Plasma Fibrinogen: Determination, Normal Values, Physiopathologic Shifts, and Fluctuations

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The determination of plasma fibrinogen, either as clottable protein or protein precipitable with glycine or ammonium sulfate, is evaluated in terms of principles of analysis, analytic error, normal and abnormal ranges, physiologic stability, and pathologic variability of fibrinogen concentration. The quantitative comparison of analytic error, population ranges, and individual variability should permit more precise interpretation of clinical data than previously has been possible.

**Keyphrases** clottable protein • thrombin • fibrin • ultraviolet absorption, 282 nm • glycine precipitant • ammonium sulfate precipitant • turbidimetry • intraindividual constancy • pregnancy and plasma fibrinogen • diabetes • vascular and blood-clotting diseases • arthritis • liver disease • blood clotting • normal values • homeostasis

**Determination of Plasma** fibrinogen is potentially useful for evaluating the clinical status of patients with a wide variety of disorders, and for assessing the effectiveness of particular courses of treatment (1–5). However, the rapid method of analysis commonly used in clinical laboratories, which is based on the measurement of precipitable protein (4, 5), is subject to large, unavoidable errors, and yields results of uncertain significance (6). Consequently, if determination of plasma fibrinogen is to achieve its potential usefulness in clinical medicine, a more reliable method of analysis must be used.

This report compares the determination of fibrinogen as precipitable protein and as clottable protein, evaluates the reliability of the latter procedure, and indicates its broad clinical applicability.

**Materials and Methods**

**Determination of Fibrinogen as Clottable Protein** (7)

**Principle.** Dilute plasma is treated with thrombin to convert fibrinogen to fibrin. The fibrin clot is collected as a thin film, washed free of plasma protein, and dissolved in urea solution. Fibrinogen is determined by measurement of the absorbance at 282 nm. This method is similar in principle to the method of Swain and Feders (8).

**Special equipment.** Porcelain crucibles (Coors No. 00); 4 mm × 160 mm glass rods; 75 mm (3 inch) squares of white nylon cloth (about 170 threads per 6.25 square inch, available at any yardgoods store).

**Reagents**

**Phosphate buffer (0.015 mole of sodium phosphate per liter of 0.075M sodium chloride, pH 6.35).**

Dissolve 2.07 g of NaH2PO4·H2O in 950 ml of 0.075M NaCl, adjust to pH 6.35 with sodium hydroxide (about 0.4 ml of a 50 g/100 ml solution), and dilute to one liter with 0.075M NaCl.

**Saline solution (0.15 mole of sodium chloride per liter).** Dissolve 8.78 g of NaCl in 1 liter of distilled water.

**Thrombin** (100 N.I.H. units/ml). Bovine thrombin (Parke-Davis, topical, 5000 N.I.H. units) is dissolved in 5 ml of glycerol solution (50 ml of glycerol plus 50 ml of water) to provide a stock solution containing 1000 units/ml. Prepare a working solution containing 100 units/ml by diluting 1 ml of stock solution with 9 ml of saline solution. The stock solution is stored at −10°C; the working solution is kept refrigerated for no longer than one week.

**Alkaline urea reagent** (40 g of urea per 100
ml of 0.2n sodium hydroxide). Dissolve 200 g of reagent grade urea in distilled water and dilute to 450 ml. Dissolve 4 g of sodium hydroxide (AR) in 50 ml of distilled water and add to the urea solution. This solution slowly deteriorates, with formation of ammonia, but is usable for one month if it is stoppered at room temperature.

Procedure

Conversion of Fibrinogen to Fibrin. Pipet 0.50 ml of plasma and 1.5 ml of phosphate buffer into a porcelain crucible and mix by gentle swirling. Add about 0.15 ml of the thrombin solution (100 units/ml) and mix immediately by swirling. Mixing should be completed within 10 s after adding thrombin, and the crucible should then be left undisturbed for 30 min. Precaution: the mixing of plasma, buffer, and thrombin are critical steps; incomplete mixing produces a nonhomogeneous clot, which will not collapse completely to a thin film and cannot be washed free of contaminating plasma protein. For the same reason, swirling must be no longer than 10 s after the addition of thrombin, as this will interfere with the formation of a uniform gel structure.

The pH of the buffer is 6.35 because this is within the pH range for maximum thrombin activity but is at the lower limit of effective plasma antithrombin activity (9, 10).

Recovery of Fibrin. The clot is freed from the wall of the crucible by tapping the tilted crucible sharply against the bench top several times; the clot is then carefully poured onto a piece of nylon cloth, which is on a pad of absorbent paper towels. As the fluid of the clot is drawn into the towels, the clot collapses upon the cloth as a thin fibrin film. The nylon cloth with adhering fibrin film is then laid across a small funnel, which drains into a large Erlenmeyer flask, and is washed with 25 ml of saline solution delivered dropwise to the entire surface of the film and the surrounding cloth. Precaution: Because fibrinogen constitutes only 4 to 10% of the total plasma protein, thorough washing is essential. The clot must be completely collapsed (that is, there must be no residual gel structure) because the saline wash does not remove plasma entrained within a gel.

The cloth with its washed film of fibrin is laid upon a paper towel to remove residual wash fluid. The edge of the film is then picked up with a glass rod, to which it adheres strongly, and the entire film is lifted from the cloth and rolled loosely onto the rod. The rod is then placed in a test tube containing 3.0 ml of the alkaline urea reagent.

The nylon cloth is soaked in saline solution, rinsed with distilled water, and dried for reuse.

Measurement of Fibrin. Solution of the fibrin in the alkaline urea reagent requires about 1 h, with occasional stirring. When solution is complete, the glass rod is rinsed with 4.00 ml of saline solution while it is withdrawn from the tube. The urea and saline solutions are mixed by repeatedly inverting the tube, and the absorbance (A) at 282 nm is measured vs. a urea–saline blank. The absorbance is constant for at least 72 h.

Calculation. Fibrinogen is calculated from the equation:

\[ \text{Mg of fibrinogen per 100 ml of plasma} = \frac{A_{282}}{16.5} \times \frac{V_2}{V_1} \times V_3 \times 10 \]  

where \( A_{282} \) is the measured absorbance; \( V_1, V_2, \) and \( V_3 \) are the respective volumes of the plasma sample, the solution analyzed, and 100 ml of plasma; and 16.5 is the specific absorbance (absorbance of a 1 g/100 ml solution measured at 282 nm in a cuvet with a 10-mm light path, at 20°C) of purified human fibrinogen in the urea–saline solvent (11). In this procedure (i.e., with 0.50 ml plasma and a final volume of 7.0 ml), Equation 1 reduces to:

\[ \text{Mg of fibrinogen per 100 ml of plasma} = 848 \times A_{282} \]  

Determination of Fibrinogen by Nonspecific Precipitation with Ammonium Sulfate

Parfentjev's modification (5) of the procedure of Fowell (4) was used. In this procedure plasma is mixed with ammonium sulfate solution, and the resulting turbidity is measured and expressed as fibrinogen concentration by means of a previously determined empirical relationship.

In certain experiments (e.g., those illustrated in Figures 1 and 2) the precipitated protein was collected by centrifugation, dissolved in the alkaline urea reagent, the absorbance at 282 nm measured, and the concentration of fibrinogen actually recovered was calculated by Equation 1.

Determination of Fibrinogen by Specific Precipitation with Glycine

This method is entirely analogous to the Parfentjev procedure, but is based on the specific precipitation of fibrinogen in 2.1M glycine (12); 2.33M glycine is used instead of ammonium sulfate as the precipitant. The precipitate was collected by centrifugation, dissolved in alkaline urea reagent, the absorbance at 282 nm was measured, and fibrinogen concentration was calculated by Equation 1.

Construction of Population Distribution Curves

Fibrinogen determinations from a population were arranged in rank order and the percentage of the initial population remaining at various fibrino-
fibrinogen concentrations was calculated. The percentage remaining was graphed against fibrinogen concentration on probability paper, and the best line through the data points was drawn. The concentration range was divided into about 20 equal segments to provide a satisfactory increment of change (18). The change in percentage remaining (dN) for successive increments in fibrinogen concentration (dF) was then read from the graph. The latter values (i.e., dN/dF) were graphed against fibrinogen concentration to obtain the apparent distribution curve for the population (Figure 8).

In contrast to the apparent population distribution curve, the normalized distribution curve (Figure 7, normal population) was obtained by graphical analysis of the initial plot on probability paper, as described by Neumann (14), before reading off the values of dN/dF.

Results

Comparison of Methods

Specificity of precipitation reactions. The specificities of ammonium sulfate and glycine as precipitants for fibrinogen were compared by varying the concentration of precipitant added to aliquots of a plasma. The precipitates obtained at each concentration were dissolved in alkaline urea solution, and the absorbance at 282 nm was measured. In addition, the clottable protein of the plasma was determined. The results (Figure 1) illustrate the high and low specificities, respectively, of glycine and ammonium sulfate.

The concentration of ammonium sulfate (0.9 M) used in the Parfentjev method is apparently optimal for the determination of fibrinogen. However, Figure 1 shows that, at this concentration of ammonium sulfate, gross contamination by coprecipitation of globulins must occur. Electrophoretic analysis of the precipitate from normal plasma has shown that contaminating β- and γ-globulins constitute about 15% of the total precipitate. Precipitation with 0.9 M ammonium sulfate appears to be quantitative (Figure 1) because this concentration of ammonium sulfate precipitates only 80 to 85% of the total clottable protein (see Figure 2). Thus, ammonium sulfate causes incomplete precipitation of fibrinogen as well as partial precipitation of other globulins.

In contrast, nearly quantitative precipitation of fibrinogen is obtained with glycine, and the precipitate is contaminated only by a small amount of entrained plasma.

Analytical results. Each of the three methods can be made to yield apparently accurate, reproducible results when applied to normal plasmas. However, with plasmas from patients large discrepancies can occur. To illustrate these differences, a series of patient plasmas was analyzed by each of the three methods.

All determinations were made by measuring the absorbance at 282 nm, and results were calculated as fibrinogen was actually recovered. The results (Figure 2) demonstrate that even though the results obtained with the three methods generally correlate, there is excessive deviation in individual plasmas.
In a similar study, plasmas were analyzed by both the ammonium sulfate turbidimetric procedure and the clottable protein method, and even greater discrepancies were noted (Figure 3). The following studies show that these discrepancies are related to variability in the precipitation characteristics of fibrinogen as it occurs in normal and patient plasmas.

**Effect of limited proteolysis of fibrinogen on its precipitability and coagulability.** In vivo, fibrinogen is subjected to the action of two specific proteolytic enzymes, thrombin and plasmin, and can exist in partially degraded forms (15, 16). The effect of partial degradation of fibrinogen by thrombin on the determination of fibrinogen is shown by the following experiment.

Plasmas from several healthy subjects were pooled, and the pool was divided into two portions, labeled A and B. A small amount of thrombin, insufficient to cause coagulation of all of the fibrinogen, was added to pool B. After 10 min, the fibrin clot was removed by winding it onto a glass rod. Five minutes later, a second clot was removed, and the plasma was then left undisturbed for 45 min to permit complete inactivation of thrombin by plasma antithrombin. Thrombin had been inactivated, since there was no further clot formation, even though a substantial amount of clottable protein was still present (as shown by subsequent analysis, Figure 4). Aliquots of plasmas A and B were placed in a series of tubes that contained increasing amounts of a reference fibrinogen solution. These specimens were then analyzed for fibrinogen by the Blomback clottable protein method (7) and the Parfentjev turbidimetric procedure (5). The results of these analyses (Figure 4) show:

(a) Treatment of plasma B with thrombin diminished the concentration of fibrinogen significantly, as assayed as either clottable protein or precipitable protein.

(b) One milliliter of the reference fibrinogen solution added to plasmas A and B should have increased the determined value by 4.00 mg/ml. From the slope of the best lines drawn through the experimental points, the recovery of fibrinogen added to plasma A was 100% when assayed as either clottable or precipitable protein.

(c) The recovery of fibrinogen added to plasma B was 100% when assayed as clottable protein, but only 60% when assayed as precipitable protein. Apparently the presence of fibrinogen partially degraded by thrombin affected the precipitation of native fibrinogen added to the plasma in such a way that quantitative recovery was not possible.

Thus, the clottable protein assay gave consistent results whether native fibrinogen (plasma A), modified fibrinogen (plasma B), or a mixture of native and modified fibrinogen (plasma B with added fibrinogen) was present. The precipitable protein assay gave apparently reliable results with native fibrinogen (plasma A), but gave erroneous results with modified fibrinogen (plasma B) and with a mixture of native and modified fibrinogen (plasma B with added fibrinogen).

To investigate the effect of plasmin on the fibrinogen assay, I incubated a solution of purified fibrinogen (12) with plasmin. Samples were with-
drawn at various times for the determination of clottable protein and of protein precipitable with ammonium sulfate or glycine. The results (Figure 5) make it evident that very limited digestion with plasmin renders fibrinogen nonprecipitable with either ammonium sulfate or glycine, but has little effect on its coagulability with thrombin.

These experiments show that the naturally occurring enzymes, thrombin and plasmin, can induce subtle alterations of the fibrinogen molecule, which are insufficient to affect the coagulation of fibrinogen significantly but can strongly influence its precipitability and, consequently, cause erroneous assay results.

Analytical error of the clottable protein assay. Reproducibility and stability of the clottable protein method was assessed by analyzing 0.30-ml and 0.50-ml aliquots of specimens from about 50 patients. These specimens were collected over a period of several weeks, and the 0.30-ml and 0.5-ml aliquots were independently analyzed.

In Figure 6, the results from the 0.30-ml and 0.50-ml samples are plotted on the abscissa and ordinate, respectively. The standard deviation over the range of fibrinogen concentration is ±7.2 mg/100 ml.

The accuracy of the method was evaluated in conjunction with the above study by determining the recovery of fibrinogen added to 30 of the specimens. A known fibrinogen solution, 0.2 ml, was added to a 0.30-ml sample of each specimen. From the concentration of the known fibrinogen solution it was calculated that each analytical value should have increased by 128 mg/100 ml. The determined increase was 128 ± 8.6 mg/100 ml. Thus, the clottable protein assay is both accurate and reproducible over a wide range of fibrinogen concentration.

Physio-Pathological Fluctuations of Fibrinogen

Normal range. Specimens from 88 healthy blood donors under 45 years of age were analyzed by the clottable protein procedure. The distribution curve for this population is shown in Figure 8. No significant difference between males and females was observed. Since the curve appears to have two components, it was analyzed as described by Neumann (14), and a "normalized" distribution curve (Figure 7) was derived. If I use limits of ±2 standard deviations, the apparent normal range is

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Fig. 5. Effect of limited proteolysis by plasmin on the recovery of fibrinogen

Fig. 6. Precision of the clottable protein assay

Fig. 7. Comparison of distribution curves of fibrinogen values in rheumatoid arthritis and chronic lung disease (silicosis) with the normalized curve of a healthy population
from 170 mg/100 ml to 410 mg/100 ml with a mean value of 290 mg/100 ml.

**Physiologic variability.** Three subjects having low, average, and high fibrinogen values were selected from the healthy population and were analyzed repeatedly. The "low" subject was analyzed nine times during one year; the "average" subject was analyzed every other day for one month; the "high" subject was analyzed every other day for one month, and at monthly intervals for one year. The results of these analyses are given in Figure 8 ("normal individuals") and show that healthy individuals maintain a characteristic fibrinogen level, which is stable within approximately ±10% of the individual's mean value.

**Abnormal values.** In general, the patients' results were accumulated and evaluated, retrospectively, in conjunction with a review of medical records or consultation with clinicians.

Some of the specimens had come from special clinics or study groups and provided categorized patient populations. Distribution curves for those populations having at least 30 individuals are compared with the normalized normal distribution curve in Figure 7. Results of analyses of other specimens are summarized in Figure 8. Some of these specimens were repeat analyses and provided information on the stability of plasma fibrinogen concentration in various circumstances. Briefly, the principal findings were as follows.

**Polycythemia Vera.** Four patients; all had normal fibrinogen levels.

**Pregnancy.** Twelve patients were analyzed during the last month of pregnancy. The mean value for 10 of these patients, whose pregnancies were unremarkable, was about 100 mg/100 ml above the normal mean. Two patients, with diabetes and toxemia of pregnancy, had markedly increased fibrinogen concentrations. Apparently, fibrinogen concentration is moderately elevated during a normal pregnancy, but can reach high concentrations when complications are present.

**Diabetes Mellitus.** Five patients; all had elevated fibrinogen levels. One patient had an initial value of 710 mg/100 ml, a value of 510 mg/100 ml two days later, and died the following day.

**Thrombophlebitis.** Three patients, analyzed on the second and third days of hospitalization; all had similar high normal fibrinogen values initially. Two had been "under observation," and the fibrinogen concentrations decreased about 100 mg/100 ml to fall within the low normal range. The third had been given anticoagulant therapy (heparin) and the fibrinogen concentration increased to a frankly abnormal value.

**Cardiomyotom.** This was a patient undergoing surgical treatment of a congenital heart defect; his fibrinogen concentration before surgery was 380 mg/100 ml. During surgery ε-amino-caproic acid was administered to prevent excessive fibrinogenolysis. During the next several days, clots formed retroperitoneally and in one leg; the clots were removed surgically and the patient was given therapeutic doses of heparin for five days. At the time of heparin withdrawal, a second plasma specimen had a fibrinogen concentration of 620 mg/100 ml. About two weeks later the patient died with massive thrombosis at the site of the heart operation.

**Pulmonary Embolism.** Six patients; one had a normal fibrinogen level, four had clearly elevated levels, and one was initially normal but increased in 24 h to a frankly elevated level.

**Coronary Thrombosis.** One patient, admitted because of myocardial infarction; initial fibrinogen

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**Fig. 8.** Comparison of analytic error, normal range, and physiologic variability of plasma fibrinogen with values observed in a categorized hospital population

Open circles indicate patients who died within four weeks after analysis. Arrows indicate how individual values changed during the observation period.

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was 540 mg/100 ml. After one week of hospitalization fibrinogen had decreased to 400 mg/ml. The patient’s clotting time was stabilized with warfarin and he was checked as an outpatient at weekly intervals. After two months, fibrinogen was still about 400 mg/100 ml and fibrinogen determinations were discontinued. Checkups continued every two weeks, and the patient’s clotting problem was considered well controlled on the basis of prothrombin-time determinations. However, eight months later the patient was readmitted with a second myocardial infarction at which time his fibrinogen concentration was 760 mg/100 ml.

RHEUMATOID ARTHRITIS. Two outpatients, in the acute phase; their initial fibrinogen levels were about 600 mg/100 ml. After one-week, decreases of 90 and 180 mg/100 ml had occurred, and a week later one patient had a rise in fibrinogen, associated with amelioration of her discomfort. Apparently, fibrinogen concentrations are high in patients with arthritis, and fluctuate periodically.

ARTERIOSCLEROSIS. Thirteen elderly patients whose diagnoses included generalized arteriosclerosis. Five of these patients died within four weeks of the date of analysis. Most of these 13 patients had high fibrinogen concentrations, and repeat determinations on two of them revealed wide fluctuations, which were correlated with the clinical suspicion of recurrent intravascular coagulation.

CHRONIC LIVER DISEASE WITH THROMBOCYTOPENIA. Sixteen patients with chronic liver disease, and considered likely to have recurrent hemorrhagic episodes, were classified as “quiescent” or “active,” respectively, on the basis of a normal (Figure 8, group a) or elevated (Figure 8, group b) serial thrombin time test (17). The quiescent group had abnormally high fibrinogen concentrations; the active group tended to have values in the low part of the normal range. Wide fluctuations of fibrinogen concentration were observed in two patients whose plasmas were analyzed during their active and quiescent phases. Apparently, fibrinogen rises to high concentrations during the quiescent phase and is decreased to very low concentrations by activation of the fibrinolytic system during the active phase.

Discussion

Reliability of Fibrinogen Determination

In principle, the basic reliability of a chemical determination is assured by utilizing procedures or measurements that are specific for the component of interest (18). In the determination of fibrinogen as precipitable protein (4–6), this fundamental principle is compromised. In normal plasma the precipitation of native fibrinogen by ammonium sulfate is neither quantitative nor specific (Figure 1), and in other plasmas fibrinogen can exist in a modified form which is precipitated abnormally by ammonium sulfate or glycine (Figures 4, 5). Because of these fundamental deficiencies, the determination of fibrinogen as precipitable protein is inherently unreliable and in practice yields grossly erroneous results (Figures 2, 3).

The determination of fibrinogen as clottable protein makes use of two reactions specific for fibrinogen: the limited proteolysis by thrombin, and fibrin polymerization. The former reaction is dependent on the natural specificity of thrombin for fibrinogen, and the latter reaction depends on the unique molecular architecture and self-affinity of the fibrin monomer (19).

In the present procedure both reactions are carried out under optimal conditions; fibrin is recovered in a form easily freed of contaminants and is determined by measuring its absorbance. The specific absorbance of fibrinogen (and fibrin) is a physicochemical constant, which is characteristic of it and has a value three times that of albumin and about two times that of other plasma globulins. The use of specific absorbance allows accurate and consistent standardization of the method. Thus, the determination of fibrinogen as clottable protein is conceptually sound, and in practice does yield accurate and reproducible results (Figure 8).

Significance of Fibrinogen Determination

Studies summarized in Figures 7 and 8 were designed to provide a broad perspective of the range of values and magnitude of changes in fibrinogen which occur in a general hospital population. An interpretation of the results must be based on present understanding of the functioning of the coagulation system, and recognition of the uniquely favorable position of fibrinogen within this system to serve as an internal monitor of certain physiologic processes.

The coagulation system is structured biochemically (20) to moderate the utilization of fibrinogen, the central component of the system (Figure 9). The utilization of fibrinogen is believed to be due to the activities of thrombin and plasmin generated in blood in response to platelet or tissue activation, and the activity of these enzymes is limited by plasma antithrombin and antiplasmin (9, 10, 21, 22). Fibrinogen and other major pro- and anticoagulant components of the system are synthesized by the liver and secreted into the circulation (23 24), where they are continuously available for interaction with tissue substances at the vascular-extravascular interface.

Physiologic utilization of fibrinogen (fibrination)
(Figure 10) is believed to occur primarily through local activation of the coagulation system by disintegrating platelets (25–27), with the microparticles of platelet debris and fibrin being removed by phagocytosis (28). Pathologic utilization of fibrinogen occurs when tissue substances cause excessive or prolonged activation of either prothrombin or plasminogen (29, 30).

Thus, the concentration of fibrinogen in plasma reflects the net balance between the rate of its biosynthesis and secretion by the liver, and the rate of utilization resulting from challenges to the coagulation system by platelets and substances of extravascular origin. These processes are dynamic, for fibrinogen and platelets are normally used and replaced at the rate of 20 to 25% per day (31, 32).

The data summarized in Figures 7 and 8 provide a kaleidoscopic view of this dynamic balance as it operates in health and disease, and the following conclusions can be drawn:

(a) Individuals who are apparently healthy maintain a stable level of plasma fibrinogen over extended periods of time (Figure 8), and the level is characteristic of the individual.

(b) The general population is comprised of subgroups of individuals having various characteristic levels of fibrinogen, and the distribution of observed values (Figure 8) depends on the size of the various subgroups. The majority of individuals nevertheless comprise a population with Gaussian distribution for their plasma fibrinogen concentration, the mean being 290 mg/100 ml (Figure 7); in contrast, about 15% of the normal population comprise a distinct subgroup having a mean fibrinogen level of about 410 mg/100 ml.

The latter population may represent individuals in whom the balance has been altered for various reasons, resulting in a stable shift of the mean fibrinogen concentration. Individuals having latent coronary heart disease are known to have moderately elevated fibrinogen levels (53, 34). In addition, individuals having early subclinical manifestations of some of the conditions listed in Figures 7 and 8 (i.e., diabetes, arteriosclerosis, arthritis, liver disease, lung disease) might be expected to have moderately elevated fibrinogen values.

(c) A change in physiologic state (for example, during pregnancy) results in an increase of about 100 mg/100 ml in the mean fibrinogen value. This temporary shift is probably a result of enhancement by estrogen of fibrinogen biosynthesis, but could also result (Figure 10) from a decreased utilization of fibrinogen secondary to diminished tissue thromboplastic stimulation associated with changes in plasma volume and fluid compartmentalization which occur in pregnancy (35, 36). Exacerbation of the shift may be observed in complicated pregnancies.

(d) In some chronic conditions (e.g., rheumatoid arthritis, diabetes, chronic lung, or liver disease, and generalized arteriosclerosis), marked elevation of fibrinogen can occur associated with wide fluctuations of fibrinogen concentration. The changes in arthritis are periodic and are believed to be related to the inflammatory process; plasma fibrinogen has been proposed as a useful parameter to monitor the inflammatory process in arthritis (37, 38), and therapeutic measures designed to stabilize the fibrinogen level have been reported to ameliorate the acute phase of rheumatoid arthritis (39).

(e) Therapeutic measures, intended to control
the coagulation system in patients susceptible to hemorrhagic or thrombotic episodes, may result in extreme, unsuspected changes in fibrinogen concentration and possibly contribute to serious complications when the therapy is terminated. By the same token, the fibrinogen determination should be helpful in evaluating the status of these patients more accurately, in regulating therapy more effectively, and in devising more effective treatment.

In summary, this comparison of analytic error, range, and stability of fibrinogen in healthy individuals and in patients provides a basis for more precise interpretation of clinical data than has been previously possible. The determination of fibrinogen has little diagnostic value because it is altered in many different situations. However, normalcy for a particular individual can be accurately defined, and changes from normalcy easily detected. The quantitative determination of fibrinogen should find application in evaluating a particular patient’s deviation from normalcy, in controlling the deviation, and in achieving a restoration to normalcy.

References