kininogen)
B. Monitoring heparin therapy
C. Screening for inhibitors of Factors VIII, IX, or XI
D. Screening for the presence of a lupus anticoagulant
E. Diagnosis of disseminated intravascular coagulation (DIC), although it is a less sensitive test for DIC than the prothrombin time.

II. PRINCIPLE OF TEST: **A mixture of phospholipid (in partial thromboplastin) and calcium is incubated with citrated plasma and the time until clot formation is measured. The PTT may be performed as a one-step procedure without an activator, or may utilize an activator such as silica or kaolin (activated PTT or "aPTT") The majority of laboratories in the U.S. perform the aPTT, the normal range of which is much shorter than that of the PTT. Therefore, "PTT" is usually synonymous with "aPTT."**

III. PATIENT PREPARATION; COLLECTION/HANDLING OF SPECIMEN: **No patient preparation needed. Venous blood is collected in citrate (blue top Vacutainer). Specimens should be centrifuged at 1,500 x g, the plasma transferred to a plastic test tube, and then preserved on ice until the time of testing. DO NOT COLLECT BLOOD THROUGH A HEPARIN LOCK OR OTHER HEPARINIZED LINE. The presence of clot in the specimen is cause for rejection of the sample.**

IV. PROCEDURE

A. Reagents/Materials
1. General Diagnostics aPTT Reagent, or any commercially available aPPT reagent
2. Normal control plasma—one such plasma is General Diagnostics Verify Normal
3. Abnormal control plasmas—such as General Diagnostics Verify Abnormal I and II, which differ in their degree of abnormality
3. Patient plasma
4. Fibrometer (BBL) with attached 37°C heat block or any instrument used for automatic clot detection, such as the Coag-a-Mate X-2 (General Diagnostics).
5. 0.025 M CaCl2

B. Method—Fibrometer
(Method for automated testing is instrument dependent)
1. Reconstitute the PTT reagent with the recommended amount of distilled water.
2. Add 1 ml distilled water to each of the controls.

3. Put CaCl2 into a test tube and incubate it in the Fibrometer well at 37°C for at least 5 minutes.
4. Into a Fibrometer cup, pipet 0.1 ml patient plasma and 0.1 ml PTT reagent. Begin timing, shake to mix, and incubate in a fibrometer well at 37°C for 3 minutes.
5. At exactly 3 minutes, add 0.1 ml CaCl2 and simultaneously start timing. Record seconds until clot formation.
6. Each test should be performed in duplicate.

C. Calculations: Average the seconds for the duplicate specimens and report this as the patient's PTT.

D. Normal range: Each laboratory should establish its own normal range based on the PTT values of 50-100 normal subjects.

V. COMMENTS

A. Common causes of acquired deficiencies of one or more of the intrinsic pathway factors include:
1. Severe liver disease
2. Vitamin K deficiency

B. Inhibitors of Factors VIII and IX occur predominantly in severe hemophilia A and hemophilia B, respectively. However, they may occur spontaneously in other diseases. Inhibitors generally produce a marked prolongation in the PTT (See section on "Factor VIII Inhibitors.")

C. To distinguish a factor deficiency from an inhibitor in a patient with a prolonged PTT, an inhibitor screen ("1:1 mixing study") is performed, which consists of a PTT using equal volumes of normal plasma and patient plasma. If the PTT corrects completely, a deficiency of an intrinsic pathway factor should be suspected; if the PTT does not correct, an inhibitor should be suspected.

D. Deficiences of factors in the common pathway prolong the PT more than the PTT (in general); thus, although the PTT may be prolonged by a common pathway factor deficiency, the PT is used as a screening test for these deficiencies.

REFERENCE

1. Langdell RD, Wagner RH, Brinkhous KM: Effect of antihemophilic factor on one-stage clotting tests: A presumptive test for hemophilia and a simple one-stage antihemophilia factor assay procedure. J Lab Clin Med 41:637-647, 1953.
2. Proctor RR, Rapaport SI: The partial thromboplastin time with kaolin. Am J Clin Pathol 36:212-219, 1961.

1:1 Mixing Study for Prolonged PT (Inhibitor Screen)

I. USE: To determine if a prolonged PT is due to a deficiency of Factor II, V, VII, or X, or due to the presence of an inhibitor.

II. PRINCIPLE OF TEST: Equal portions of patient plasma (with a prolonged PT) and normal plasma are combined and incubated for various lengths of time, typically 0 minutes (immediately after mixing), 30 minutes, 60 minutes, and 120 minutes. A PT is performed with this mixture of plasmas. If the patient's prolonged PT corrects (is within the normal range) with the addition of normal plasma, a deficiency of one or more of the aforementioned coagulation factors is the cause of the prolonged PT; if the PT corrects partially or not at all, the prolonged PT is due to the presence of an inhibitor.

III. PATIENT PREPARATION; COLLECTION/HANDLING OF SPECIMEN: No patient preparation is necessary; blood is collected in citrate (blue-top Vacutainer tube). BLOOD MUST NOT BE COLLECTED THROUGH A HEPARIN LOCK OR OTHER HEPARINIZED LINE.

IV. PROCEDURE

A. Reagents/Materials