PLATELET ADHESIVE INDEX STUDIES IN MULTIPLE SCLEROSIS AND OTHER NEUROLOGIC DISORDERS*

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DURING the past two decades considerable thought has been given to venule thrombosis as a possible pathogenesis for lesions in multiple sclerosis. Pathologic studies have been convincing to some investigators[1] but not to others.[2] Attempts to show increased coagulability of the blood have been for the most part inconclusive.[3, 4]

In 1949, Moolten and Vroman[5] devised a test for platelet adhesiveness, that is, the tendency for platelets to stick to one another or to stick to other substances. They demonstrated that under conditions which produced thromboembolism, there was a rise in the platelet adhesiveness.[6] Considering the possibility that an alteration in the blood clotting mechanism may be a factor causing disseminated lesions in the central nervous system, this test was done on a series of patients with multiple sclerosis and compared to a series with chronic and acute neurologic disorders.

Method: Platelet adhesiveness was measured by the technique of Moolten and Vroman. Using siliconized glassware, a platelet count and a red blood count are done on citrated blood. Ten minutes after the blood is drawn it is passed through a glass wool filter and washed through with citrate and saline. The filter has an affinity for platelets. A platelet count and a red blood count are done on the filtrate. The ratio of red cells to platelets is obtained from the pre- and post-filter counts. The adhesive index is calculated by dividing the second ratio by the first. An adhesive index of one indicates that an equal proportion of red cells and platelets have passed through the filter. Higher indices indicate increased retention of platelets in the filter. Exact details of the procedures and calculations may be found in Moolten and Vroman's

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TABLE I

	No. of Cases	No. of Determinations	Adhesive Index Average	Range	Normal	Abnormal
MULTIPLE SCLEROSIS						
1. Stationary	26	30	1.16	1.00-1.47	24(80%)	6(20%)
2. Fluctuating	28	45	1.50	1.20-2.07	8(18%)	37(82%)
3. Exacerbations	6	15	1.81	1.18-2.64	1(7%)	14(93%)
	60	90				

paper. It is interesting to note that the number of platelets is not related to the adhesiveness.

Material: One hundred and thirty-two patients were studied. Of these, 60 had multiple sclerosis, 33 had other chronic neurologic disorders, and 39 had acute neurologic disorders. In addition, determinations were made on 12 healthy subjects at varying intervals during the investigation. The adhesive indices of the normal subjects followed closely the normal range found by Moolten and Vroman and also Eisen and his associates.[7] This range was from 0.90 to 1.25.

Sixty patients with multiple sclerosis were selected from the Multiple Sclerosis Research Clinic of Bellevue Hospital. They were divided into three groups, based on clinical activity, namely: stationary, fluctuating, and acute exacerbation. The patients considered stationary (26) were those who had had no new symptoms or signs for at least six months preceding the investigation. The fluctuating group (28) consisted of patients who reported frequent new symptoms, or fluctuations of old symptoms that often could not be corroborated by neurologic examination. The group classified as acute exacerbation (6) were patients who complained of new symptoms, and had clinically verifiable objective signs which had not been present before.

Ninety determinations were done on the 60 patients, 24 returning for repeat tests. The intervals ranged from two days to three months. Two patients in acute exacerbation were followed closely until clinical remission occurred.

The 33 patients with other chronic neurologic disorders, and 39 patients with acute neurologic disorders, were selected from the medical

TABLE II

	Number of Cases	Adhesive Index Average	Range	Normal	Abnormal
CHRONIC NEUROLOGIC DISORDERS (Other than Multiple Sclerosis)					
1. Amyotrophic Lateral Sclerosis	4	1.01	0.96-1.10	4	0
2. Subacute Combined Degeneration	3	0.97	0.78-1.13	3	0
3. Syringomyelia	3	1.28	1.20-1.38	2	1
4. Parkinsonism	5	1.27	0.99-2.03	4	1
5. Other Extra-Pyramidal Disorders	4	1.07	0.00-1.17	4	0
6. Presenile Dementia	7	1.10	1.02-1.20	7	0
7. Idiopathic Epilepsy	5	1.05	0.90-1.19	5	0
8. Undiagnosed Disease of Spinal Cord	2	1.50	1.40-1.60	0	2
	33				

and neurologic services of Bellevue Hospital. The type and number are indicated in the tables.

Results: 1. Multiple Sclerosis Group (Table I).

Of the 30 determinations done on 26 patients who were considered as stationary, 80 per cent were normal and only 20 per cent abnormally high. However, of the 45 determinations on the fluctuating group, only 18 per cent were normal and 82 per cent were abnormal. Similarly, 15 determinations on the group of acute exacerbations indicated that 14 were abnormal and only one determination was normal and this on a patient who was already showing objective and subjective improvement.

The range of values also showed a significant difference, the highest values being found in the group of cases in exacerbation. The average adhesive index for the stationary group was within the normal range, 1.16. The average for the fluctuating group was 1.50 and for the group in exacerbation 1.81.

2. Chronic Neurologic Group (Table II).

Of the 33 patients studied only four showed an abnormally high adhesive index. Two of these four patients had spinal cord disease of undetermined etiology, all laboratory studies including myelogram having been negative. History and neurologic findings failed to give evidence of disseminated lesions and therefore these cases were not considered to

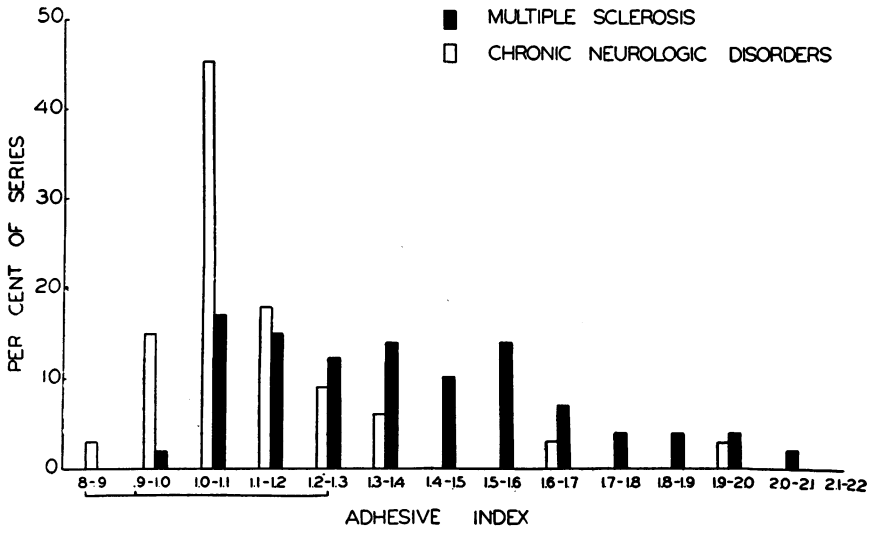

Figure 1—Frequency distribution of the multiple sclerosis series compared to other chronic neurologic disorders. The normal range of the adhesive index is 0.90-1.25.

TABLE III

	Number of Cases	*Adhesive Index Average*	*Range*	*Normal*	*Abnormal*
ACUTE NEUROLOGIC DISORDERS					
1. Head Trauma	5	1.40	1.25-1.61	1	4
2. Brain Tumors	8	1.45	1.01-1.72	2	6
3. Cerebro-vascular accidents	10	1.00	0.76-1.22	10	0
4. CNS Syphilis	7	0.97	0.88-1.11	7	0
5. Meningoencephalitis	5	1.05	0.84-1.31	4	1
6. Guillain-Barré Syndrome	4	1.65	1.52-1.80	0	4
	39				

be multiple sclerosis. The future course of these two patients may give us the answer. The striking difference between the chronic neurologic disorders and the multiple sclerosis group is shown in the frequency distribution graph (Fig. 1).

3. Acute Neurologic Disorders (Table III).

Cerebrovascular accidents and inflammation of the central nervous system gave uniformly normal values, the highest value being 1.31, just

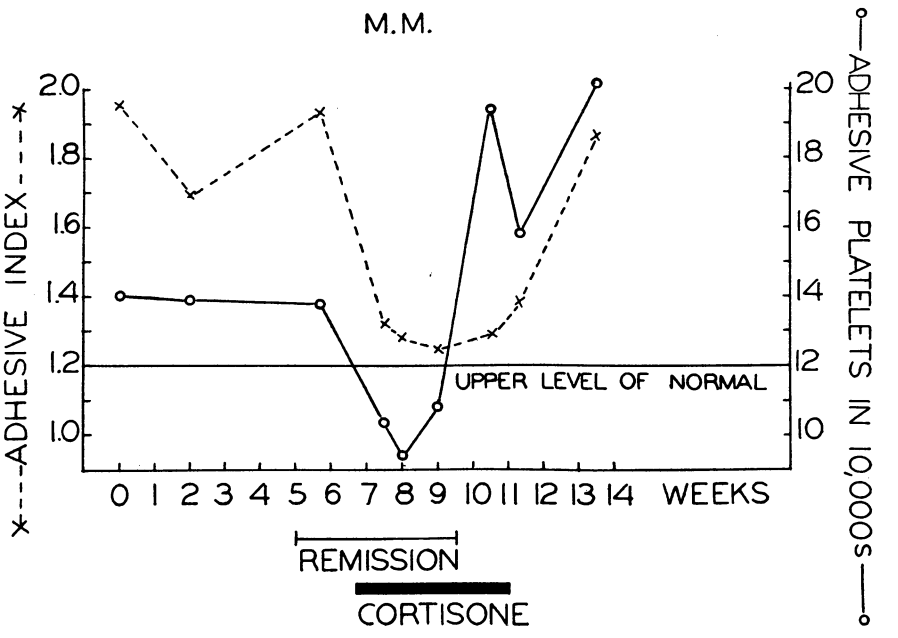

Figure 2—Patient M. M. The platelet adhesiveness followed during an exacerbation of multiple sclerosis, a remission and another exacerbation. The second attack of retrobulbar neuritis occurred during the ninth week while on cortisone.

outside the normal range. Six of the eight proven brain tumors had abnormally high adhesiveness and four of five acute head injuries also had raised adhesiveness several days following the trauma. However, although the platelet adhesiveness was elevated, it did not reach the range of the exacerbations of multiple sclerosis. Four cases of Guillain-Barré syndrome all showed a high adhesive index during the period of activity of the disease which was in the range of active multiple sclerosis.

Two cases of multiple sclerosis were followed closely through an exacerbation and a remission. One of them is of special interest because determinations were made prior to and during administration of cortisone (Fig. 2). A twenty-six year old man diagnosed as multiple sclerosis suddenly began to complain of marked pain behind the right eye and dimness of vision in that eye. On examination, two days later, he had a large right central scotoma which had not been present before. At this time and for several weeks following he had an abnormally high adhesive index. The vision of his right eye improved gradually and the

central scotoma disappeared. Six weeks following the onset of disturbance of the right eye, he complained of "almost blindness" of the left eye. There was complete remission in three weeks. At this time he was admitted to the hospital and started on 100 milligrams of cortisone per day. His adhesive index and adhesive platelets remained about normal for several weeks and he showed no new signs or symptoms. While on cortisone he then had another attack of acute retrobulbar neuritis in his right eye. Shortly following this, his adhesive index rose to a very high level and cortisone was stopped. Eisen et al[7] have shown that cortisone has no effect on the platelet adhesiveness.

Discussion: Analysis of the data presented reveals a striking difference between multiple sclerosis and other chronic neurologic disorders both in number of abnormally high indices and in the extent of the increase of the platelet adhesive index. Since these high values were found almost entirely among the fluctuation and exacerbation groups, the implication is that a high adhesive index parallels the clinical activity of the disease. This was confirmed in the two cases followed closely.

As to the high values in brain tumors, Moolten and Vroman have indicated that in patients with malignancy there is a change in adhesiveness. Similarly, trauma to any part, or surgical procedures result in a rise of platelet adhesiveness over a period of 4 to 10 days. This has been confirmed. Therefore, it may be concluded that the increased adhesiveness in brain tumors and head trauma is non-specific for the nervous system. However, the fact that in 4 out of 4 cases of the Guillain-Barré syndrome high values were obtained suggests the possibility of a similar process of activity in multiple sclerosis.

The consistent normal values found in cerebral vascular accidents and inflammatory processes in the central nervous system speak against these factors as pathogenetic in multiple sclerosis.

The role of the platelets in the clotting mechanism is unclear and particularly the role of platelet adhesiveness is unknown. Preliminary studies by Savitsky and Greenwald[8] suggest that clot retraction is very closely correlated with platelet adhesiveness and not with the platelet count, within the normal range of platelets. It is interesting to note that Henstell, Henstell, Smalens and Ornitz[9] in a study of various tests of the clotting mechanism in multiple sclerosis observed that the only changes were in platelet agglutination and in clot retraction. Whether thrombosis is an etiologic factor in multiple sclerosis can not be inferred from this

evidence. Eísen and his associates[7] have demonstrated that in active thromboangiitis obliterans there is an elevation in the platelet adhesiveness which is comparable to the rise in adhesiveness found in multiple sclerosis.

As far as the diagnostic value of this test is concerned, a high value can not rule out a brain tumor, nor does a low value indicate the absence of multiple sclerosis. It can be said that this test has value as an indicator of activity in multiple sclerosis and that this may be important in evaluating new therapy.

Summary

The platelet adhesive index was studied in a series of patients with multiple sclerosis and other chronic and acute neurologic disorders. The platelet adhesiveness was found to be elevated during periods of activity of multiple sclerosis and in the Guillain-Barré syndrome. It was also elevated in brain tumors and following head trauma. There was no change in the other neurologic disorders.

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