Adhesiveness of Blood Platelets in Arteriosclerosis Obliterans, Thromboangiitis Obliterans, Acute Thrombophlebitis, Chronic Venous Insufficiency and Arteriosclerotic Heart Disease

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Total and adhesive platelet counts were made on normal individuals and on patients with myocardial infarction, thromboangiitis obliterans, and other peripheral vascular diseases. Tests were made in several cases while patients smoked and after abstaining from tobacco. Repeated tests were done while patients were receiving dicumarol anticoagulant therapy. A rise in adhesive platelet counts was found in cases of thromboangiitis obliterans, particularly with activity of the disease, and in cases of thrombophlebitis. Cessation of cigarette smoking in cases of thromboangiitis obliterans resulted in a significant decrease in platelet adhesiveness.

THE PURPOSE of this paper is to present statistical evidence of the clinical significance of the glass wool filter test of adhesiveness of blood platelets described by Moolten and associates,3, 4, 5 in 125 cases of peripheral vascular and arteriosclerotic heart disease. At first this test was utilized in patients with existing or impending coronary thrombosis in an attempt to correlate it with the clinical and electrocardiographic findings. We were unable, however, to duplicate the results of Moolten and Vroman in this field or to find any correlation. The glass wool filter test was then applied to cases of various types of peripheral vascular disease and striking differences were found. We are indebted to Sylvan Moolten for instruction in the exacting technic of this test.

METHOD

The method described by Moolten and co-workers was used. This method was chosen rather than that of Helen P. Wright3 because of its greater simplicity and speed. A specimen of citrated venous blood was filtered through a fiber glass wick.

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Pre- and postfiltration red cell and platelet counts were performed. From this data the number of adhesive platelets was calculated, using a simple formula devised by Moolten.

FACTORS AFFECTING ADHESIVENESS

It has been demonstrated by Wright, Moolten and others3-5 that the following factors increase the adhesiveness of platelets: accidental and surgical trauma, the postpartum state, carcinoma and hemorrhage. Conversely, the following conditions decrease platelet adhesiveness in vivo and in vitro: increased concentrations of citrate, oxalate, heparin and dicumarol.

ORIGIN OF PLATELETS AND FUNCTION

Platelets are derived from megakaryocytes in the bone marrow and constitute the basic foundation of a white thrombus, which is the initial stage of intravascular clotting. It is believed by Wright3 that fibrinogen is converted into fibrin on the surface of the platelets and that adhesiveness is the result of this change. It seems reasonable to assume that increased adhesiveness of platelets suggests the presence or imminence of thrombosis. A secondary function of platelets in the white thrombus may be liberation of a vasoconstrictor substance.
FACTORS AFFECTING THE ADHESIVE PLATELET COUNT

Anticoagulant therapy in the form of dicumarol was found to produce a marked decrease in the adhesive platelet count in active thromboangiitis obliterans associated with or without superficial migratory phlebitis and a subsidence of clinical manifestations. When dicumarol was discontinued, the adhesive platelet count became elevated.

In active thromboangiitis obliterans the adhesive count was markedly increased whereas in inactive thromboangiitis obliterans the count was elevated above the normal range but was not as high as in the active cases.

Of our control series of 100 normal subjects, it was found that approximately 70 per cent were smokers. Adhesive platelet tests performed on this group of smokers were in the same range as those found in normal nonsmokers. About 35 per cent of this group of normal smokers completely refrained from smoking for periods of one to two weeks and tests made at the end of this period revealed no change from the previous adhesive platelet counts. Serial tests were performed in the clinic and in private practice on many of the arteriosclerotic peripheral vascular patients who smoked and revealed no change from the normal count. Twenty-five of the arteriosclerotic patients who smoked refrained from smoking for periods of one week and tests taken at the end of this time revealed no change in their adhesive counts.

In the thromboangiitis obliterans series most of the patients claimed to have stopped smoking, but in this group the adhesive count was elevated whether the patient smoked or not. In the case of W. K. there was a history of myocardial infarction which preceded the onset of thromboangiitis obliterans by one year. This patient was a heavy smoker at the time of his coronary thrombosis. He recovered but continued to smoke heavily. A test done while smoking revealed an exceptionally high adhesive platelet count. When he refrained from smoking for only three days there was a sharp decrease of 50,000 adhesive platelets.

In a few other cases of thromboangiitis obliterans with ulceration, serial tests revealed a decrease in adhesiveness on cessation of smoking with a coincidental improvement in ulcers. When smoking was resumed, the platelet adhesiveness was increased.

The group of patients with arteriosclerotic peripheral vascular disease associated with arteriosclerotic heart disease showed no change from the normal range of platelet adhesiveness. An adhesive platelet test was done on a private male patient aged 62 years, suffering from arteriosclerotic heart and peripheral vascular disease, and revealed a normal count. Two days later he complained of acute substernal distress of a few hours duration. A count was done immediately but no significant change was found. The first count was 65,000 and the second, 67,000. The next day the patient died of acute coronary thrombosis.

In our series of one case with acute deep thrombophlebitis and 6 cases of chronic venous stasis resulting from deep thrombophlebitis, adhesive platelet counts were all significantly elevated. In lymphedema, although the lower extremity is also swollen, the adhesive count falls within the normal range.

In an acute flare-up of thromboangiitis obliterans or deep thrombophlebitis in the form of superficial migratory phlebitis, there was found to be a marked elevation in the adhesive platelet count.

Serial tests were done on 5 cases of lupus erythematosus disseminatus before and during cortisone therapy to determine if the dramatic response to this therapy was due in any part to its effect on platelet adhesiveness. There was no change in total or adhesive platelet counts during cortisone therapy.

RESULTS

We felt that in order to derive any clinical significance from the adhesive platelet counts in specific pathologic conditions, it was essential to have a large series of normal adhesive counts from which to determine the mean normal adhesive count and the standard deviation. Over 100 normal individuals ranging in age from 20 to 45 years were tested and approximately 200 tests were performed on these normal subjects. It was found that the normal mean was 67,000 adhesive platelets with a
standard deviation of 18,000. Our normal figures were appreciably lower than those found by Moolten\(^{3-5}\) (fig. 1).

In a series of 36 cases of thromboangiitis obliterans in which seventy tests were performed, there was found to be an increase in adhesiveness of platelets, with a mean count of 111,500 and a standard deviation of 40,000. This series was subdivided into the following groups: those with ulceration, diabetes, coronary thrombosis, combined arteriosclerotic peripheral vascular disease and thromboangiitis obliterans, uncomplicated (fig. 1).

While the majority of all these groups showed a markedly elevated adhesive platelet count, this was most striking in a young patient with a combination of thromboangiitis obliterans and arteriosclerotic heart disease. He was also a very heavy cigarette smoker. This particular case was in marked contrast to our series of 12 cases of acute myocardial infarction in which fifty-five tests were done; these did not reveal any significant increase in platelet adhesiveness. Tests were performed daily on these cases and we were unable to determine any essential difference from those of our series of 100 normal cases.

In a series of 60 cases of arteriosclerotic peripheral vascular disease in which approximately seventy-five tests were performed, the mean adhesive platelet count was 75,000 with a standard deviation of 19,000 (fig. 1). This series was also subdivided into five groups similar to those applied to cases of thromboangiitis obliterans.

In a group of 7 cases, one of acute deep thrombophlebitis and 6 of residual venous stasis resulting from thrombophlebitis, the mean adhesive platelet count was 166,000 (fig. 1).

From the above data it is apparent that the patients with arteriosclerotic peripheral vascular disease have an adhesive platelet count only slightly above the normal range, whereas those with thromboangiitis obliterans and deep thrombophlebitis have a marked elevation of adhesiveness. It is of interest to note that the presence of gross ulceration complicating arteriosclerotic disease caused no appreciable increase in platelet adhesiveness, while in thromboangiitis obliterans there was a very significant increase in platelet adhesiveness in the presence of ulceration.

In the cases of combined thromboangiitis obliterans and arteriosclerotic peripheral vascular disease, the adhesive count usually fell into the range of the cases of arteriosclerotic disease, since by the time these patients reached the age of development of arteriosclerosis, the activity of the thromboangiitis obliterans process had subsided.

**DISCUSSION**

In our series of 12 cases of coronary thrombosis on which fifty-five serial tests were performed we were unable to confirm the findings of Moolten and associates\(^{3-5}\) concerning the rise and fall of adhesive platelets in this condition.

Anticoagulant therapy in the form of dicumarol was found to produce a marked decrease in the adhesive platelet count in active cases of thromboangiitis obliterans. When dicumarol was discontinued, the adhesive count rose sharply. This differs from the work
of Moolten and associates, who found little effect on platelet adhesiveness from dicumarol therapy.

As stated by Moolten and co-workers, marked platelet hyperadhesiveness predisposes to thrombosis. This is a generally accepted fact. It is of interest that we found such hyperadhesiveness in active thromboangiitis obliterans and in acute deep thrombophlebitis but not in coronary thrombosis or arteriosclerotic peripheral vascular disease. Possibly this may assist in differentiating these two types of peripheral vascular disease in doubtful cases.

All previous laboratory tests done on patients with thromboangiitis obliterans, including a variety of blood chemistry studies, have revealed no difference in the blood of these patients when smoking and not smoking. Patients with this disease who continue to smoke have a progressive disease, whereas in those who have stopped smoking, the disease becomes completely arrested. In patients with thromboangiitis obliterans who smoke, we found an increase in platelet adhesiveness, which falls with cessation of smoking.

**Summary and Conclusions**

(1) Four hundred and ninety-seven adhesive platelet tests were performed in this study.

(2) Two hundred of these tests were made on over 100 normal individuals. The normal adhesiveness platelet count was found to be between 42,000 and 72,000.

(3) Two hundred and thirty-two tests were performed on 125 cases of peripheral vascular disease which included thromboangiitis obliterans, 35 cases; arteriosclerotic peripheral vascular disease, 60 cases; arteriosclerotic heart disease, 12 cases; thrombophlebitis, 7 cases; miscellaneous disease, 12 cases.

(4) Fifty-five tests on 12 cases of acute myocardial infarction did not reveal any abnormal response in platelet adhesiveness.

(5) Serial tests on 5 cases of lupus erythematosus disseminatus treated with cortisone did not reveal any change in total or adhesive platelet counts.

(6) Sustained hyperadhesiveness of platelets was found only in thromboangiitis obliterans and thrombophlebitis; this may be used as an aid in differential diagnosis.

(7) Dicumarol produces a decided marked decrease in platelet adhesiveness.

(8) Cigarette smoking does not affect platelet adhesiveness in normal individuals or those with arteriosclerotic peripheral vascular disease.

(9) Cessation of cigarette smoking in 5 cases of thromboangiitis obliterans which we tested resulted in a very significant decrease in platelet adhesiveness.

(10) This is the first biologic test which has shown a difference in patients with active and inactive thromboangiitis obliterans.

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**References**

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