REFERENCES

1. BAARS, H.: Variabiliteit van paraproteinen bij de ziekte van Kahler. Utrecht, Holland. Schotanus & Jens. 1955.

2. BAYNE-JONES, S., and WILSON, D. W.: Immunological reactions of Bence-Jones proteins. I. Differences between Bence-Jones proteins and human serum proteins. *Bull. Johns Hopkins Hosp.* 33: 37-43, 1922.

3. BAYNE-JONES, S., and WILSON, D. W.: Immunological reactions of Bence-Jones proteins. II. Differences between Bence-Jones proteins from various sources. *Bull. Johns Hopkins Hosp.* 33: 119-125, 1922.

4. CAMPBELL, D. H.; LUESCHER, E., and LERMAN, L. S.: Immunologic adsorbents. I. Isolation of antibody by means of a cellulose-protein antigen. *Proc. Nat. Acad. Sc.* 37: 575-578, 1951.

5. COLLIER, F. C., and JACKSON, P.: The precipitin test for Bence-Jones protein; further studies of clinical evaluation of the test employing antibody prepared by the adjuvant technic. *New England J. Med.* 248: 409-414, 1953.

6. DENT, C. E., and ROSE, G. A.: The Bence-Jones protein of multiple myelomatosis: its methionine content and its possible significance in relation to the aetiology of the disease. *Biochem. J.* 44: 610-618, 1949.

7. GITLIN, D.: Use of ultraviolet absorption spectroscopy in the quantitative precipitin reaction. *J. Immunol.* 62: 437-451, 1949.

8. GUTMAN, A. B.: The plasma proteins in disease. *Advances Protein Chem.* 4: 185-250, 1948.

9. HARDY, S., and PUTNAM, F. W.: Proteins in multiple myeloma. IV. Interaction with metabolic nitrogen. *J. Biol. Chem.* 212: 871-878, 1955.

10. HERTORN, I., and WELLER, W. H.: Immunological differences of crystalline Bence-Jones proteins. *Biochem. J.* 34: 487-489, 1940.

11. JACOBSON, B. M., and MILNER, L. R.: The detection of urinary Bence Jones protein. *Am. J. Clin. Path.* 14: 138-149, 1944.

12. KORNGOLD, L., and LIPARI, R.: Immunological studies of Bence-Jones proteins. (Abstr.) *Proc. Am. A. Cancer Research* 2 (1): 29-30, 1955.

13. KORNGOLD, L., and LIPARI, R.: Tissue antigens of human tumors grown in rats, hamsters, and eggs. *Cancer Research* 15: 159-161, 1955.

14. KORNGOLD, L., and LIPARI, R.: Multiple-myeloma proteins. I. Immunological studies. *Cancer* 9: 183-192, 1956.

15. LOHR, F., and HITTMANN, G.: Myelom-Plasma-Proteine, IV. Mitteilung. Zur Immunochemie der α- und β- Myelomproteine. *Ztschr. f. Naturforsch.* 8b: 706-711, 1953.

16. LOHR, F.; WEILER, E., and HITTMANN, G.: Myelom-Plasma-Proteine, III. Mitteilung. Zur Immunochemie der γ-Myelom-Proteine. *Ztschr. f. Naturforsch.* 8b: 625-631, 1953.

17. MOORE, D. H.; KABAT, E. A., and GUTMAN, A. B.: Bence-Jones proteinemia in multiple myeloma. *J. Clin. Investigation* 22: 67-75, 1943.

18. OUCHTERLONY, Ö.: Antigen-antibody reactions in gels. IV. Types of reactions in coordinated systems of diffusion. *Acta path. et microbiol. Scandinav.* 32: 231-240, 1953.

19. PUTNAM, F. W., and HARDY, S.: Proteins in multiple myeloma. III. Origin of Bence Jones protein. *J. Biol. Chem.* 212: 961-969, 1955.

20. PUTNAM, F. W., and MIYAKE, A.: On the non-identity of Bence-Jones proteins. *Science* 120: 848-849, 1954.

21. PUTNAM, F. W., and STELOS, P.: Proteins in multiple myeloma. II. Bence-Jones proteins. *J. Biol. Chem.* 203: 947-958, 1953.

22. ROBINSON, S. H. G.: An investigation of the antigenic properties of four specimens of Bence-Jones protein obtained from cases of myelomatosis. *Brit. J. Exper. Path.* 8: 454-456, 1927.

23. RUNDLES, R. W.; COOPER, G. R., and WILES, R. W.: Multiple myeloma. IV. Abnormal serum components and Bence Jones protein. *J. Clin. Investigation* 30: 1125-1142, 1951.

24. SLATER, R. J.; WARD, S. M., and KUNKEL, H. G.: Immunological relationships among the myeloma proteins. *J. Exper. Med.* 101: 85-108, 1955.

25. WOHLMANN, F. H.; WUNDERLY, C., and HAAG, A.: Immunological investigations in ten cases of plasmacytoma. *Brit. J. Exper. Path.* 31: 507-514, 1950.

ADDITIONAL REFERENCES

26. DEUTSCH, H. F.; KRAUPPNER, C. M., and REIF, A. E.: Immunochemical relation of Bence Jones proteins to normal serum proteins. *J. Biol. Chem.* 216: 103-111, 1955.

BLOOD-VOLUME MEASUREMENTS IN CANCER USING THE Cr^{51} RED-BLOOD-CELL TAGGING METHOD

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DURING a series of tumor-host studies in rats and mice, we noted that the animals developed anemia relatively soon after implantation of the tumor. This association between malignant tumors and anemia has been observed previously by a number of investigators, as cited by Ewing in 1940. Later studies by Sandberg et al. reported the occurrence of a severe secondary anemia in neoplastic disease. Strong and Francis have reported that strains of mice susceptible to tumors had lower hemoglobin levels than nonsusceptible mice.[8] They reported also that the hemoglobin level progressively decreased with age in susceptible mice.[9] In a report on the relationship of tumor growth and hemoglobin levels, Taylor and Pollack concluded that the decrease in hemoglobin is a direct, rather than a secondary, effect of the malignant tumor.

A series of blood-volume measurements was initiated on tumor-bearing rats in order to determine whether the observed anemia was the result of excessive red-cell destruction or of an expansion of plasma volume. Because of the relatively small red-cell mass of the rat, determinations were made by the method of Gray and Sterling,[2,3] which utilizes Cr^{51} as a red blood cell tag to measure the circulating red-cell mass. At a later date, when Cr^{51} with a sufficiently high specific activity to warrant its use in man became available commercially (Abbott Laboratories), measurements on patients with various types of cancer were included in the expanded program. The value of Cr^{51} as a clinical aid in estimating the red-cell mass and whole-blood volume has been reported by us earlier.[5]

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METHOD

Animal Studies. Blood-volume determinations were made on twenty-two control and on twenty-nine tumor-bearing Sloniker rats. The tumor used was a transmissible fibrosarcoma that has been described.[7] Subcutaneous isografts were made by bilateral inoculation of a suspension of tumor cells. Inoculation of this particular tumor has produced a high percentage of takes. The resultant tumors have never been observed to regress but to grow rapidly and overwhelm the host in a period of from three to four weeks.

The Cr^{51} used in these studies was produced in the cyclotron by bombarding a vanadium target with protons to form carrier-free radiochromium as a result of the p,n reaction. In some cases, microgram quantities of sodium chromate carrier were added to effect a more satisfactory tagging of the red blood cells. The uptake of Cr^{51} by red cells was found to be less when carrier-free Cr^{51} was used. It was suspected that the minute quantities of hemoglobin present in the saline in which the cells were suspended sequestered the small amount of carrier-free Cr^{51}, thus making it unavailable for diffusion into the red cells.

An aliquot of the tagged cells was set aside as a primary standard. A known volume of the tagged cells, 0.1 to 0.2 cc., was then administered to normal and tumor-bearing rats via the external jugular vein, which was exposed by a small incision in the skin lying directly over the clavicle. A mixing time of thirty minutes was allowed and a sample of cardiac blood, 1 to 4 cc., was withdrawn. Each sample was counted on a scintillation counter, using a thallium-activated sodium iodide crystal in conjunction with a 5819 R.C.A. photomultiplier tube. The efficiency of the scintillation counter was such that 11 to 14 per cent of the gamma rays emitted by the Cr^{51} were registered as counts. The samples were counted for a sufficient period of time to reduce any variation owing to statistical fluctuation to ± 3 per cent.

The blood volume was calculated by com-

puting the dilution of the Cr^{51}-tagged cells in each sample of cardiac blood. Determination of the red-cell mass and approximate plasma volume was made from hematocrits of the samples.

Additional studies were undertaken to determine the fate of Cr^{51} at one and sixteen days after the intramuscular injection of carrier-free Cr^{51} (Table 1) and at eighteen days after the intraperitoneal administration of 1 mg. of labeled sodium chromate (Table 2). The data obtained showed that Cr^{51} was not localized to any appreciable extent in any of the tissues examined but was slowly and continuously excreted in the urine and to some extent in the feces. These results indicated that the administration of tracer doses of Cr^{51} would not be hazardous to patients, since the small amount of radiation received would not be localized in any tissue but would be shared by the whole body.

Human Studies. The red-cell mass, plasma volume, and whole-blood volume were determined in eighty-seven normal subjects (providing eighty-seven tests) and 175 hospitalized patients with various types of cancer (providing 213 tests). The presence of a cancer was confirmed by one or more of the following: unequivocal clinical and laboratory (including roentgenographic) findings, surgical exploration, biopsy, and autopsy. For purposes of evaluation, the cases were divided by the same criteria into cancers with extensive spread (196 cases) and nonmetastatic cancers (twenty-one cases). They were further subdivided according to the location of the tumor as follows: forty-three pulmonary carcinomas, nineteen carcinomas of the colon, fifteen cases of leukemia, and thirteen cases of Hodgkin's disease.

TABLE 1

DEPOSITION OF CARRIER-FREE $Na_2Cr^{51}O_4$ IN THE RAT ONE AND SIXTEEN DAYS AFTER INTRAMUSCULAR INJECTION

Values Are Expressed as Per Cent of the Absorbed Dose Recovered in Wet-Weight Tissues

Tissue	One day*		Sixteen days*	
	% in organ	% per gm.	% in organ	% per gm.
Heart	0.20	0.22	0.06	0.06
Lung	0.68	0.44	0.17	0.11
Spleen	0.48	0.48	0.30	0.30
Plasma	3.92	0.72	0.04	0.06
Red cells	0.70	0.09	0.06	0.06
Liver	3.31	0.39	1.70	0.21
Kidney	1.39	0.81	1.27	0.68
Adrenals	0.04	—	0.06	—
Thyroid	0.04	—	0.06	—
Lymph gland	—	0.44	—	0.30
Pancreas	0.04	0.24	0.17	0.08
Brain	0.04	0.04	0.06	0.06
Stomach	0.22	0.17	0.06	0.06
Small intestine	0.68	0.13	0.23	0.06
Skeleton	10.6	0.68	8.64	0.55
Muscle	7.36	0.06	4.53	0.04
Skin	6.01	0.15	3.71	0.08
Gonads	0.54	0.33	0.30	0.13
Urine	56.2	—	65.6	—
Feces	1.66	—	14.7	—
Unabsorbed at injection site	47.2		32.9	

*Average values of three rats.

TABLE 2

DEPOSITION OF 1 MG. OF Na_2CrO_4 TAGGED WITH Cr^{51} IN RATS EIGHTEEN DAYS AFTER INTRAPERITONEAL ADMINISTRATION

Values Are the Averages of Three Rats. Total Recovery 90.3 Per Cent of Administered Dose. Data Are Expressed as Per Cent of the Dose per Organ and Gram Wet Weight

Tissue	% in organ	% per gm.
Adrenals	0.007	—
Bone (femur, tibia, fibula)	—	0.14
Heart	0.10	0.07
Kidneys	1.61	0.52
Gastrointestinal tract	2.26	0.07
Liver	2.57	0.02
Lungs	0.17	0.08
Muscle	—	0.03
Skin	1.45	0.03
Spleen	1.25	1.00
Blood	3.14	0.14
Balance	7.57	0.04
Time, hr.	**%, urine**	**%, feces**
First 24	20.6	10.1
24–49	7.5	9.7
49–216	10.6	7.8
216–432	3.6	2.3
TOTAL	42.3	29.9

Tagging of Red Cells. Human red cells were tagged by a method similar to that used in the tests on rats.[5] Heparinized blood (8 to 10 cc.) was seeded with known amounts of sodium chromate and shaken on a mechanical agitator for at least forty-five minutes. The plasma was withdrawn and the cell mass washed twice with normal saline to remove the trapped plasma. The volume was reconstructed with normal saline; a small aliquot was taken to determine the number of Cr^{51} counts to be injected and the remainder given to the patient intravenously. Earlier studies had shown that one hour allowed adequate time for complete mixing of the tagged cells. At the end of this period another heparinized sample of blood (5 to 10 cc.) was withdrawn. A measured volume of the sample was assayed for its Cr^{51}-tagged red cells with a scintillation crystal counter. The blood volume was computed as follows:

$$\frac{\text{total counts/sec. injected}}{\text{counts/sec./cc., final blood sample}} = \text{cc. apparent blood volume.}$$

Hematocrits were made in order to calculate the relative plasma volumes and the red-cell mass from the whole-blood volume.

All data are expressed as the mean for any series of observations ± the standard error. The mean ± the standard error was calculated by $\sqrt{\frac{\Sigma dev.^2}{n(n-1)}}$. The significance of any difference between two groups was calculated by finding the variance (v) between groups:

$$v = \frac{\Sigma dev.^2 \text{ (for group 1)} + \Sigma dev.^2 \text{ (for group 2)}}{(n_1) + (n_2 - 2)}.$$

The standard error of difference = $\sqrt{\epsilon_1^2 + \epsilon_2^2}$.

The value for Fisher's $t = \frac{\text{mean}_1 \pm \text{mean}_2}{\text{S. E. D.}}$.

The probability of any difference between groups was obtained by using a standard table for t.

RESULTS

Animal Studies. The average body weight, blood volume, and packed-cell volume of the tumor-bearing rats and their controls are presented in Table 3. The average whole-blood volume of the twenty-nine tumor-bearing rats averaged 7.1 ± 0.25 per cent of the body weight. This was significantly greater than that of the controls, which averaged 5.37 ± 0.18 per cent of the body weight. The increased blood volume of the tumor-bearing rats resulted primarily from an expansion of the plasma volume ($P = 0.01$). The red-cell mass was increased slightly.

Human Studies. In the majority of patients with cancer, the whole-blood volume was not significantly different from normal (Table 4), 67.62 ± 0.82 vs. 65.5 ± 0.70 cc. per Kg. ($P = 0.1$). No significant increase was noted in the group with extensive metastases; in the patients with nonmetastatic cancer, however, the whole-blood volumes were significantly lower than normal ($P = 0.01$). All cases of cancer, including those categorized as being extensive, showed a significant reduction of red-cell mass, as well as an expansion of plasma volume ($P = <0.01$). The plasma volumes in the group with nonmetastatic cancers were not significantly increased ($P = 0.3$).

Analysis of the data in the groups classified according to the type or location of the predominant tumor showed normal blood volumes in the patients with pulmonary cancer and Hodgkin's disease, whereas significantly greater than normal blood volumes were found in the patients with leukemia, carcinoma of the stomach and esophagus, and carcinoma of the colon ($P = 0.02$, <0.01, and <0.01 respectively).

In all of the various categories of cancer shown in Table 4, the red-cell masses were lower than normal and the plasma volumes greater than normal to a significant degree, except in the group with carcinoma of the colon. In these patients, the red-cell mass was essentially normal.

Hematocrits in all patients with cancer, including those patients with leukemia and Hodgkin's disease, were lower than normal.

DISCUSSION

Results of the present study showed that, whereas the whole-blood volume was not expanded in the presence of a malignant tumor in man, the plasma volume was significantly increased. Conversely, greater than normal volumes were found in tumor-bearing rats. The average red-cell mass of all cancer patients was significantly lower than that of normal subjects, 25.88 cc. per Kg. and 29.6 cc. per Kg. respectively. A similar decrease was not observed in the experimental rats; however, the rapid growth of the transmissible tumor used for implantation may have occurred in too short a period to interfere appreciably with hematopoiesis or have much influence on the existing red cells in the blood stream.

A comparison of the blood volumes of all of the cancer patients with the controls showed that the reduction in red-cell mass was balanced by an expansion of the plasma volume and resulted in whole-blood volumes that were approximately normal. These results

TABLE 3

COMPARISON OF THE BLOOD VOLUMES OF CONTROL AND TUMOR-BEARING RATS USING THE Cr^{51} RED-CELL-TAGGING METHOD*

Rats	Blood vol., % body wt.	Hematocrit	Av. body wt., gm.
Tumor-bearing			
(29)	7.1 ± 0.25	35.9 ± 0.81	207.0
Range	5.4 – 9.5	22.0 – 46.	
Control			
(22)	5.4 ± 0.18	48.1 ± 0.97	176.0
Range	4.1 – 7.7	43.0 – 55.	

*Size of tumors ranged from 8 to 35 gm.

Averages given = mean ± standard error $\sqrt{\frac{\Sigma dev.^2}{n(n-1)}}$

TABLE 4

COMPARISON OF DATA ON THE BLOOD VOLUME OF NORMAL SUBJECTS AND PATIENTS WITH CANCER, USING Cr^{51} AS A RED-BLOOD-CELL TAG
Values Presented Are Means ± Standard Error

Diagnostic categories	No. of tests	Hematocrit	Red-cell mass	Plasma volume	Whole-blood volume
Normals (87 patients)	87	45.10±0.38	29.6±0.26	35.9±0.47	65.5±0.70
All Cancers (175 patients)					
Total number tests	213	38.25±0.45	25.88±0.47	41.6±0.70	67.6±0.82
P value*			<0.01	<0.01	<0.01
Extensive	196	38.06±0.49	25.87±0.50	42.2±0.69	68.0±0.96
P value			<0.01	<0.01	0.10
Nonmetastatic	21	40.55±1.11	25.80±1.12	37.3±1.33	63.0±1.91
P value			<0.01	0.30	0.01
Special Groups					
Carcinoma of lung	43	39.02±0.85	25.93±0.93	41.1±1.25	67.0±1.83
P value			<0.01	<0.01	0.90
Hodgkin's disease	13	33.19±3.21	24.56±1.65	44.1±1.97	68.7±3.12
P value			<0.01	<0.01	0.20
Leukemia	15	28.8±3.29	23.73±2.38	50.4±5.1	74.0±7.1
P value			<0.01	<0.01	0.02
Carcinoma of stomach and esophagus	13	40.77±5.27	26.17±1.75	46.6±2.19	72.8±3.41
P value			0.01	<0.01	<0.01
Carcinoma of colon	19	41.05±1.56	28.26±1.62	41.1±1.76	69.44±2.78
P value			0.20	<0.01	<0.01

*P value represents statistical comparison with corresponding normal value.

confirm those reported earlier by Kelly et al., who used T1824-tagged plasma and I^{131}-labeled albumin in similar studies.

SUMMARY

To determine whether anemia observed in cancer results from excessive red-blood-cell destruction or from an expansion of plasma volume, the whole-blood volume and hematocrit were measured in tumor-bearing rats and in patients with various types of cancer.

The whole-blood volume of twenty-nine Slonaker rats bearing a transmissible fibrosarcoma was found to be greater than normal. This was the result of an increase in plasma volume; the red-cell mass was increased slightly.

Similar determinations in 175 patients with various types of cancer and eighty-seven normal control subjects showed no significant expansion of whole-blood volume in cancer, but did demonstrate a significant expansion of plasma volume and a decrease in red-cell mass, especially when the cancer was widespread.

REFERENCES

1. EWING, J.: Neoplastic Diseases; a Treatise on Tumors, 4th ed. Philadelphia, W. B. Saunders Co. 1940, p. 55.

2. GRAY, S. J., and STERLING, K.: Determination of circulating red cell volume by radioactive chromium. *Science* 112: 179-180, 1950.

3. GRAY, S. J., and STERLING K.: The tagging of red cells and plasma proteins with radioactive chromium. *J. Clin. Investigation* 29: 1604-1613, 1950.

4. KELLY, K. H.; BIERMAN, H. R., and SHIMKIN, M. B.: Blood volume, body water, and circulation time in patients with advanced neoplastic diseases. *Cancer Research* 12: 814-817, 1952.

5. REILLY, W. A.; FRENCH, R. M.; LAU, F. Y. K.; SCOTT, K. G., and WHITE, W. E.: Whole blood volume determined by radiochromium-tagged red cells; comparative studies on normal and congestive heart failure patients. *Circulation* 9: 571-580, 1954.

6. SANDBERG, M.; GROSS, H. and HOLLY, O. M.: Changes in retention of copper and iron in liver and spleen in chronic diseases accompanied by secondary anemia. *Arch. Path.* 33: 834-844, 1942.

7. SCOTT, K. G.; BOSTICK, W. L.; SHIMKIN, M. B., and HAMILTON, J. G.: Distribution of globulin bound thyroid fractions of iodine in normal and tumorous animals after intravenous administration using radioiodine as a tracer. *Cancer* 2: 692-696, 1949.

8. STRONG, L. C., and FRANCIS, L. D.: The blood of female mice (breeders) of cancer susceptible (A) and cancer resistant (CBA) strains. *Arch. Path.* 23: 202-206, 1937.

9. STRONG, L. C., and FRANCIS, L. D.: Differences in hemoglobin values in the blood of breeder female mice; a comparison between cancer-susceptible and cancer-resistant strains. *Am. J. Cancer* 38: 399-405, 1940.

10. TAYLOR, A., and POLLACK, M. A.: Hemoglobin level and tumor growth. *Cancer Research* 2: 223-227, 1942.

BILATERAL ADRENALECTOMY FOR ADVANCED BREAST CANCER

A Report of Eleven Cases

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THE PRESENT clinical investigation at Brooke Army Hospital was originally stimulated by the work on bilateral adrenalectomy in advanced carcinoma of the breast performed by Huggins in Chicago and at Memorial Center for Cancer and Allied Diseases in New York City. Previous efforts to palliate this disease have led to the recognition of the influence of hormones on the growth of mammary cancer, and the effect of castration and administration of estrogens and androgens has previously been found to be beneficial. The similarity of adrenal hormones to those of the gonads has led investigators to postulate that they might also influence these particular neoplasms. It was believed that removal of these hormones with resultant alteration of the physiological environment of the tumor might cause clinical remission. The lack of adequate replacement therapy for the life-supporting adrenal glands, however, prevented the use of bilateral adrenalectomy until the development of cortisone. In about 1951 Huggins first employed bilateral adrenalectomy in far-advanced carcinoma of the breast and prostate, as did a group in Memorial Center. Prior to the beginning of our investigation, each group had reported a small series of cases indicating that most patients achieved subjective benefits for weeks to months, while about 50 per cent of patients also demonstrated objective improvement, as manifested by shrinkage of tumor masses, new bone formation in osteolytic lesions, decrease in pleural effusion, and gains in weight and strength. The same investigators also tried the operation in other cancers but found no evidence of benefit.

The clinical experience at Brooke Army Hospital from January 1, 1953, through July 1, 1955, is limited to eleven patients, all of whom had advanced mammary cancer, with clinical and laboratory evidence of distant metastases.

METHOD

The adrenal glands were removed in all patients through the posterolateral approach, through the bed of the twelfth rib on either side, both glands being removed at the same operative procedure. In all instances, there had been previous surgical or roentgen-ray castration. The present replacement therapy for the adrenal glands is as follows: one day preoperatively, 50 mg. cortisone intramuscularly every four hours; operative day, 50 mg. cortisone intramuscularly every four hours and 100 mg. orally at 6:00 A.M.; first postoperative day, 50 mg. cortisone intramuscularly every six hours; second and third postoperative days, cortisone 50 mg. intramuscularly every twelve hours; fourth, fifth, and sixth postoperative days, 25 mg. cortisone orally every eight hours; seventh postoperative day, and thereafter, 25 mg. cortisone orally every twelve hours. The maintenance dose of oral cortisone is 50 mg. a day in two divided doses.

In the early part of our investigation, it was our custom to administer intramuscular deoxycorticosterone acetate (DOCA) prior to and on the day of surgery, along with sodium chloride; however, these procedures have been found to be unnecessary and have contributed to the accumulation of excessive body fluid manifested by ascites and peripheral edema. We still advocate the use of DOCA and intravenous sodium chloride in the operative or postoperative course in patients having difficulty with maintenance of blood pressure; however, in properly prepared patients, we have had no difficulty to date in supporting the blood pressure. Other drugs that have been recommended are nor-epinephrine, adrenocortical extract, and intravenous hydrocortisone. All eleven patients in this series tolerated the adrenal surgery well and their

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