THE MECHANISM OF THE INFLAMMATORY PROCESS.*

I. The Electrophoresis of the Blood Cells of the Horse and Its Relation to Leucocyte Emigration.

By HAROLD A. ABRAMSON,† M.D.

(From the Kaiser Wilhelm Institute for Physical Chemistry and Electrochemistry, Berlin-Dahlem, Germany.)

(Received for publication, July 6, 1927.)

The present status of the relationship between the electrokinetic potential of leucocytes and the potential differences existing between injured and uninjured tissue zones, points to a situation which is not alone unsolved quantitatively but also qualitatively; but its solution presents, perhaps, a hopeful answer to the question of leucocytic migration in response to injury.

HISTORICAL.

Dineur (1) (1893) seems to have been the first investigator who attempted to study the electrical charge on white blood cells. He placed platinum wires that had been sealed into glass capillaries into the normal and inflamed peritoneal cavities of the frog. Leucocytes tended to enter the capillaries in the absence of a current. In normal frogs, upon the passage of a current, more leucocytes went to the anodal capillary, but just the reverse occurred in frogs with peritoneal exudates. In the latter, the leucocytes seemed to be positively charged, wandering in greater numbers to the cathode. From that time until the present no work has apparently been done which defines *quantitatively* the speed of leucocytic migration and a possible ζ potential. Further, the conditions of the previously undertaken investigations have been so ill defined according to our present knowledge of the behavior of charged colloidal particles, that the investigators' statements seemingly disagree even as to whether leucocytes wander to the anode or to the cathode.

Lillie (2) (1903) studied the white blood cells of the frog suspended in isotonic

* Unless otherwise stated in this and the following papers, the word "inflammation" is used in a strictly limited sense; *i.e.*, the wandering of a white blood cell to a point of injury.

† Fellow in Medicine, National Research Council.

sugar-NaCl solution. Under these conditions it was found that lymphocytes wandered to the anode; the polymorphonuclear leucocytes to the anode or cathode, or even remained stationary. Höber (3) the following year maintained that frog leucocytes were negatively charged. In 1914, Schwyzer (4), overlooking the definite results of Lillie and Höber, stated that the work of Dineur was untrustworthy, and that his own efforts to produce cataphoresis of leucocytes in tissues were unsuccessful. Schwyzer, however, was the first to hint that electrical differences of potential may play a part in producing the appearances of inflammation. He states: "Der Weg zur Emigration wird durch die Elektronenströme angedeutet, und die Pseudopodien werden durch diese Ströme in der schwachsten Stelle der Membran [capillary wall] gerichtet. Die Leucocytenwanderung im Gewebe wird also *chemotaktisch* aufgefasst, konnte aber auch durch Ionenwirkung erklärt werden." Mendelssohn (5) observed that leucocytes wandered to the cathode. The work done by Höber and his coworkers later leads him to state (6): "Dies hängt damit zusammen, dass nach der Kataphoresegeschwindigkeit und nach der Entladbarkeit mit La^{+++} beurteilt, das ζ potential der Leucocyten nur schwach, negativ, null, oder schwach positiv ist." Eliasoph (7) found that gelatin suspensions of leucocytes wandered to the platinum anode, and that if the electrodes were buried in splenic tissue, there was also anodal migration. Unfortunately, non-polarizable electrodes were not used by Eliasoph. Feringa (8) (1922, 1924) mentions qualitative experiments with rabbit and other white cells. He found them to be negatively charged, but no quantitative data are given concerning speed or potential. Feringa states that lymphocytes do not move as quickly as leucocytes cataphoretically. This will subsequently be shown to be probably a misinterpretation. This author, agreeing with Schwyzer, believed that the potential difference between injured and uninjured tissues caused leucocytic migration to a point of injury, the basis of this taken as pH changes. His observations that leucocytes in general move with ameboid movements toward the anode on an agar floor had not been noted by Abramson (9) on a glass floor for a small potential difference. However, studies on the *floor* of an electrophoresis chamber are complicated by at least the following: (1) the nature of the floor and its influence on the particle itself; and (2) the fact that the suspending medium is also charged relative to the floor. In general, alkaline fluids near the floor of a cataphoresis chamber are positively charged and move toward the cathode. Before one can state, therefore, that ameboid motion is influenced by an electric current, it must be ascertained whether leucocytes would migrate against a moving stream of fluid as occurs in the instance of spermatozoa which move *against* the ciliary stream in the ducts of the female generative organs.

Abramson (9, 10) during the same year (1924) published studies on human lymphocytes suspended in serum. He found human lymphocytes to be definitely negatively charged and estimated the mean

cataphoretic velocity (C.V.) semiquantitatively at 0.3μ per volt per cm. per sec. Further, lymphocytes kept on ice during a period of 30 hours did not appreciably alter the speed of migration. The work on human lymphocytes was undertaken in order to test a hypothesis then proposed which attempted to correlate *quantitatively* the order of magnitude of the potential differences in injured tissues and the speed of white cell cataphoresis (see Fig. 2). The researches of Du Bois-Reymond (11), Biedermann (12), and Hermann (13) pointed to the fact that negative electricity could be conducted from injured tissue surfaces. Potential differences between injured and uninjured surfaces up to about .1 volt had been recorded. With this in mind, it seemed possible that the border of a zone of injury relative to the comparatively uninjured cells, capillary wall, and blood stream could be positively charged. As the surrounding tissue and tissue fluids are conductors, a continuous current must flow between uninjured and injured tissues, the energy coming from the metabolic changes incidental to injury. It was then shown that the order of magnitude of the potential drop between uninjured and injured tissues was probably the same as that necessary to cause white blood cell migration as far as lymphocytes were concerned. That this is also true for polymorphonuclear leucocytes as well will be shown in this communication, and data will be presented concerning the absolute velocities of horse polymorphonuclear leucocytes and lymphocytes in plasma and serum. Observations also have been made concerning cataphoresis in gels and their viscosity. The significance of these data in relation to the inflammatory process will be demonstrated.

Methods.

The method in detail of determination of the C. V. of cell migration is presented elsewhere in connection with the more physical aspects of the present studies (14). In brief, a microscopic method, similar to that used by Northrop (15), was employed which permitted fairly accurate measurement of red cell velocity at different levels in the cataphoresis chamber. From these data the velocity of the medium, V_m, in a given level of the cell could be calculated. The actual velocity of the white cells, V, is then,

$$V = V_o - V_m$$

where V_o is the observed velocity in the particular level. The potential drop in the cell during the measurements was usually of the order of 15 volts per cm.

The Calculation of ζ Potential and the Viscosity of the Suspending Medium.

As is well known (16) the flow of certain colloidal solutions through a capillary, in particular the lyophilic sols, does not follow the Poiseuille formula. That is, with different pressures exerted on the moving column, different values of "viscosity" are obtained. The smaller

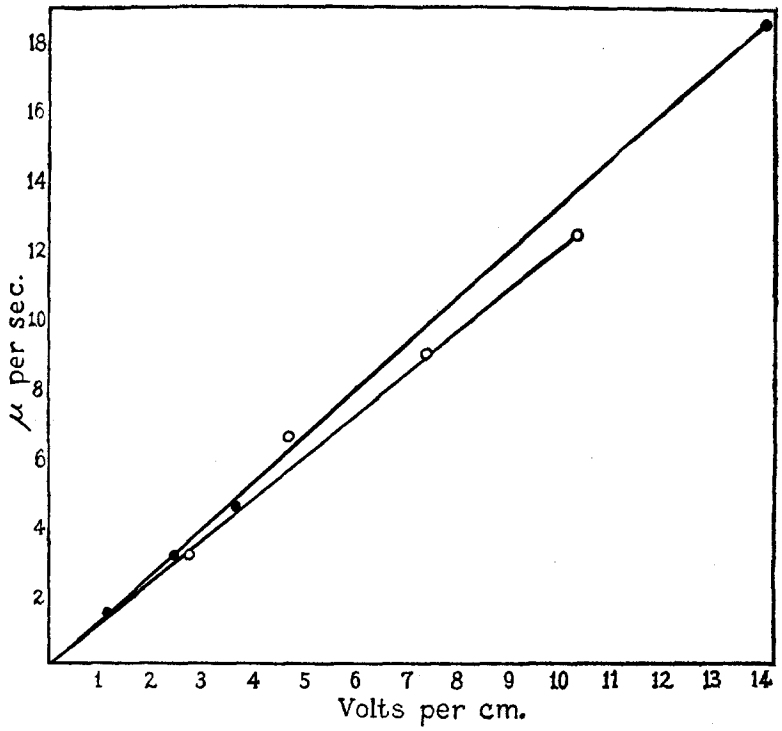

FIG. 1. The C. V. of red cells in plasma is proportional to the applied P. D. The same linear relationship exists for serum.

the pressure, the greater is the "elasticity" of the solution. Blood shows this elastic effect to a slight degree.

From consideration of the Helmholtz-Lamb equation, $v = \frac{HK\zeta}{4\pi\eta}$ (v = velocity, K = dielectric constant of the medium, H = potential drop per cm., ζ = electrokinetic potential, η = viscosity)

(all units are electrostatic), it follows that in a system where the elasticity of the medium could hinder migration, v would not be proportional to H.

Fig. 1 shows that marked differences in H produce a particle velocity which follows the conventional Helmholtz-Lamb equation, and consequently demonstrates that under these conditions plasma and serum have no "elasticity." Accordingly taking the value of .02 for η,[1] 85 for K (Fürth), and the observed values for the other factors, it follows that for a drop in potential of 1 volt per cm. at 18° the electrokinetic potential

$$= \frac{4 \times 3.14 \times .02 \times (300)^2}{85}$$

$$= (26.5 \times \text{velocity in } \mu \text{ per sec.}) \text{ millivolts.}$$

Evidence has also been obtained by Freundlich and Abramson (14) that the migration of the micellæ of certain "elastic" gelatin gels has the same speed in the gel that is found in the sol. In this instance, a linear relationship between H and C.V. has also been found. This strongly suggests that extremely small differences of potential existing in tissues could produce particle migration even though a viscous gel-like medium was present.

The Electrophoresis of Erythrocytes.

Plasma suspensions of leucocytes and red cells were obtained by oxalating 1 litre of freshly shed horse blood with 8.5 cc. of the saturated solution of the potassium salts. Table I gives the C.V. of red cells in plasma obtained from seven different horses. The mean value .98 μ per volt per cm. per sec. for plasma agrees quite well with the mean value, 1.01μ per volt per cm. per sec. obtained in serum from ten other horses. The data for serum[2] are published elsewhere (14).

[1] The viscosity of serum is actually 5–10 per cent lower than that of plasma. This difference is here neglected.

[2] The data for serum include studies made on aggregates of red cells and red cell rouleaux. It was found that the C. V. of different shaped aggregates were identical with one another and with single cells. The significance of these facts is discussed (14).

Keeping the cells on ice during a period of 3 days or less did not change the C.V. It may be recalled that the isoelectric point of fibrinogen is in the region pH 8.0. Plasma contains .1 to .4 per cent of this protein. The isoelectric point of the other proteins present is in the region pH 5.0. As the isoelectric points of the proteins influence the ζ potential, different C.V. could have been expected from plasma and serum cell suspensions.

TABLE I.

The Electrophoresis of Red Cells in Plasma. Seven Different Horses.

Plasma	Age of cells	Speed	ζ potential
	hrs.	*μ per sec. per volt per cm.*	*millivolts*
A	30	1.04	27.5
B	30	1.02	27.0
B		.90	24.0
C	6	1.07	28.0
C serum	6	1.06	28.0
C	30	1.01	27.0
F	6	.97	26.0
F serum	6	.94	25.0
H	6	.91	24.0
I	6	.90	24.0
I		1.01	27.0
J	6	.95	25.0
Mean plasma		.98	26.0
Mean serum (10 horses)		1.01	27.0

The Electrophoresis of White Cells.[3]

Polymorphonuclear leucocytes (P) wander in plasma (Table II) with a mean C.V. of .54μ per volt per cm. per sec. (seven horses). This value is about half that found for red cells from the same group

[3] The C. V. of blood platelets has also been studied and will be presented in a subsequent communication.

(98:54). The calculated mean ζ potential is 14.5 millivolts. Small lymphocytes (SRC) wander in plasma about 20 per cent faster than polymorphonuclear cells. Because of the presence of blood platelets, optimal optical conditions were not present for differentiation of polynuclear cells and round cells. For this reason, serum was studied in greater detail; but it was quite clear that the same relationships held for serum and plasma. In both instances, as found previously for human lymphocytes, keeping the cells on ice up to 48 hours did not alter the C.V.

TABLE II.

The Electrophoresis of White Blood Cells in Plasma (Seven Horses).

(P) = polymorphonuclear leucocyte. (SRC) = small lymphocyte.

Plasma	Age of cells	Corrected speed	ζ potential
	hrs.	*μ per volt per cm. per sec.*	*millivolts*
1 (P)	30	.51	13.5
1 (SRC)		.61	16.0
2 (P)	6	.46	12.0
3 (P)	6	.59	15.5
3 (P) serum	6	.50	13.5
3 (P)	30	.57	15.0
4 (P)	6	.57	15.0
5 (P)	6	.47	12.0
5 (SRC)	6	.60	15.5
6 (P)	6	.58	15.5
7 (P)	6	.58	15.5
Mean (P).....		.54	14.5

$$\frac{\text{Red cell}}{\text{P}} = \frac{98}{54} = 1.8$$

Table III is a summary of experiments with cells in serum taken from six different horses; the mean velocity of polymorphonuclear leucocytes observed in this series of experiments was .51μ per volt per cm. per sec. The calculated ζ potential was 13.5 millivolts. Lymphocytes have given a mean velocity of .60μ per volt per cm. per sec. with a ζ potential of 17.0 millivolts. It is preferred to take the values given in the tables for large round cells (LRC) as approximate because of the difficulties incidental to differentiation of unstained cells.

TABLE III.

The Electrophoresis of White Blood Cells in Serum. Six Different Horses.

(LRC) = large round cell.

Type of cells	Age of cells	Corrected mean (V)	ζ potential	Remarks
		μ per volt per cm. per sec.	*millivolts*	
1 P	30 hrs.	.50	13.0	P is a mean of 3 values .49, .58, .43 obtained from *different* levels in cell. These do not agree as well with one another as those given below taken in the midregion.
SRC		.59	15.5	
2 P	6 "	.51	13.5	Although a different chamber than above was used in this experiment, the agreement is excellent P — SRC are mean of 2 experiments.
SRC		.60	17.0	
2a P	30 "	.50	13.0	
SRC		.62	16.5	
LRC		.55	14.5	
3 P	3 days	.61	16.0	In this serum, 3 days old, although higher values have been noted, the ratio P/SRC is practically the same as above.
SRC		.74	14.5	
4 P	2 "	.55	14.5	
SRC		.66	17.5	
5 P	6 hrs.	.47	12.5	
SRC		.54	14.0	
6 P	6 "	.54	14.5	
Mean as above: 1 P 2 P 2a P 4 P 5 P 6 P		.51	13.5	$\frac{\text{SRC}}{\text{P}} = \frac{17.0}{13.5} = 1.25$
1 SRC 2 SRC 2a SRC 4 SRC 5 SRC		.60	17.0	$\frac{\text{Red cells}}{\text{P}} = \frac{27}{13.5} = 2.0$

TABLE IV.

Typical Protocols of Experiments to Determine Leucocyte Velocity. Horse Serum and Cells.

Column 1, 6 hrs. old. Column 2, 30 hrs. old.

No.	Type	V_o	V	ζ potential		No.	Type	V_o	V	ζ potential	
				millivolts						*millivolts*	
1	P	.73	.48	12.5		1	P	.76	.54	14.0	
2	P	.68	.45	12.0		2	P	.70	.48	12.5	
3	SRC	.87	.62	16.5	Chamber	3	P	.72	.50	13.5	
					refilled	4	P	.69	.45	12.0	
4	P	.71	.48	12.5		5	SRC	.82	.60	16.0	
5	P	.75	.55	15.0		6	LRC	.79	.55	14.5	
6	P	.77	.57	15.0		7	LRC	.81	.60	16.0	
7	P	.77	.57	15.0		8	SRC	.90	.67	18.0	
8	P	.68	.47	12.5		9	SRC	.76	.56	15.0	
9	P	.71	.51	13.5		10	SRC	.97	.72	19.0	
10	SRC	.85	.64	17.0		11	LRC	.76	.51	13.5	
11	LRC	.65	.44	11.5		12	SRC	.82	.61	16.0	
12	SRC	1.01	.81	21.5		13	SRC	.90	.65	17.5	
13	P	.69	.49	13.0							Refilled
14	P	.74	.53	14.0		14	P	.63	.47	12.5	
15	P	.67	.46	12.0		15	P	.68	.41	12.5	
16	P	.93	.73	19.0		16	SRC	.76	.61	16.0	
					Refilled	17	P	.79	.46	12.0	
17	SRC	.79	.59	15.5		18	P	.74	.52	14.0	
18	P	.76	.54	14.5		19	P	.74	.52	14.0	
19	P	.68	.48	13.0		20	P	.74	.52	14.0	
20	P	.76	.57	15.0		21	P	.69	.47	12.5	
21	P	.75	.54	14.5		22	SRC	.79	.54	14.5	
22	SRC	.83	.62	16.5		23	SRC	.86	.61	16.0	
23	P	.70	.49	13.0		24	P	.79	.55	14.5	
24	SRC	.90	.69	18.5		25	LRC	.79	.57	15.0	
25	LRC	.90	.66	17.5		26	SRC	.84	.63	16.5	
26						27	P	.69	.45	12.0	
						28	SRC	.83	.60	16.0	
						29	P	.76	.53	14.0	
						30	P	.76	.53	14.0	
Mean P.....			.51	13.5							
Mean SRC.....			.66	17.5							
						Mean P.....			.50	13.0	
						Mean SRC.....			.67	16.5	
						Mean LRC.....			.55	14.5	

The C.V. of single polynuclear cells in serum and plasma was quite constant. In the same preparation (Table IV, Column 1) all but one cell of this type wandered with a speed which varied between .45 and .57μ per volt per cm. per sec. This variation appears to be much less from *qualitative* observation. Three or four leucocytes accidentally suspended at the same level migrate with the same velocity. The mean value, therefore, of the sixteen cells closely approaches the true value of the absolute velocity for the preparation, .51μ per volt per cm. per sec. The mean ζ potential, calculated as described heretofore is (26.5 $\times$ .51) 13.5 millivolts.

The behavior of the lymphocytes is as interesting as it is inexplicable. Although a smaller variation in velocity was expected because of the regularly spherical shape, as the table indicates, the velocity of these round cells varies considerably. In general, it may be stated the small lymphocytes wander about 15 to 30 per cent faster than polymorphonuclear cells. The six lymphocytes whose velocities are noted had a mean speed of .66μ per volt per cm. per sec. The calculated potential is (26.5 $\times$ .66) 17.5 millivolts. Frequently, round cells are observed which migrate more slowly than polymorphonuclear leucocytes. Cell 11, for example, was of the large mononuclear type (LRC). Its migration speed was only .44μ per volt per cm. per sec. On the other hand, Cell 6, a polymorphonuclear leucocyte, migrated with a velocity of .73 per sec. These differences are all the more striking when observed. The lymphocytes overtake the leucocytes; the red cells go swiftly by with a velocity practically twice as fast; and then suddenly, one may observe a round cell overtaking another round cell, or a leucocyte exhibiting the unusual property of migrating faster than a lymphocyte. This, however, is rare. On the other hand, although potential drops per cm. as high as 30 volts had been used, leucocytes (20° C.) that had settled to the glass exhibited no movement in either direction and could not be removed by a powerful stream of saline forced through the electrophoresis chamber. Feringa's experiments with an agar floor were not repeated because of the questionable influence of water flow on the ameboid movements of the cells mentioned previously. The data, however, given in the tables represent *absolute* velocity within the cells irrespective of the water flow and of ameboid movements.

DISCUSSION.

It has been stated that the present study was a continuation of the work previously done on human lymphocytes in an attempt to correlate *quantitatively* the electrokinetic potential of white blood cells with the differences of potential passing between injured and uninjured tissues (9, 10).

The following discussion is in continuation of this attempt to establish a quantitative basis for this theory of the mechanism of inflammation. It may be again emphasized here that other views, such as those of chemotaxis, of surface tension, etc., are not meant to be excluded. As will be shown, however, there are two quantities: (1) the speed of white cells per volt per cm., per sec.; and (2) the P.D. existing in living injured tissues, whose order of magnitude can be presented with a fair degree of certainty—a degree of certainty which will permit of a correlation of the two, and of a definition in a limited sense of several physicochemical factors incidental to the inflammatory process.

The preceding data lead one to suspect that mammalian white cells are negatively charged and move with an appreciable velocity under a P.D. of 1 volt per cm. toward the anode. With this in mind, the nature and order of magnitude of the P.D. between injured and normal tissues will be described. It is well known that the *surfaces* of injured tissues are negative to the uninjured surface (15). That the uninjured surface of an injured muscle is comparable to the uninjured underlying tissue is shown by the following experiment. If a carefully dissected frog muscle be cross-sectioned, the injured surface at the moment after cutting shows only a small fraction of the maximum E.M.F. which appears only after a considerable interval (17, 11, 13).

Differences in potential arising in tissues incidental to injury cannot have their sources in electrode potentials as no metal is present. Consequently the currents passing between injured and uninjured tissues must have their origins either in: (1) diffusion potentials which are based upon differences in ionic molarities, or (2) membrane potentials, potentials produced by intervening phases—most probably both. From the former, slight electromotive forces are to be expected not greater than .01 volt. On the other hand, membrane potentials are

usually of the order of .02 to .1 volt. Michaelis' discussion of the physiological significance of diffusion potentials does not give them a particularly important position (18). In the instance of an injured tissue zone, the presence of a new phase would, it is true, produce in all

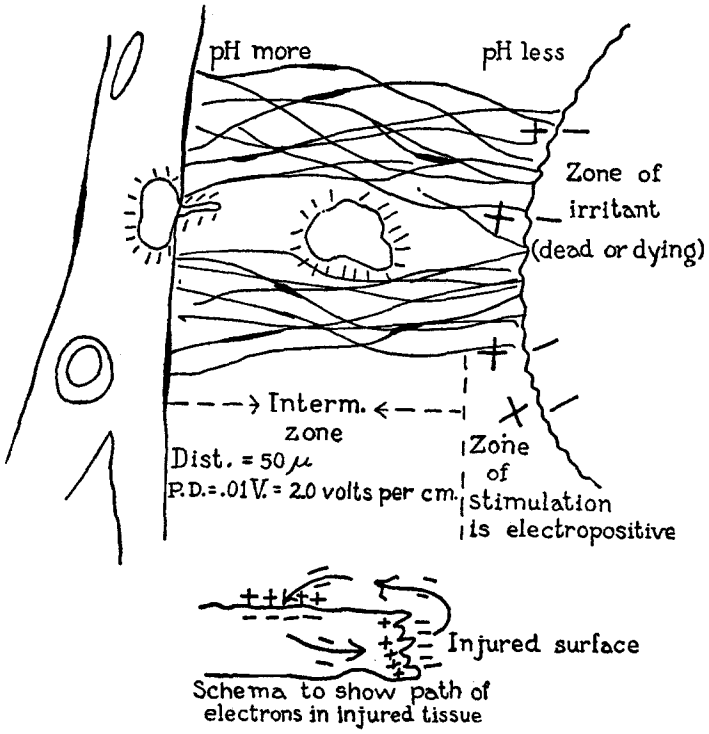

FIG. 2. Note the absence of intervening membranes in the spaces where leucocytic migration occurs between injured area and capillary wall. This *structural* homogeneity lends aid to the supposition that the conductivity and hence the drop in potential is fairly uniform. For further description see text.

probability potential differences of the order of magnitude possessed by membrane potentials.[4] The main drop in potential, however, may be across the phase producing the potential. A particle, migrating

[4] As for example in muscle. A resting muscle is isoelectric. With the production of an injured surface the varying permeability of the membrane of the muscle cells for anions and cations may produce P. D. of the order of magnitude of membrane potentials.

cataphoretically, would thus be out of range of the main drop in potential except when migrating through the phase—*e.g.*, the wall of a capillary. That diffusion potentials may play a significant rôle in the production of cataphoretic migration is shown by the following.

Reference to Fig. 2 shows that negative electricity is drawn from an injured surface. Consequently electrons flow from uninjured tissue zones to injured tissue zones, making the injured area electropositive. That an injured area is relatively positive is made all the more probable by the fact that injured tissues have a lower pH than the blood in the

TABLE V.

This table demonstrates that even with minimum potential differences between injured and uninjured zones appreciable drops in potential per cm. should be found, even with maximum distances.

Distance between injured zone and capillary or normal tissue	100 μ	50 μ	25 μ	10 μ
Possible potential differences between injured and uninjured tissue	Drop in potential in tissue			
volts	*volts per cm.*	*volts per cm.*	*volts per cm.*	*volts per cm.*
.001	.1	.2	.4	1.0
.005	.5	1.0	2.0	5.0
.010	1.0	2.0	4.0	10.0
.050	5.0	10.0	8.0	20.0
.100	10.0	20.0	40.0	100.0

capillaries and adjoining normal tissues (19). Consequently, the higher hydrogen ion concentration (see Fig. 2) again would lead one to believe that injured tissue was electropositive.

Before discussing the order of magnitude of the P.D. existing between injured and uninjured zones, it should be recalled that P.D. is expressed in *volts per cm.* A picture of the forces at play which may influence a charged leucocyte is appreciated only if the drop in potential is converted by estimation of the distance from the injured point to the nearest capillary, to P.D. per cm. Table V shows the estimated order of magnitude of the P.D. per cm. with different distances and different potential differences. The fall across the injured tissue to capillary area would have to be divided inversely proportionally to the resistance of the tissues. As relatively normal tissues have a high resistance

and as the tissue fluids similarly are not good conductors, it is fair to assume that even though the total drop in potential is not uniform, a portion of it, sufficiently great to influence migration of a charged particle, is present. It should be noted that *the inflammatory process takes place in connective tissue*, and leucocytic migration occurs in the capillary spaces between fibrous tissue bands where the P.D. is unhindered by the presence of cell membranes existing in muscle. From the point of view of the structure of the intracellular fluids in connective tissue, one may assume for the present that the thinness and conductivity of phases or membranes present do not make the curve of potential drop sufficiently unlinear to reduce the probability of the correctness of the order of magnitudes to be considered.

Table V shows that even with a P.D. of .001 volt between injured zone and a capillary wall .1 mm. away, the P.D. per cm. is .1 volt. Of course, this is an extreme instance. The potentials measured between cut surface and uninjured surface vary between .030 and .100 volt, and if membranes (phases) are present in the injured zone, this order of magnitude of potential would be expected. If, however, only diffusion potentials incidental to the enormous rise of metabolism which occurs (20) are present and if the P.D. in that instance be only 5 millivolts, with a distance of .05 mm., the P.D. per cm. is *1 volt*,—a force sufficient to bring a leucocyte moving in plasma at the rate of .5μ per volt per cm. per sec. to the point of injury in 2 minutes.

Why do not the red cells and lymphocytes also migrate at once toward the point of injury? Some of them do, but the great difference between these cells and polymorphonuclear leucocytes is that the ameboid cells stick to the capillary walls and are uninfluenced by the rush of blood going by (see Paper II of this series). The speed of blood in capillaries is remarkably constant throughout the vertebrate kingdom. One may expect in mammals a speed of about .5 mm. per second of the cells passing through certain capillaries (21). Even if the P.D. per cm. between blood and injured zone were 20 volts, the speed of a cell moving toward the zone of injury at a rate of .5μ per volt per cm. per sec. would be only 10μ per sec. Thus, there would be a force exerted on the blood cell in the direction of the blood stream fifty times as great as that exerted in the direction of the point of injury (Fig. 2). When, however, a white cell is trapped by the capillary wall, the electromotive

or other forces are dominant and the forward pressure of the blood stream on the adherent cell is negligible. This presupposed, of course, that leucocytes are able to wander through the wall, as they can. The same phenomena are readily seen in an electrophoresis chamber of the kind described above. At *room* temperature, on the floor of the cell, are stationary polymorphonuclear leucocytes, and hovering about apparently suspended in the immediate fluid strata are lymphocytes and red cells. Even though the P.D. on occasions has been 30 volts per cm., the leucocytes which have stuck to the glass remain there uninfluenced by the difference of potential while the round cells and red cells move swiftly by just as in a blood vessel.

One further point at present remains to be discussed—the electrophoresis of water. Granting the difference of potential and the other factors that have been previously discussed, it follows that the movement of the tissue fluids would also be influenced. As the experiments of Mudd (22) have conclusively shown, animal membranes are negatively charged when the medium is serum or any other alkaline fluid. The significance of this in relation to the inflammatory process is at once evident. There should be adjacent to the strands of connective tissue and in the pores of the connective tissue a cathodal flow of water. But, these strands of connective tissue form capillary spaces. If these spaces are closed systems, as in an electrophoresis chamber, in the absence of structural irregularities, there may be in the midregions of these capillary spaces a return anodal flow to assist leucocyte migration where the capillary spaces are not too small.

SUMMARY.

1. The velocity of cataphoretic migration of blood cells in plasma and serum is proportional to the potential drop applied.

2. The cataphoretic velocity of red cells, polymorphonuclear leucocytes, small lymphocytes, and large lymphocytes is described for serum and plasma.

3. The relation between the electrokinetic potential of white blood cells and the differences of potential probably existing in injured tissues are correlated quantitatively.

4. This correlation suggests that migration of leucocytes to a point of injury is, in part, dependent upon the electromotive forces at play in the tissues.

The writer wishes to express his thanks to Professor H. Freundlich for his constant guidance and criticisms, and to Dr. Ettisch for his unceasing interest.

BIBLIOGRAPHY.

1. Dineur, *Bull. Soc. belge micr.*, 1893, xxviii, 113.
2. Lillie, *Am. J. Physiol.*, 1903, viii, 273.
3. Höber, *Arch. ges. Physiol.*, 1904, ci, 607; cii, 196.
4. Schwyzer, *Biochem. Z.*, 1914, lx, 454.
5. Mendelssohn, *Compt. rend. Acad.*, 1916, clxii, 52.
6. Höber, R., Physikalische Chemie der Zelle und der Gewebe, Leipsic, 6th edition, 1926, 756.
7. Eliasoph, *Z. ges. exp. Med.*, 1924, xli, 317.
8. Feringa, *VIII Réunion ann. Physiol. néerl. Amsterdam*, 1922, xii, 28; *Arch. ges. Physiol.*, 1924, cciii, 672.
9. Abramson, H., *Am. J. Med. Sc.*, 1924, clxvii, 102.
10. Abramson, H., *J. Exp. Med.*, 1925, xli, 445.
11. Du Bois-Reymond, E., Untersuchungen über thierische Electricität, Berlin, 1848. See also Luciani, L., Human physiology, translated by Welby, F. E., London, 1915, iii, 75.
12. Biedermann, Elektrophysiologie, Jena, 1895, 274.
13. Hermann, L., Handbuch der Physiologie, Leipsic, 1879, i, 192.
14. Freundlich, H., and Abramson, H. A., *Z. physik. Chem.*, 1927, cxxviii, 25.
15. Northrop, J. H., *J. Gen. Physiol.*, 1922, iv, 629.
16. Freundlich, H., Kapillarchemie, Leipsic, 3rd edition, 1923, 741.
17. Biedermann, *Ergebn. Physiol.*, 1903, ii, pt. 2, 264.
18. Michaelis, L., Die Wasserstoffionenkonzentration, Berlin, 1922, 177.
19. Schade *et al.*, *Z. ges. exp. Med.*, 1921, xxiv, 11.
20. Gessler, H., *Arch. exp. Path. u. Pharmakol.*, 1922, xcii, 273.
21. Tabulæ biologicæ, Berlin, 1925, i, 133.
22. Mudd, S., *J. Gen. Physiol.*, 1925, vii, 389.