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## Relation Between Prothrombin Concentration and Retraction of the Blood Clot.\*

P. M. AGGELER AND S. P. LUCIA.

*From the Division of Medicine, University of California Medical School, San Francisco, California.*

It has long been known that one of the salient features of the bleeding tendency in obstructive jaundice is a fragile, non-retractile blood clot. Quick<sup>1, 2</sup> showed that the essential defect in the plasma of patients with the bleeding tendency of obstructive jaundice was a deficiency of prothrombin. Boyce and McFetridge<sup>3, 4</sup> found that in normal subjects the volume of serum expressed from the blood clot in 4 hours at room temperature was equal to half the total volume of the specimen. In patients with obstructive jaundice the volume was significantly less. They expressed this relationship as the serum volume index, in which the volume of serum is divided by half the total volume of the specimen. The index is corrected for deviations from the normal erythrocyte count. The serum volume index for normal subjects was 1.00; the highest index at which a patient with obstructive jaundice bled was 0.71; the lowest index at which hemorrhage did not occur was 0.78. Mettier and Witts express the measurement of clot retraction as the clot retraction index. In their test<sup>5</sup> the volume of serum expressed from the clot in one hour at 37°C is divided by the total volume of the specimen; to this is added the packed cell volume and the final result is divided by two. In normal subjects the clot retraction index ranged from 38 to 50. We have used both the clot retraction index and serum volume index. Although the trend of the results with either test is the same, the clot retraction index is perhaps a better measure of this phenomenon, because it eliminates variables due to fluctuation in temperature and mean corpuscular volume.

It is obvious that the degree of retraction of the blood clot depends upon at least 2 factors: the amount of prothrombin and the amount

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<sup>1</sup> Quick, A. J., Stanley-Brown, M., and Bancroft, F. W., *Am. J. M. Sc.*, 1935, **190**, 501.

<sup>2</sup> Quick, A. J., *J. A. M. A.*, 1938, **110**, 1658.

<sup>3</sup> Boyce, F. F., and McFetridge, E. M., *J. Lab. and Clin. Med.*, 1937, **23**, 202.

<sup>4</sup> Boyce, F. F., and McFetridge, E. M., *New Orleans Med. and Surg. J.*, 1939, **91**, 357.

<sup>5</sup> Mettier, S. R., and Witts, L. J., in press, personal communication.

TABLE I.

Samples	No. of tests	Prothrombin Concentration		Clot Retraction Index		Correlation Coefficient
		Mean	Sigma	Mean	Sigma	
A	85	72	37	38	5	.450 ± .09
B	44	80	25	39	6	.634 ± .09
C	41	78	25	39	6	.641 ± .09

of thromboplastin. the volume of the corpuscles under ordinary circumstances playing a minor rôle. The amount of prothrombin can be estimated by the method of Quick.<sup>2</sup> The amount of thromboplastin in a sample of blood is conditioned by the number and quality of the platelets, and the amount of tissue juice expressed from traumatized tissues.

We have recorded the clot retraction index and prothrombin concentration of 85 samples of blood. The blood was obtained from normal subjects and from patients suffering from obstructive jaundice and from a variety of diseases affecting the liver. Patients with hemophilia and thrombocytopenic purpura were excluded. Calculated statistical values are shown in Table I.

*The Prothrombin Concentration.* By the terms of this test the variable factor apparently is the quantity or quality of the prothrombin contained in the test sample. The test can be accurately performed; our experimental error in repeated estimations of the prothrombin concentration in the same subject is not greater than 5%. It is a delicate test, as is apparent from the value of the spread around the mean.

*The Clot Retraction Index.* In this test there are at least 2 variable factors, one the prothrombin content, and the other the quantity of thromboplastin in the blood sample. This test is less delicate as can be seen from the narrowness of the spread of the values around the mean. When done at the same time and on the same sample of blood which is used for the prothrombin time, the fluctuation in the clot retraction index for a given prothrombin concentration will apparently be due to fluctuations in the quantity of thromboplastin.

*Correlation Coefficients.* Sample A—85 tests were performed on samples of blood obtained from 44 persons including both normal and pathologic individuals. Of these, 50 samples were obtained from 9 individuals before and after recovery from prothrombinemia. The correlation coefficient of  $0.450 \pm 0.09$  is positive and significant, and indicates that on the average as the prothrombin concentration is lowered, the clot retraction index is also lowered, that is, the 2 factors fluctuate in the same direction simultaneously.

Sample B—Because sample A was weighted by 50 tests from 9 individuals, it was decided to select only one reading (the lowest prothrombin concentration) from each individual, normal or pathologic. The final sample included 44 tests. The correlation coefficient of  $0.634 \pm 0.09$  indicates to a greater degree the same relationship found in sample A.

Sample C—A further reduction of sample B made by eliminating the tests on the three normal individuals ( $N = 41$ ) slightly raised the correlation coefficient ( $r = 0.641 \pm 0.09$ ).

An example of the close correlation, which may be observed in some patients, between the prothrombin concentration and the clot retraction index is given in Fig. 1.

Clinical bleeding from mucous membranes occurred when the prothrombin concentration dropped to 10% and the clot retraction index to 30. When the prothrombinemia was corrected by the parenteral administration of Vitamin K, both the prothrombin concentration and clot retraction index returned to normal.

The following example, however, illustrates the error which may be

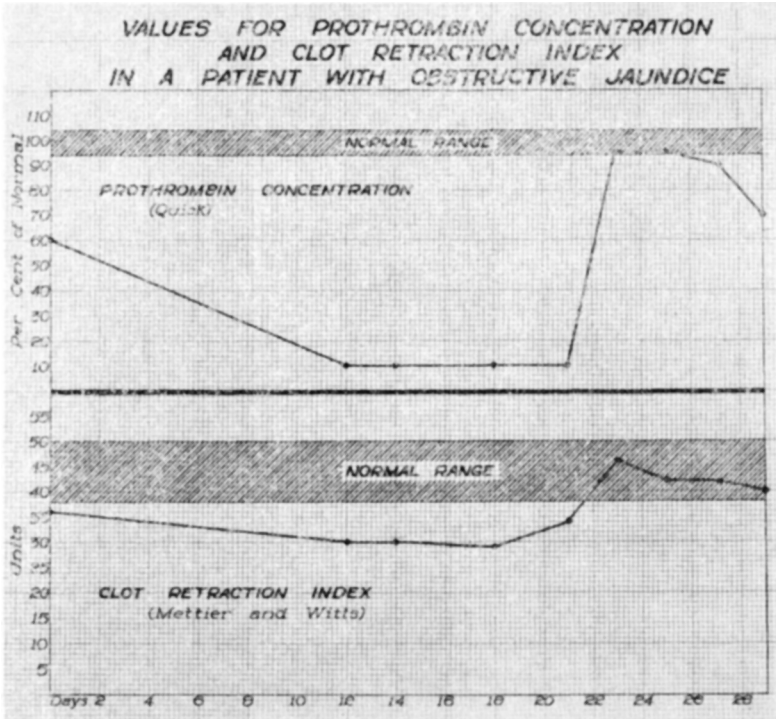


FIG. 1.

made in ascribing to prothrombinemia alone the deficient clot retraction observed in some cases of liver damage. A patient entered the hospital because of recurrent icterus. She was found to have marked hepato-splenomegaly. Icteric index 25. Whole blood coagulation time  $7\frac{1}{2}$  minutes. Prothrombin concentration 100%. Clot retraction index 31. The capillary fragility was markedly increased, and the platelet count was 65,000  $\text{mm}^3$ .

It is obvious that the deficiency in clot retraction was probably due to decreased thromboplastin and not to any alteration in prothrombin concentration.

*Summary.* A relationship has been established between the prothrombin concentration and the clot retraction index. This should not be interpreted as a direct cause and effect relationship, inasmuch as other variables may influence both tests in common. In the case of the clot retraction index, thromboplastin, as well as prothrombin plays an important rôle in the reaction. The variation of the prothrombin concentration, when evaluated in terms of diagnosis, appears to be a more sensitive index than the clot retraction index.

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#### Age and the Rate of Venous Enlargement under Increased Venous Pressure.\*

T. ADDIS AND W. LEW.

*From the Department of Medicine, Stanford University Medical School, San Francisco.*

By tying the vena cava of rats above the entrance of the renal veins an intense venous congestion is produced in the kidneys. The formation of urine stops and the blood urea concentration rapidly rises. In surviving animals a small amount of dilute urine containing a high concentration of protein and many renal failure casts is excreted after 24 hours, but the blood urea concentration still rises until 48 hours after operation it is more than 300 mg per 100 cc. Thereafter the volume of urine increases, the concentration of urea rises in the urine and falls in the blood, the proteinuria diminishes, the casts disappear and in a week after operation there is no evidence of any renal lesion.

The mechanism of the process of restoration is dependent on the

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