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A STUDY ON HYPERCOAGULABILTIY USING HEPARIN LOADING TEST

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During recent years increasing attention has been paid to the role of hypercoagulability in the pathogenesis of arteriosclerosis and intravascular thrombosis. Since there are several reviews and publications on this extensive research field, we shall not discuss the literature in detail.

In order to reveal "hypercoagulability" many workers introduced several methods. We suggested[17,18] "heparin loading test" for this purpose. We are going to discuss in this paper the results which we obtained using this method in the cases of arteriosclerosis, ischaemic-heart disease, myocardial infarction, essential hypertension and thrombophlebitis.

METHODS AND MATERIAL

The coagulation time was measured with the method of Lee and White[3], one-stage prothrombin time with the method of Quick[13], antithrombin time with the method of Studer[15] and Winterstein, and heparin clotting time with the method of Rosenthal[14] were performed. The thromboplastin generation test was used according to Biggs[2] and Douglas.

The heparin loading test according to Ulutin[17,18] and Sestakof was performed as follows: 100 mg. heparin† was given intravenously before, and 15, 30, 60, 90, 120, 180, and 240 minutes later venous blood was obtained and thromboplastin formation was followed by means of thromboplastin generation test of Biggs and Douglas. We used the serum after 4 hours of clotting incubated in 37° C waterbath.

In the simplified heparin loading test blood samples were taken before heparin injection, 20 and 60 minutes after.

Cholesterol and total lipid were determined and lipidogram was performed. These experiments were made on ten normal subjects and twenty-two patients.

RESULTS

Antithrombin time shortened in 7 cases out of 12, and in 5 cases out of 14 heparin clotting time diminished. We noticed also that in 14 cases out of 22 the thromboplastin curve was higher than the normal with the thromboplastin generation test. With heparin loading test we observed the following results; in 7 out of 10 normal subjects the antithromboplastic effect of heparin continued 90 - 180 minutes (Fig. I). In three subjects out of ten the mild antithromboplastic effect lasted 60 - 90 minutes.

In 16 cases out of 22 the antithromboplastic effect of heparin lasted 15 - 30 minutes and at 60 - 90 minutes we obtained normal curve (Fig. 2).

However, in six cases antithromboplastic effect of heparin could not be found in the blood even 15 minutes after the injections (Fig. 3).

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†Liquemin "Roche" and Heparin Vitrum were used.

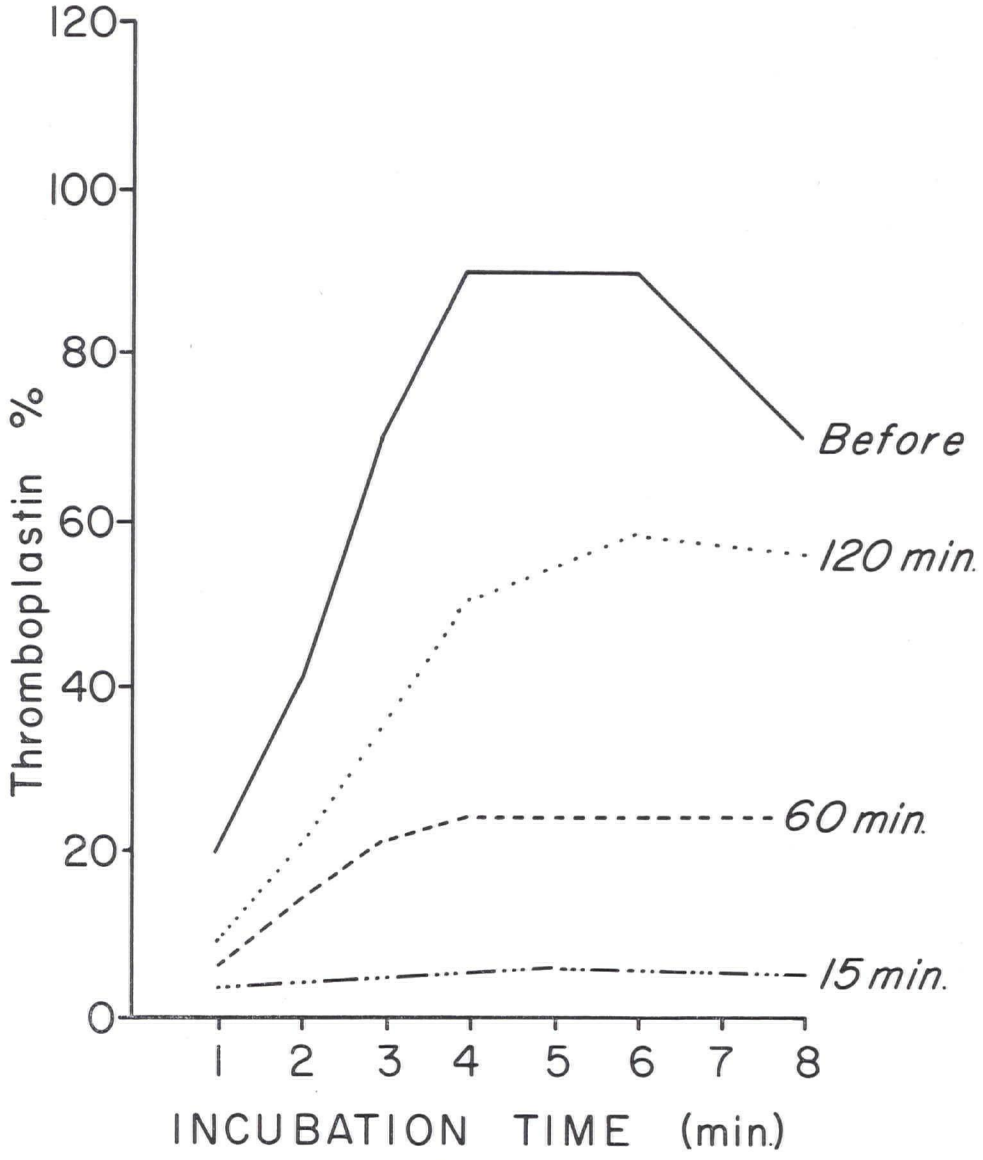

Figure 1

DISCUSSION

Biggs[3], Douglas and MacFarlane in 1953 have shown that heparin inhibits the formation of blood thromboplastin. In 1954 MacMillan[6] and Brown confirmed the antithromboplastic effect of heparin, and they also observed that intravenous heparin causes a defect in serum fraction. Douglas[4] in 1956 showed that in the blood which was taken after injecting heparin AHG, Factor V and prothrombin were not consumed.

In 1957 we confirmed[17] that in the blood taken after heparin injections the generation of thromboplastin was inhibited, and we pointed out that the continuation of

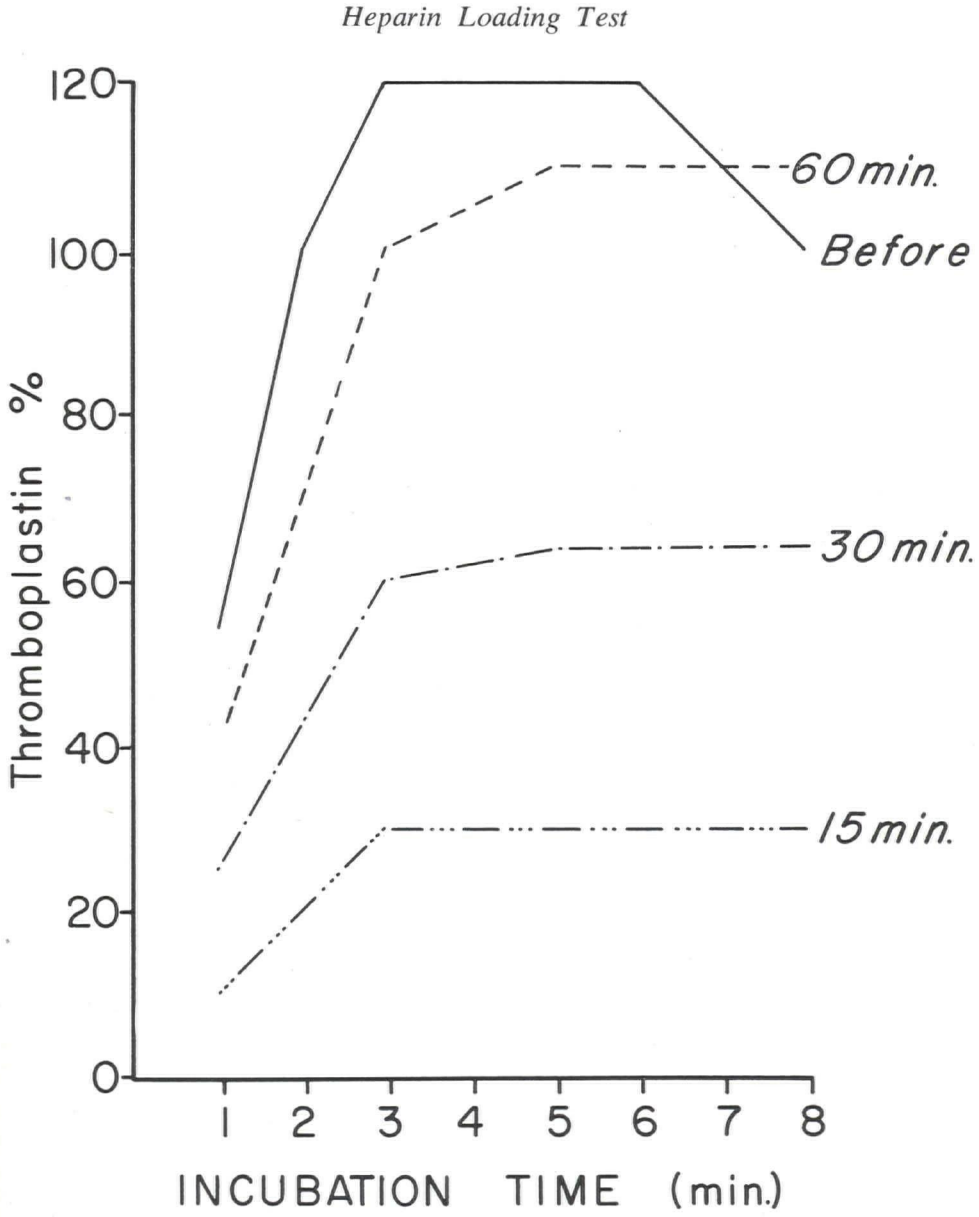

Figure 2

antithromboplastic effect of heparin was different in normal persons and in some patients. In several patients having arteriosclerosis, ischaemic heart disease and thromboplebitis the antithromboplastic effect of heparin lasted for a short time or did not appear at all. In other words, heparin was either consumed or neutralized rapidly.

In cases showing hypercoagulability, according to the heparin loading test, after three or six months of strict low-fat diet and anticoagulant treatment, hypercoagulability decreased or became normal[16] (50 mgs heparin twice weekly intravenously). In

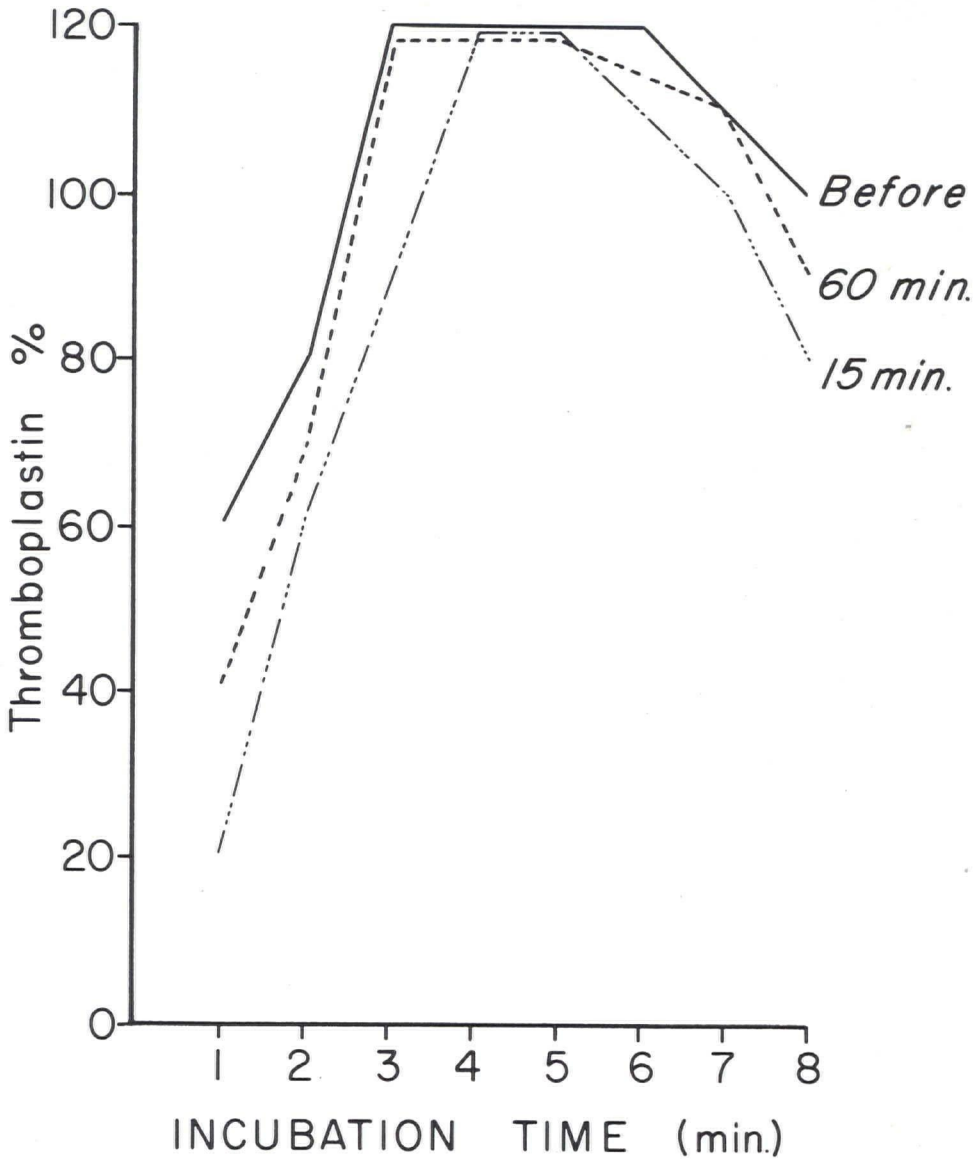

Figure 3

these so-called hypercoagulability cases cholesterol and blood lipid level increased. Lipidogram showed a decrease in A lipids and an increase in B lipids.

In 1957 McDonald[7,8] and Edgill in such cases obtained a shortening of Stypven time, an increase of platelet stickiness and a higher thromboplastin curve in thromboplastin generation test. Authors dwell upon the relation between the increase of cholesterol level and platelet-stickiness.

Heparin Loading Test

In 1957 Kirk[5] and others and in 1958 Berenson[1] have shown that vascular endothelium is lined with a heparin-like mucopolysaccharides, and this substance has an anticoagulant activity.

In 1958 O'Brien[11,12] showed that heparin influenced the Christmas factor. According to author, heparin has affinity for platelets, the Christmas factor and lipoproteins. On the other hand Mustard[9,10] showed that in patients with arteriosclerosis activity of the Christmas factor was increased.

In our opinion there is a close relation between the results of the heparin loading test and recent findings in the literature.

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