A Useful Modification of the Prothrombin Time

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A useful modification of the prothrombin time test is described. It compares favorably with the usual Quick prothrombin time method in results and has the advantages of universal applicability, even for difficult or problem cases, and convenience for patient and physician.

The introduction by Quick (1) of the prothrombin test supplied the medical profession with a very useful tool. This test is widely used today for control of anticoagulant therapy, as a preoperative test of hemostatic function, and as a liver function test, both in geriatric and pediatric practice. However, the methodology of the usual procedure either excludes or limits its employment for certain types of patients: the patient with poor or thrombosed veins, the apprehensive acute cardiac on anticoagulant treatment who becomes agitated upon venipuncture, the pediatric patient requiring repeated determinations, and others. This has given impetus for devising a modification of the prothrombin test which would have the advantages of being simple, dependable, universally applicable, and of supplying the physician with results in a short time, even in a large hospital service. It is the purpose of this paper to describe a modification of the prothrombin test which has been found applicable to every type of patient, employs a minimum amount of blood, and allows an accurate result to be recorded within 3–4 min. after obtaining the specimen.

Materials and Methods

1. Water bath Thermolyne Dri Bath† mounted on a small cart (Fig. 1)

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2. Pipets 0.1-ml. Alpha Pette*  
3. Lancets Redi-lance† sterile blood lancets (disposable)  
4. Thromboplatin Human brain thromboplastin prepared as described previously (2)  

![Fig. 1. Mobile prothrombin laboratory containing supplies, thermometer, electric bath, and light source.](image)

5. Calcium chloride 0.005M. solution made isosmotic with NaCl solution. This may be conveniently prepared by adding 17 ml. of 0.85% (w/v) NaCl solution to 5.0 ml. of 0.022 M. calcium chloride, which is usually used for the standard prothrombin time test.  

Determinations of Prothrombin Time

Equal volumes of thromboplastin and .005 M. calcium chloride solution were added to a clean, dry test tube, which was inverted gently several times for mixing and placed in the Dri Bath which was kept at a constant temperature of 37.5°. The mixture was allowed to incubate for at least 5 min. prior to use. The patient’s third or fourth finger was wiped with 70% alcohol and allowed to dry completely. Then a deliberate clean sharp puncture to the side of the finger was made using a sterile, disposable lancet. The patient’s finger was then gently squeezed, and a large drop of blood was allowed to run into a clean glass pipet by capillary action to the 0.1-ml. mark. The blood was then

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blown into a clean test tube (1-cm. I.D., 7.5 cm. long) containing 0.1 ml. of the thromboplastin calcium chloride mixture. A stop watch was started immediately upon contact of the blood with the thromboplastin-calcium chloride. The tube was twirled and, after 8 sec., it was removed and tilted for observation of the end point, which was a solid coagulum as in the usual prothrombin time technic.

Conversion of Clotting Time

Conversion of clotting time to "per cent prothrombin" was accomplished simply by preparing plasma having different percentages of prothrombin from various combinations of normal and "prothrombin-free plasma (3). Thereafter, the well-washed cell mass was added to the plasma in the proportion indicated by the hematocrit. The clotting times obtained from such known per cent prothrombin reconstituted whole-blood samples, were used to construct the curve of Fig. 2. Because of the one-ninth volume of 3.8% citrate used to collect such blood samples a modified calcium concentration of .022 M. made isosmotic with sodium chloride was employed in obtaining this curve.

Results

In Fig. 2 may be seen a calibration curve used to convert the clotting times obtained to "per cent prothrombin." In our hands the variation in clotting time determinations at the 100–75% prothrombin range

![Fig. 2. Prothrombin calibration curve used to convert clotting time to "per cent prothrombin." Nature of curve is highly dependent on thromboplastin reagent used in test.](image-url)
averaged approximately 0.7 sec. This equals ± 8% prothrombin. At the 20% prothrombin range, variation of repeat determinations was approximately 0.9 sec. This is equal to ± 1% prothrombin. In Fig. 3 may be seen a chart of the anticoagulant record of a patient controlled with this modification of the prothrombin test. The patient was a 56-year-old white male, who had had a myocardial infarction 1 year previously and was being maintained on Coumadin.* He was of apprehensive temperament and in addition had veins that were difficult to palpate. The numerous unsuccessful attempts at venipuncture led to the undesirable situation of a rebellious, apprehensive patient, in poor control. The incomplete record of his prothrombin response to anticoagulant therapy was an erratic sawtooth curve. At the start of using this modified test, his prothrombin was 66% of normal. Figure 3 indicates the dose-response curve obtained with this test. Not indicated are the patient's response and physician's response, both of which were much more gratifying. In Fig. 4 may be seen a correlation between the prothrombin times of the hospital laboratory done by Quick's method and those obtained with this modification. The line of theoretically perfect correlation is shown. Its formula is \( y = 1.00x + 0.00 \). The actual regression formula was \( y = 0.94x - 1.74 \). In view of the variability of prothrombin determinations done in most routine hospital laboratories, the correlation is fairly acceptable. It must be emphasized that the laboratories, personnel, methods, blood samples,

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**Fig. 3.** Dose-response curve record of patient. Because of difficulties of venipuncture and temperament, patient was in poor control prior to use of this modification of prothrombin time test.
reagents, and calibration curves were entirely different. Furthermore, the operational procedure was quite different. In the case of this modification of the test, one technician was sent to the hospital floors early in the morning, with a cart containing, in essence, a mobile

![Graph](image)

**Fig. 4.** Correlation between prothrombin results of hospital laboratory and modification of prothrombin time test. Laboratories, personnel, methods, blood samples, reagents, and calibration curves were entirely different for the two tests.

prothrombin laboratory (Fig. 1). In the patient’s room, the electric Dri Bath was connected to the room receptacle, the patient’s finger punctured, duplicate determinations performed, and results read directly from a calibration curve, recorded, and left at the nurses’ station for the physician’s morning rounds.

**Discussion**

A useful modification of the prothrombin time test has been described. It has been found to have definite technical and practical advantages over previously described micro methods (4–10). It was applicable to all patients, including such problem cases as those with poor veins, the obese, the apprehensive cardiac, the pediatric case requiring multiple or daily determinations, and others. It presents the further advantage of using only a minimum of blood, of eliminating the time and effort of collection of specimens, and of providing information to the physician in 3–4 minutes. Variation in hematocrit has been found to have minor and negligible effect on results.

The test has no theoretical advantages over the usual Quick method. It supplies no more information than the usual prothrombin time test. Further, it is subject to the same errors and precautions as the Quick prothrombin time test.
The greatest variable in both cases is the thromboplastin reagent. It is generally preferable to avoid commercial reagents prepared from or containing lung or other highly vascular tissue, since blood contamination and insensitivity to Factor X depresses results. Furthermore, batch differences and time deterioration are associated with such products. Animal brain or human brain preparations are preferable.

The degree of control in anticoagulant therapy is not superior (11), except in those cases where required venipuncture is difficult or inadvisable. The main advantages of this modification are universal applicability and convenience for both patient and physician.

References