periments in that no blood NPN elevation occurred in our experiments.

Implantation of liver, skeletal muscle, cardiac muscle, spleen, and boiled kidney had only a transient depressor effect upon the blood pressure of hypertensive dogs.

Experiments are under way to determine the nature of this renal principle and to discover whether or not similar effects can be obtained with other tissues.

Summary. Our results suggest that transplanted kidney tissue undergoing degeneration exerts an antagonistic action upon the renal hypertension mechanism.

11455

Effect of Serum Proteins on the Polarographic Curve.*

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The first attempt to apply the polarographic method to cancer diagnosis was reported by Brdicka.[1] Since then various others have used this technique as a test for the detection of changes in cancer sera.[2-4] A difference has been demonstrated between normal and cancer blood by these workers, but it appears that this difference is chiefly a statistical one. Our own results fully confirm this difficulty. In a survey of 150 cases, individuals were divided into 3 general groups: normal, non-cancerous diseases and cancer.[5] The values obtained were expressed as the height of the polarographic curve. There was considerable overlapping in all groups, making it impossible to distinguish any individual case as being representative of normal, cancerous or non-cancerous.

During the course of these studies, serum proteins were determined in some of the specimens which also were examined polarographically. There appeared to be a general parallelism between the amount of the serum protein and the height of the polarographic

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1 Brdička, R., *Nature*, 1937, **139**, 330.

2 Bergh, F., Henriques, Q. M., and Wolffbrandt, C. G., *Nature*, 1938, **142**, 212.

3 Wedemeyer, H. E., and Daur, T., *Z. f. Krebs.*, 1939, **49**, 10.

4 Walker, A. C., and Reimann, S. P., *Am. J. Ca.*, 1939, **37**, 585.

5 Rusch, H. P., Klatt, T., Meloche, V. W., and Dirksen, A. J., in press.

curve. A more extended survey was therefore made of various types of pathological as well as normal bloods, and the polarographic results correlated with variations in the albumin and globulin content as determined by chemical methods. A brief description of the apparatus and the principles underlying its operation has been recently reported by Walker and Reimann.[4]

The blood samples were obtained from fasted subjects. After clotting the serum was withdrawn and aliquots taken for the determination of the serum proteins and for the polarographic test. The serum proteins were determined by Greenberg's colorimetric method. The aliquot used for the polarographic test was treated as follows: 0.1 cc of serum was hydrolyzed by adding 2.5 cc of a 0.05N HCl solution containing 2.5 mg pepsin and incubating at 40°C for 15 min. 0.1 cc of this mixture was then added to 5 cc of a buffer solution which was composed of 10 cc 1N NH_4OH; 10 cc 1N NH_4Cl; 10 cc 0.01N cobaltic chloride and 10 cc water. Stock solutions of the various constituents of this buffer were kept in separate bottles and were added together in appropriate amounts just prior to each test. The polarographic measurements were made immediately after the test solutions were prepared.

In order to determine which fraction of the serum protein gave the typical curve, the proteins were precipitated from aliquots of serum with $(NH_4)_2SO_4$ and the precipitate divided into albumin and globulin fractions by solution in dilute salt and by coagulation of the globulin on dialysis against distilled water. The crude protein fractions were then replaced separately, and in combination, into appropriate amounts of deproteinized serum and polarographic measurements made as before. Only the albumin fraction yielded a typical curve; the characteristic waves obtained with intact serum were not observed in the globulin fraction, nor did the addition of globulin materially alter the shape of the albumin curve.

TABLE I.
Relation of Level of Serum Albumin to Polarographic Curve.

No.	Diseases	Albumin %		Height of polarographic curve in mm	
		Avg	Range	Avg	Range
7	Nephritis	2.1	1.3-3.1	21.0	13.5-28.0
3	Vomiting of Preg.	2.2	2.0-2.5	22.5	20.5-23.5
3	Osteomyelitis	2.5	1.4-3.6	25.0	13.5-36.0
6	Cancer	2.8	2.5-3.3	26.0	23.0-29.5
22	Miscellaneous*	2.6	1.1-3.8	25.8	17.5-34.5
18	Cardio-vascular	3.0	1.8-4.1	28.0	18.2-34.5
7	Normal	3.5	3.6-4.0	36.5	28.0-44.5

*There were no more than 2 of the same disease in this group.

There was a total of 66 cases in this series, the results of which are listed in Table I. When the average results of the serum from various diseases were compared, a direct correlation was found between the level of serum albumin and the height of the polarographic curve. There was, however, a considerable overlapping of the individual cases in each group (Table I). Nevertheless, the individual results also demonstrated a very close parallelism between the amount of the serum albumin and the polarographic response (Fig. 1). Wedemeyer and Daur have reported a similar correlation.[3]

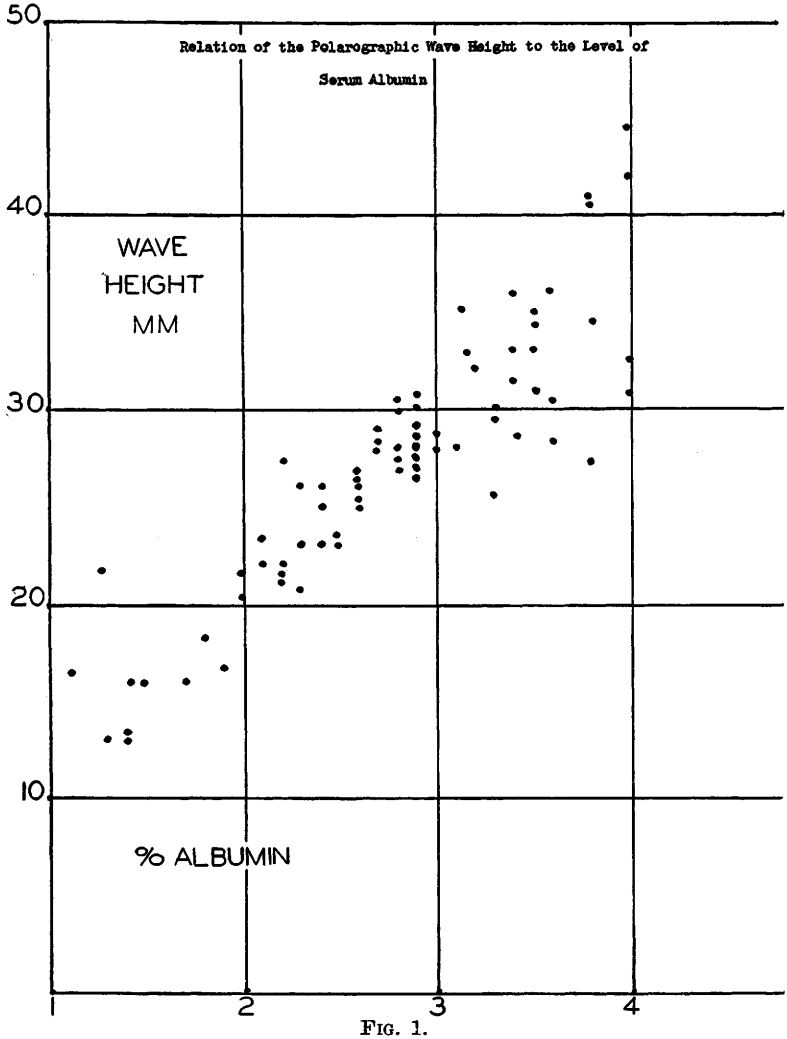

FIG. 1.

The use of the polarograph as a method for cancer diagnosis depends on the measurement of certain sulfur-containing amino acids present in the proteins in the blood serum. The level of these constituents is reported to differ in normal and cancer sera. Brdicka explains the production of the polarographic curve as being due to the catalytic liberation of hydrogen at the dropping mercury cathode induced by the S-H group of cysteine and the S-S linkage of cystine. While this reaction is said to be catalytic, the amount of hydrogen deposited is quantitatively proportional to the concentration of these amino acids. Brdicka also demonstrated that the cystine group gives a wave height twice that for cysteine when equivalent molecular concentrations are used.[1,6,7] Various workers have determined the cystine content of serum globulin as being about 1.5-3.5% and that of serum albumin from 2.5-6.0%. If we take the usual figures given for the level of albumin as from 4-5 g per 100 cc and those for globulin as 2-2.8 g per 100 cc, we find that the cystine content of the albumin from 100 cc of serum is approximately 0.1-0.3 g while that for the globulin of the same amount of serum is about 0.03-0.09 g. These figures may, in part, explain our findings in regard to the curves obtained with these two separated fractions.

It is interesting to note in passing that various workers have reported a higher sulphydryl content in rapidly growing tissues than in those proliferating slowly.[8] This has been demonstrated to be the case in embryonic cells, root tips as well as in certain tumors.

Summary. The effect of the serum proteins on the polarographic curve was made on blood sera obtained from 66 normal and pathological individuals. The height of the polarographic curves was found to be directly proportional to the level of the serum albumin. It is obvious, therefore, that the polarographic method is of limited value in cancer diagnosis since changes in serum albumin are by no means specific for neoplastic diseases.

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6 Brdička, R., *Nature,* 1938, **142**, 617.

7 Brdička, R., *Klin. Wochschr.,* 1939, **18**, 305.

8 Reimann, S. P., and Hammett, F. S., *Am. J. Ca.,* 1936, **26**, 554.