that we should find considerable trouble with Sir William Ramsay over the relative apportionment between the two investigators of the radium which was allotted for their use by the Kaiserliche Akademie der Wissenschaften of Vienna. However, the work proceeds with ever-increasing acceleration, the further unravelling of the details of radioactive phenomena and the determination of radioactive constants adding prestige to Rutherford's name, until he was rewarded in 1908 by the receipt of the Nobel Prize.

It was while at Manchester that Rutherford developed his ideas concerning the existence of a central atomic nucleus of small size. We read of his various contacts with colleagues the world over, of his interest in public affairs, and then of that period during the great World War in which, of course, much of his attention was devoted to war work. It is interesting to note that even during this period of stress, we find communications going on in friendly spirit between Rutherford and some of his former collaborators who were then in the ranks of the enemy. It would indeed be difficult to make a war out of such men, if they alone peopled the lands of the earth.

When Sir J. J. Thomson retired from the Cavendish professorship at Cambridge, England, Rutherford was the natural successor, and he accepted the appointment in 1919. Sir J. J. Thomson became Master of Trinity, but still retained some activities as professor of physics without stipend "with rooms and mechanics essential to the continuance of his research work." It is not unnatural to find Rutherford's dominant personality, coupled with J. J. Thomson's long control of affairs, the cause of some little necessity of adjustment. But all was soon amicably settled, and Rutherford drafted a statement by way of agreement. It is quoted as one "full of alterations, erasures, additions, all uninitialled; it was a document which would make a lawyer weep, but there are the initials at the bottom, J.J.T., E.R. It was sufficient; it worked."

We may sense Rutherford's impulsive yet humorous attitude from the following quotation concerning a conversation with his well-known assistant, Crowe: "Now, Crowe, have some mica absorbers ready tomorrow with stopping power equivalent to 50 cm of air." "Yes, sir." On the next day: "Now, Crowe, put in a 50 cm screen." "Yes, sir." "Why don't you do what I tell you—put in a 50 cm screen." "I have, sir." "Put in 20 more." "Yes, sir." "Why the devil don't you put in what I tell you—I said 20 more." "I did, sir." "There's some damned contamination." "Put in *two* 50's." "Yes, sir." "Ah, it's all right; that's stopped 'em! Crowe, my boy, you're always wrong until I've proved you right! Now we'll find their exact range!"

In treating of the period at Cambridge, the author naturally covers at the same time the history of the main developments which the Cavendish Laboratory brought forth during what is approximately the last twenty years of Rutherford's life. There are accounts of the famous experiments on nuclear disintegration by alpha particles, of the disintegration of matter by artificial means, of the discovery of the neutron, of the work of Kapitza and of Aston. We read of his increasing responsibilities and distinctions, and the book, after reviewing the circumstances attending his last illness, concludes with a brief summary of his achievements and a list of his honors.

We can, perhaps, conclude this review no better than by citing the following characterization of Rutherford quoted by the author from *Nature* (19 July, 1906):

> His own successes as an investigator may be traced to a few well-marked characteristics. The first is his pertinacious and reiterated assault at the particular point which he wishes to attack. He has also an instinctive insight which often makes his initial point of view more trustworthy than the deliberate conclusion of some befogged experimenter. Most noteworthy of all is the extreme simplicity and directness of his experimental methods. Some observers seem to grow happier as their apparatus becomes more complex.

Professor Eve has produced a work dealing with the life of one of the most distinguished men in all the history of science, a work which teems with interest for the physicist, both as a chronicle of achievement and as a picture of the personality of the central figure.

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SPECIAL ARTICLES

STUDIES ON THE FATE OF PLASMA PROTHROMBIN[1]

THE published studies on the metabolism of plasma prothrombin have been directed only at its site of formation; no report has described its site of destruction. That plasma prothrombin is being continuously destroyed in, or lost from, the circulating blood is indicated[2] by following the level in the blood after

[1] This study was carried out under a grant from the John and Mary R. Markle Foundation. From the Department of Surgery of the New York Hospital and Cornell University Medical College, New York.

[2] W. DeW. Andrus, J. W. Lord, Jr., and R. A. Moore, "The Effect of Hepatectomy on the Plasma Prothrombin and the Utilization of Vitamin K." *Surgery,* Vol. 6: 899–900, Dec., 1939.

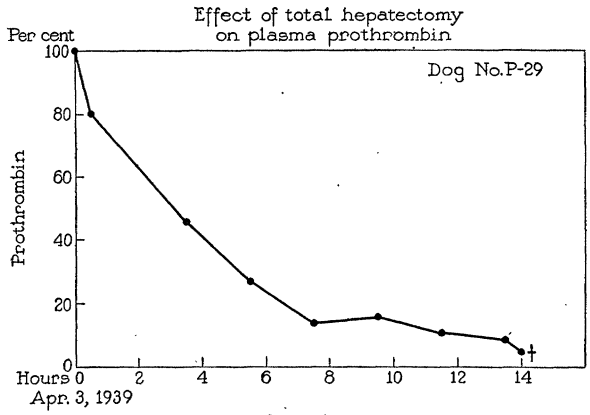

FIG. 1

total hepatectomy in the dog. The characteristic curve of plasma prothrombin after total hepatectomy (Fig. 1) shows a rapid fall to 50 per cent. of the pre-operative level three hours after operation, and a more gradual fall to approximately 5 per cent. of normal by the fourteenth hour post-operatively. Other experiments have shown that this fall is in no way altered when massive doses of vitamin K and bile salts are injected into the small intestine at the time of operation. These experiments suggest the following conclusions: first, that the liver is the sole site of formation of plasma prothrombin; second, that the liver forms this substance continuously; and third, that plasma prothrombin disappears rapidly and continuously from the circulating blood. It was in an effort to find the site of this loss of plasma prothrombin that the present work was undertaken.

METHOD

Healthy mongrel dogs weighing between 10 and 20 kilo. were used in all experiments. Nembutal anesthesia was employed, supplemented by intratracheal insufflation when thoracotomy was necessary. Samples of blood were taken from the afferent and efferent vessels of the head, lung, liver, spleen, intestine, kidney and hind limbs. Samples from the right and left ventricles of the heart were used to test the values of plasma prothrombin in the blood before and after passing through the pulmonary circuit. The plasma prothrombin content was determined by the method of Warner, Brinkhous and Smith.[3]

RESULTS

The plasma prothrombin levels in the samples of blood before and after passing through the lungs showed the only consistent and significant differences. The values for the arterial and venous blood of other organs were the same—within the limits of our experimental error. The limit of error of the Warner, Brinkhous and Smith test in our hands is 3 per cent. when the blood samples are run at one sitting, as in these experiments. In 17 (85 per cent.) of 20 animals the plasma prothrombin level was from 4 to 19 per cent. lower in the blood from the left ventricle than in that from the right ventricle. In the other three experiments, the values were the same from both sides of the heart. The average loss of prothrombin, in passage through the lungs, was 10.6 per cent. in the 17 animals that showed a difference in levels. This was in marked contrast to the results obtained in series involving the other organs, in which no significant differences were found.

In order to rule out oxygenation of the blood as a factor in the destruction of prothrombin, the following experiments were performed. In four dogs blood samples from the right ventricle were divided into two parts through one of which oxygen was bubbled, and a sample of blood was taken from the left ventricle of each dog at the same time. In no instance did oxygenation change the plasma prothrombin content of blood from the right ventricle, yet the plasma prothrombin content of the left ventricle blood was, on the average, 6.5 per cent. lower in this group. Further, exposure of citrated blood samples to air for as long as six hours failed to cause any change in the prothrombin content.

In one experiment, after removing blood samples from each ventricle, the left main bronchus was tied off, causing complete atelectasis of the left lung. After a lapse of 20 minutes, determinations of plasma prothrombin showed the same degree of fall (17 per cent.) in the samples removed from the circulation of each lung. This difference in plasma prothrombin was identical with that of the samples taken before initiation of atelectasis.

DISCUSSION

These results point to the lungs as the site of disappearance of plasma prothrombin. The question arises as to the factor or factors involved in the decrease of this substance as the blood passes through the pulmonary circuit. Two mechanisms are theoretically possible: first, oxygenation of the blood may cause a decrease of plasma prothrombin; and second, a specific tissue substance may be responsible. That the first mechanism is not the explanation has been shown not only by the results of bubbling oxygen through blood without changing its plasma prothrombin content, but also by the fact that blood circulating through an atelectatic lung loses an amount of plasma prothrombin comparable to that lost in passage through a normally aerated lung. Evidently, simple elevation of the oxygen content of blood does not destroy plasma prothrombin. The second idea, that

[3] E. D. Warner, K. M. Brinkhous and H. P. Smith, *Am. Jour. Physiol.*, 114: 667–675, 1936.

a specific tissue component is involved, is supported by certain experimental data.

Thus Howell and Donahue[4] have advanced evidence to show that blood platelets are formed in capillaries of the lung, and are being discharged continuously into the blood stream. In 15 (88 per cent.) of 17 experiments they have found the number of platelets in the blood from the left side of the heart to be greater than in that from the right side of the heart, and that the increase averaged 13.3 per cent. in the 15 successful experiments. Further proof was adduced by perfusion experiments and by histological examination of the lung. In our experiments the lowering of the level of the plasma prothrombin as blood passes from the right to the left side of the heart by way of the pulmonary circuit corresponds both in frequency and in degree to the increase in blood platelets found by Howell and Donahue. The platelets disintegrate and in so doing, liberate thromboplastin. According to the present accepted mechanism of blood-clot formation, the action of thromboplastin and calcium on prothrombin changes it to thrombin. Platelets are the chief source of intravascular thromboplastin; they are fragile and are continuously undergoing disintegration. Loss of prothrombin is then dependent upon the thromboplastin and calcium. This mechanism accounts for the continued loss of prothrombin after the source of supply, the liver, has been removed.

SUMMARY

The level of the plasma prothrombin in the circulating blood is decreased during its passage through the pulmonary capillaries. In 85 per cent. of samples, plasma prothrombin has been found to be less in the blood of the left ventricle than in that from the right ventricle. This difference averaged 10.6 per cent. and ranged from 4 to 19 per cent. In no instance was the level in the right ventricle lower than that in the left. In samples of blood taken from the arterial and venous supply of the head, liver, spleen, intestine, kidney and hind limbs, no significant difference in plasma prothrombin levels was found.

A possible explanation of this role of the lung in the loss of plasma prothrombin is thought to be the production of blood platelets in this organ, as demonstrated by Howell and Donahue. Platelets, as they undergo disintegration, initiate the first stage of the clotting process by releasing thromboplastin, which, in the presence of calcium, changes prothrombin to thrombin.

WILLIAM DEW. ANDRUS
JERE W. LORD, JR.
JOSEPH T. KAUER

[4] W. H. Howell and D. D. Donahue, *Jour. Exp. Med.*, 65: 177–203, 1937.

IMPEDANCE OF BIMOLECULAR FILMS

BIMOLECULAR films having water on both sides[1] were made by bringing together, in oil, a hanging drop and a sessile drop of water with a tanned protein monolayer on each.[2] The J tube holding the sessile drop and the I tube holding the hanging drop were each about 1 cm inside diameter and each had a cylindrical platinized lead electrode 1 cm long about 2 mm from the film end. The oil was amyl acetate, purified by shaking with water and filtering to remove surface active constituents, and the aqueous phase was a dilute solution of tannic acid in M/100 KCl acidified to about pH 3. A stable film of tanned egg albumin was obtained at each interface by carrying the dry powder through the oil on a moistened glass fiber. After the two monofilms were brought together, the resistance decreased as the intervening oil was forced out and did not reach a constant value for several hours.

Alternating current impedance data were obtained on one film as described and on a second in which lecithin was added to the oil before the films were brought together. There were only minor differences between these data. The impedances were measured with a Wheatstone bridge over the frequency range from 30 to 200,000 cycles per second.[3] The data of the second experiment have been plotted[4] as series resistance, R_s, *vs.* series reactance, X_s, in Fig. 1. The

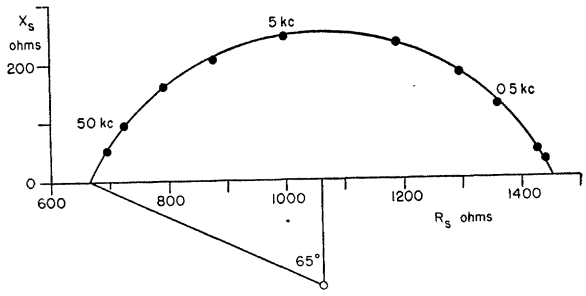

FIG. 1. Impedance locus, series resistance, R_s *vs.* series reactance, X_s, of a bimolecular tanned egg albumin and lecithin film. The frequencies indicated are in kilocycles per second. The film had an area of 0.07 cm², 790 ohms direct current resistance, 65° phase angle and 0.086 microfarads capacity at 1 kilocycle per second.

extrapolated infinite frequency resistance, R_∞, is the resistance of the electrolyte between the electrodes and the film. The difference between the extrapolated zero frequency resistance, R_0, and R_∞ is the direct current resistance of the film. From the film areas of

[1] R. B. Dean, *Nature*, 144: 32, 1939.
[2] J. H. Schulman and E. K. Rideal, *Proc. Roy. Soc.* B., 122: 29 and 46, 1937.
[3] K. S. Cole and H. J. Curtis, *Rev. Sci. Inst.*, 8: 333, 1937.
[4] K. S. Cole, *Jour. Gen. Physiol.*, 15: 641, 1932.