

ganism. In the case of the *E. typhosa* strain, this baseline was approximately 2 units and with the pneumococcus it was 0.0008 unit. It can be seen that as the baseline is moved downward the area under the penicillin-caronamide curve increases disproportionately to that of the curve produced by the administration of penicillin alone. Thus it will be seen that the advantage produced by caronamide in penicillin therapy, though very considerable against organisms of relatively high resistance, becomes even greater against highly susceptible organisms.

Many bacterial infections that have been considered to be resistant to the usual clinical penicillin dosages have been found to be caused by bacteria sensitive to amounts of penicillin that, in these experiments, inhibited *E. typhosa*. Evans¹¹ has reported that, of 66 strains of *E. typhosa*, all but one were inhibited completely by 10-25 units of penicillin per ml of culture medium. While it is not possible to translate penicillin dosage in mice into human dosage, it seems reasonable to expect therapeutic effects in man at plasma penicillin concentrations similar to those found to be effective in mice. The studies

carried out by Crosson, Boger, Shaw and Miller⁸ have indicated that such plasma penicillin concentrations may be attained in man with moderate intramuscular doses of penicillin when caronamide is administered orally. It would, therefore, seem that the use of caronamide together with penicillin may offer a means of increasing the effectiveness of penicillin treatment and bringing more bacterial infections within the limits of practical penicillin therapy.

Summary. The oral administration of 4'-carboxyphenylmethane-sulfonilide (caronamide) was found to enhance considerably the therapeutic effectiveness of intramuscularly-administered penicillin in mice experimentally infected with either Type I pneumococci or *E. typhosa*. This enhancement was 6- to 16-fold in the case of the pneumococcus experiments and approximately 4-fold for *E. typhosa*. These effects may be explained on the basis of the higher and more prolonged plasma penicillin concentrations when caronamide is administered, and do not indicate synergy between caronamide and penicillin. The significance of these observations in relation to penicillin therapy is discussed.

¹¹ Evans, R. W., *Lancet*, 1946, **2**, 113.

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Low Sodium-Forced Fluid Management of Hypertensive Vascular Disease and Hypertensive Heart Disease.*

J. MARION BRYANT AND ELMIRA BLECHA. (Introduced by Frank N. Wilson.)

From the Department of Internal Medicine and the Diet Therapy Clinic, University of Michigan School of Medicine, Ann Arbor, Mich.

One hundred patients with essential hypertension were placed for periods of several weeks to 12 months on a diet of 2200 calories containing approximately 200 mg of sodium, 2.2 g potassium, 70 g protein, 80 to 175 g

fat, 130 to 230 g carbohydrate, and vitamin supplements. A daily fluid intake of 3 liters was maintained. All were outpatients. Blood pressure readings were taken with the subject reclining, sitting and standing. They were made by one observer usually at the same time of day. No pretreatment blood pressure was below 170/100. Medical and dietary checks were ordinarily made once or twice a month.

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TABLE I.
Blood Pressure Changes in Hypertension with Surgical and Dietary Management.

Groups	Smithwick's ² post-operative classification, Diastolic reduction	Smithwick ^{2*}			Splanchnic ^{3†}			Low sodium [‡]		
		No. of cases	%		No. of cases	%		No. of cases	%	
I	30+	64	41.0	} 61.5 } 79.4	33	16.5	} 33 } 50	8	17.8	} 57.8 } 75.6
II	20 to 29	32	20.5		33	16.5		18	40.0	
III	10 to 19	28	17.9		34	17		8	17.8	
IV	to 9	17	10.9		50	25		5	11.1	
V	higher	15	9.7		50	25		6	13.3	

* Follow up on 156 patients with hypertension 1 to 5 years after surgery.

† Unpublished data. Study of 200 surviving patients of a total of 238 surgically treated with bilateral supradiaphragmatic splanchnicectomy and lower dorsal sympathetic ganglionectomy 1 to 2 years later.

‡ Forty-five unselected hypertensive patients treated for periods of several weeks to 14 months with 200 mg sodium diet—forced fluid regime.

There was a significant lowering of pressure (to or below 155/95) in approximately 20%, and of the diastolic pressure (to or below 95) in an additional 15% of the cases. A number of the patients who improved on this regime had failed to respond satisfactorily to a previous bilateral supradiaphragmatic splanchnicectomy and lower dorsal sympathetic ganglionectomy. The majority with symptoms typical of essential hypertension and hypertensive heart disease showed moderate improvement or were completely relieved of their discomfort. In most of these with angina pectoris the frequency and severity of the seizures were diminished. In all cases in which it was utilized orthodiography demonstrated a definite and progressive decrease in the size of the heart when it was enlarged. The inverted T waves frequently seen in hypertensive heart disease have in some cases become upright. Papilledema diminishes. Peripheral edema and pulmonary congestion invariably disappear. Relief of symptoms and the above described objective changes were not uniformly associated with a significant fall in blood pressure.

Several patients who originally displayed papilledema and moderately severe heart failure have been followed from 6 months to one year, have become symptom-free, and have shown a decrease in heart size and a definite fall in blood pressure. The blood

pressure has not, however, reached the normal level.

Contrary to the experience of others¹ the older patients with long standing hypertension have experienced a more striking drop in blood pressure than younger individuals.

Digitalis has seldom been prescribed unless the patient was already digitalized at the time of the first visit. It is our impression that the response of patients with congestive cardiac failure on the basis of hypertensive heart disease placed on the regime described has often been more satisfactory than that of those treated with digitalis, mercurial diuretics and ordinary "low salt diets" containing 2 to 3 g of sodium chloride. Some patients who have been taking digitalis have improved when they discontinued this drug. This has happened especially in cases of angina pectoris. A number of patients not in apparent heart failure noted a definite decrease in nocturia in spite of a fluid intake of approximately 3 liters a day.

Few instances of symptoms suggestive of sodium privation have been observed and these have usually been controlled by reducing the fluid intake. One patient with very poor renal function developed orthostatic hy-

1 Grollman, A., *J. Am. Dietetic Assn.*, 1946, **22**, 864.

2 Smithwick, R. H., *Arch. Surg.*, 1944, **49**, 189.

3 Hettig, R. C., and Lyons, R. H., unpublished observations.

potension with bradycardia and azotemia. In one obese female a psychoneurotic crisis seemed to have been precipitated; it persisted after the diet was discontinued. This regime is tolerated in warm as well as cold seasons.

Preliminary studies suggest that the results obtained by treating essential hypertension with a diet low in sodium may prove to be better than those achieved by surgical procedures (Table I). This is true particularly in patients with far advanced heart and eye ground changes. The response seems to be similar in degree to that observed by Kempner⁴ who uses drastic restriction of fluid (700 to 1000 cc), protein (20 g), fat (5 g), as well as sodium (200 mg), thus suggesting that his results, as previously pointed out,⁵ may be primarily due to sodium restriction. Compared to that used by Grollmann *et al.*,⁵ who obtained a significant reduction in blood

pressure in 2 of 6 hypertensive patients, our diet appears less inconvenient, more palatable and contains about half as much sodium.

These observations confirm the early findings of Allen and Sherrill⁶ in the treatment of arterial hypertension and the later observations of Schemm⁷ in the management of heart failure. It should be emphasized, however, that failure may be expected unless the strictest cooperation and a complete understanding over a long period of time exists between patient, dietitian and physician.

It is suggested that rigid restriction of sodium seems to have a definite place at the present time, in the management of hypertensive vascular disease. These observations, in addition may have a more important bearing on the pathogenesis of this condition.

The authors wish to express their appreciation to Dr. L. H. Newburgh and Dr. Frank N. Wilson for their aid in carrying out this study.

⁴ Kempner, W., *Nor. Car. Med. J.*, 1945, **6**, 62.

⁵ Grollman, A., Harrison, T. R., Mason, M. F., Baxter, J., Crampton, J., and Reichsman, F., *J. A. M. A.*, 1945, **129**, 533.

⁶ Allen, F. M., and Sherrill, J. W., *J. Metab. Research*, 1922, **2**, 429.

⁷ Schemm, F., *Ann. Int. Med.*, 1944, **21**, 937.

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Heterologous Transmission of a Human Lymphoma.

MACHTELD E. SANO.

From the Agnes Barr Chase Surgical Research Foundation, Temple University School of Medicine and Hospital.

Greene¹ was the first to transplant a human tumor into an animal by passage through the anterior chamber of the eye. Since 1939, at the suggestion of Dr. Lawrence Weld Smith, numerous attempts were made in this laboratory to transplant human tumors into animals by previous passage through tissue culture without any success. The work was resumed by the author and changes were made in the tissue culture medium and the type of mice used.

The tissue used for inoculation was ob-

tained from a lymphnode of a patient whose diagnosis elsewhere had been "lymphosarcoma or aleukemic leukemia." The diagnosis on section here was "possible lymphosarcoma, leukemia cannot be excluded." Bone marrow examination did neither prove nor disprove the diagnosis of leukemia. The tumor was inoculated into a tissue culture medium consisting of the patient's own plasma, mouse embryo extract and Tyrode's solution at pH around 7.6. Growth was profuse and consisted mainly of lymphocytes, occasional blast forms and a few fibroblasts and reticulocytes. A small number of mitoses were noted.

¹ Greene, H. S. N., and Murphy, E. D., *Cancer Research*, 1945, **5**, 269.