wider than the range of capillary flow rates in man (30 to 54 mm./min.[4]). However, from the standpoint of velocity, the flow in the insect wing channels much more closely approximates the capillary rate of flow in man than the speed of blood in large arteries such as the carotid in which velocities of 18,000 mm./min. (horse) and 15,600 mm./min. (dog) have been recorded.[4]

Summary. The average hemocyte velocity in the subcostal cell of the elytron of the cockroach, *Periplaneta americana* Linn., is 34.3 ± 14.4 mm. per minute. The range of normal average velocities extends from 14.5 to 65.2 mm. per minute. This range approaches the range of 30 to 54 mm. per minute found in the capillaries of man. The highest hemocyte speed observed was 65.5 mm. per minute; the lowest 10.1. No relationship was detected between variations in velocity and sex or the heart rate of the insects used for this study.

8927 C

Relation of Viscosity of Blood to Leucocyte Count, with Particular Reference to Chronic Myelogenous Leucemia.

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Studies of factors which influence the viscosity of the blood have been concerned chiefly with the effect of changes in the total volume of the red blood cells. Nygaard, Wilder and Berkson[1] have recently shown that, within certain limits, the relation between the viscosity of whole blood and the hematocrit value may be well expressed by a linear formula, providing statistical confirmation of similar observations made by Allbutt,[2] Austrian[3] and Bircher.[4] The probable importance of the white blood cells in contributing to significant changes in the viscosity of the blood has been considered by a number of workers. Bircher[4] stated that the white blood cells did not influence the viscosity of normal blood because of their

4 Howell, W. H., Textbook of Physiology, 11 edition, 1930, 493.

1 Nygaard, K. K., Wilder, M., and Berkson, J., *Am. J. Physiol.*, 1935, **114**, 128.

2 Allbutt, C., *Quart. J. Med.*, 1910, **4**, 350.

3 Austrian, C. R., *Bul. Johns Hopkins Hosp.*, 1911, **22**, 9.

4 Bircher, M. E., *J. Lab. and Clin. Med.*, 1921, **7**, 134.

small number but pointed out that if sufficiently increased they might have a marked influence. High, normal and low values for the blood viscosity in leucemia have been recorded by several observers.[2-7] This communication reports the results of a quantitative study of the relation between the white blood cell count and volume and the viscosity of whole blood, with particular reference to the leucocytosis of chronic myelogenous leucemia.

Simultaneous observations of the viscosity of whole blood, the hematocrit value and red and white blood cell counts were made in patients with chronic myelogenous leucemia at various blood levels. The viscosity was measured in relation to distilled water at room temperature by means of the Hess viscosimeter.[4] Hematocrit values

TABLE I.
Blood Counts, Hematocrit Values and Blood Viscosity in Chronic Myelogenous Leucemia.

Subject	Date	R.B.C. Millions per cu. mm.	W.B.C. per cu. mm.	Hematocrit Volumes % R.B.C.	Hematocrit Volumes % W.B.C.	Viscosity	Circulation Time sec.
E.G.	4-15	3.17	463,000	25.5	29.0	9.4	
	4-20	3.41	379,000	28.0	21.0	7.2	
	4-25	4.02	103,000	33.5	8.5	5.1	
	4-30	3.89	58,000	36.0	3.0	4.6	
	6-19	4.34	358,000	33.0	20.0	7.8	
	6-24	3.87	246,000	32.5	17.0	7.0	
	8-25	3.60	306,000	28.0	24.0	7.6	
	8-31	3.21	552,000	26.0	29.0	9.8	22
	9-8	3.79	47,000	32.5	3.5	3.8	14
J.N.	515	3.72	383,000	25.5	18.5	7.0	19
	5-19	3.17	338,000	21.0	17.0	5.5	
	5-22	2.71	252,000	23.0	14.0	4.8	
	5-28	2.92	58,000	26.0	3.0	3.4	
	6-1	2.95	14,900	28.0	1.0	3.6	13
M.T.	5-12	4.55	87,000	38.0	8.0	6.4	
	5-26	4.16	142,000	31.0	12.0	5.9	
	8-25	4.28	97,000	34.0	8.0	5.6	
E.S.	4-28	4.71	45,000	33.0	2.5	4.0	
	5-26	4.09	35,300	32.0	3.0	3.8	
	6-23	4.38	58,000	33.0	5.0	3.9	
E.R.	5-8	4.03	54,000	32.0	3.0	4.2	
	9-4	4.77	5,850	37.0	0.5	4.8	
A.S.	4-30	4.60	73,000	44.5	5.0	5.8	
M.F.	9-9	3.29	347,000	24.0	12.5	6.8	26

[5] Determan, Dr., *Z. f. klin. Med.*, 1906, **59**, 282.

[6] Retky, H., *Z. f. Heilkunde*, 1907, **28**, 106.

[7] Naegeli, O., Blutkrankheiten und Blutdiagnostik, Julius Springer, Berlin, 1931, 41.

were determined by the Wintrobe method,[8] using the anticoagulant recommended by Heller and Paul.[9] The red and white blood cell counts were determined in the usual manner. Table I shows the results of 24 such determinations. Examination of the data shows, as might be expected, that the viscosity of whole blood in myelogenous leucemia is determined not only by the level of the white blood cell count and volume but also by the relative volume of the red blood cells.

In order to study the relation of the white blood cell hematocrit to the viscosity more directly, a number of observations were made of suspensions of white blood cells in plasma. By repeated sedimentation of a large sample of oxalated whole blood obtained from patient E. G., a suspension of leucocytes in plasma, free of erythrocytes, was obtained. This suspension contained 600,000 white blood cells per cu. mm., 34% of white blood cells by volume and a viscosity of 4.4. A number of dilutions of this suspension were made by the addition of appropriate amounts of plasma (viscosity, 1.7) obtained from the same patient. Hematocrit and viscosity determinations made in each of these dilutions are shown in Fig. 1. Within the range covered by this experiment there is apparently a linear relation between the relative volume of leucocytes suspended in plasma and the viscosity of such a suspension.

As a corollary to the above experiment, the relation between the total leucocyte count and the white blood cell hematocrit of such suspensions and of whole blood was investigated (Fig. 1). The relation is apparently linear and is similar to that recorded by Wintrobe[8] in a series of determinations made in blood samples in which the predominating leucocytes were of the myeloid series. It should be noted that the observations recorded in Fig. 1 were made in bloods obtained from patients with chronic myelogenous leucemia, in which cells of the myeloid series constituted from 85 to 99% of the total leucocytes. The average size of the white blood cells, calculated from data shown in Fig. 1 was 628 cubic microns, with extremes of 417 and 920 cubic microns. The relations depicted would not be applicable to blood samples containing significantly larger numbers of lymphocytes, the volume of which has been found to be between 170 and 300 cubic microns.[8] Because of the limited number of observations and the nature of the data (varying proportions of immature and mature granulocytes in the samples examined) the determination of statistical constants was not considered feasible.

[8] Wintrobe, M. M., *Am. J. Med. Sci.*, 1933, **185**, 58.

[9] Heller, V. G., and Paul, H., *J. Lab. and Clin. Med.*, 1934, **19**, 777.

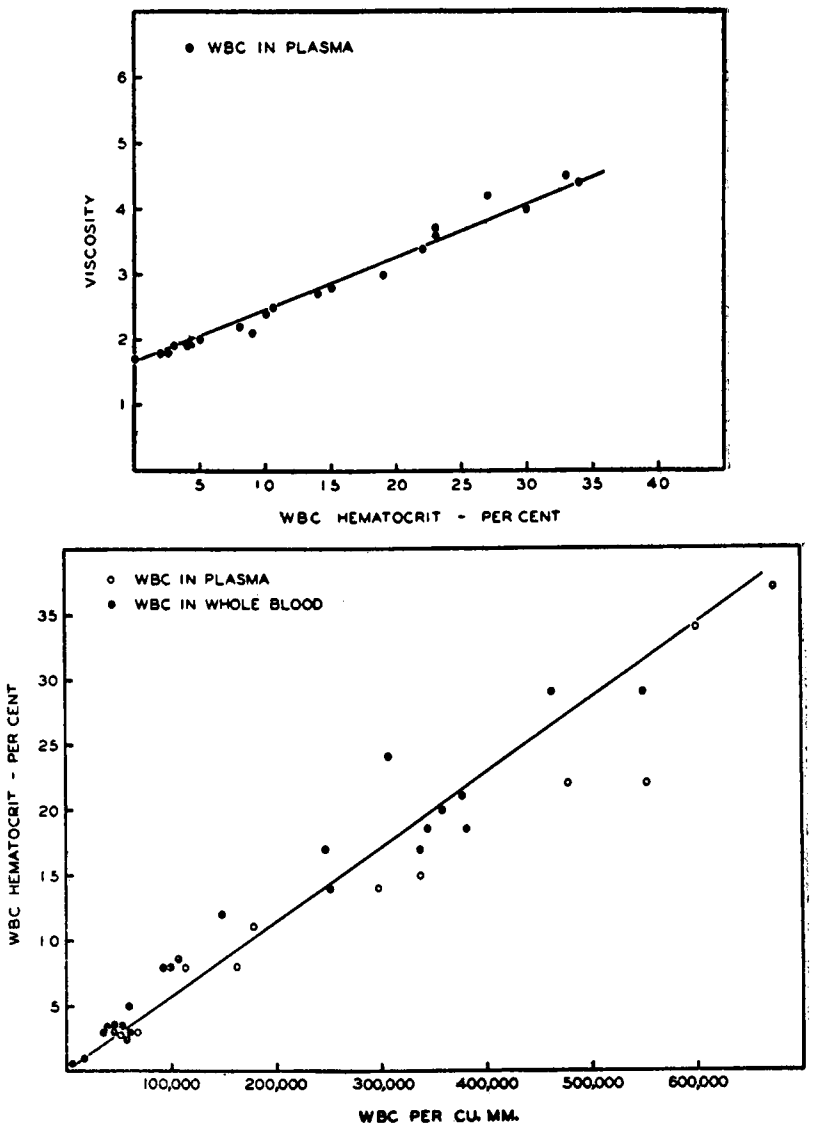

FIG. 1.

The relation of the white blood cell hematocrit to viscosity and to the total white blood cell count.

From the data presented it is apparent that the leucocytes had little effect on the viscosity of whole blood unless the total white blood cell count was in excess of 50,000 per cu. mm. and the white blood cell hematocrit exceeded 3 volumes %. With more marked elevations in the leucocyte count, significant increases in the blood viscosity were observed, the extent of which was dependent to some

degree on the relative volume of the erythrocytes. Attempts to demonstrate a constant relationship between the total hematocrit and blood viscosity were unsuccessful because of a disproportionate increase in the latter in the higher hematocrit ranges. Bircher[4] states that the influence of the various factors which determine the blood viscosity is not merely a summation but is rapidly intensified with increases in concentration. Our observations support this contention. In this regard, it is of interest that Nygaard, Wilder and Berkson[1] observed that for high values of hematocrit observed in patients who were suffering from polycythemia, the viscosity was higher than the values predicted from their formula.

In view of the very high values observed in several instances (Table I), it seems not improbable that the increased blood viscosity accompanying very high leucocyte counts in myelogenous leucemia may account for some of the symptoms observed in this disease. In chronic lymphatic leucemia normal values for the blood viscosity[7] have been observed in the presence of leucocyte counts in excess of 500,000, presumably owing to the small relative volume of the lymphocytes. Lengsfeld[10] called attention to a certain parallelism between polycythemia and myelogenous leucemia with high leucocyte count and suggested that the cerebral symptoms observed in his patient may have been due to a probable great increase in viscosity accompanying a white blood cell count of 800,000 per cu. mm. Rotenberg[11] has recently expressed the opinion that increased viscosity of the blood may play a part in the pathogenesis of priapism occurring in leucemia and other diseases.

Observations of the arm to tongue circulation time (Decholin method) were made in 3 patients with marked elevation of the leucocyte count, hematocrit and blood viscosity (Table I). Patient E. G. repeatedly complained of dizziness, roaring sensations in the ears, mental dullness and faintness during periods of marked leucocytosis. These symptoms disappeared when the white blood cell count was reduced by appropriate treatment. A circulation time of 22 seconds, which accompanied a blood viscosity of 9.4, was reduced to a normal value when the total white blood cell count, hematocrit and viscosity were lowered by means of roentgen therapy. Similar observations were recorded in the case of J. N., who had recently experienced symptoms and signs characteristic of splenic infarction. Patient M. F., who was seen through the courtesy of Dr. F. K. Holzwarth, presented the typical picture of chronic myelo-

[10] Lengsfeld, W., *Jahrb. f. Kinderheilkunde*, 1929, **126**, 289.

[11] Rotenberg, M. I., *J. D'Urologie*, 1935, **39**, 508.

genous leucemia, complicated by transverse myelitis of the thoracic spinal cord. Marked prolongation of the circulation time and increased blood viscosity accompanied a high leucocyte count and white blood cell hematocrit.

Summary. 1. Observations of the blood viscosity, hematocrit, blood counts and circulation time were made in a group of patients suffering from chronic myelogenous leucemia. 2. The relation between viscosity of the blood and the total number and volume of the white blood cells was determined. 3. The high leucocyte counts observed in chronic myelogenous leucemia are frequently responsible for marked increase in blood viscosity and prolongation of the circulation time. The probable relation of these changes to the symptomatology of the disease is briefly discussed.

8928 C

Seasonal Variation in Susceptibility of Animals to Tetanus Toxin.

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During the course of certain investigative work with tetanus toxin,* it was noted that there appeared to be a consistent variation in the susceptibility of animals to the same lot of toxin. Judging from the time of onset and the severity of the symptoms in acute and subacute poisoning in the rabbit and guinea pig, there was found an increased susceptibility during the summer months and decreased susceptibility during the winter months. Since this observation was rather incidental, it was decided to determine the actual minimal lethal dose of the toxin at various periods during the year.

For these toxicity studies, guinea pigs were used in all experiments. The toxin was kept in an icebox in small vials sealed in carbon dioxide. Approximately 100 guinea pigs were used. The work was carried on over a 2 year period.

The minimal lethal dose as determined during October and February and a year later in November was found to be from 0.004 to 0.005 mg. per kilo of body weight. This amount will kill approximately 8 out of 10 animals. All animals die with 0.006 mg. per kilo.

* The tetanus toxin for this work was kindly furnished by Dr. McCoy of the National Institute of Health, Washington, D. C.