lar reactivity since the common property of all the agents studied is the capacity to increase electrolyte excretion, primarily sodium. The failure of dichlorophenamide to alter pressor response to norepinephrine remains obscure.

The similarity of the changes in responses resulting from the several diuretics raises a question whether a singular intrinsic antipressor action is associated with chlorothiazide. Although the mechanism is not known, it is conceivable that the antihypertensive action of chlorothiazide may be due to: a) a direct effect upon peripheral vascular smooth muscle to alter its state of contraction, or b) a shift in sodium and potassium across the cell membrane resulting in a change in tonus of the vascular system, or c) its diuretic and saluretic action to alter plasma volume and electrolyte balance. Evidence available at the present time would suggest that the diuretic and saluretic action plays the most important role. Independent of changes in volume, excretion of large amounts of sodium may play a role in the antihypertensive properties of a diuretic, since low sodium diets will decrease blood pressure and increase the effectiveness of ganglion blocking drugs in hypertensive patients(5). Recently it has been reported that both chlorothiazide and mercurial diuretics appear to have an antihypertensive action that may be potentiated by a decrease in body sodium(4). In addition, an increase in electrolyte excretion associated with a diminished plasma volume has been observed to decrease the dosage of ganglionic blocking agents required in hypertensive patients(6). Results obtained in this study lend support to changes in electrolyte excretion as being a dominant factor. In each case, no change in response was noted until an interval of time had elapsed when diuresis was established. The possibility that a simultaneous decrease in plasma volume may have been an important factor can not be ruled out since measurements of this parameter were not made.

Summary. The effects on the vascular responses to norepinephrine and isopropylnorepinephrine induced by 3 diuretic agents, acetazolamide, dichlorophenamide and mercaptomerin were determined. Acetazolamide and mercaptomerin diminished vascular responses to these catechol amines similarly to the decrease previously reported with chlorothiazide administration. It is considered probable that the effect on vascular reactivity resulting from these agents is due to augmentation of sodium excretion.

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Interactions of Human Sera and Spinal Fluids with Human Brain Antigen and Antibrain Rabbit Serum. (24855)

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Investigations concerning both immunological differentiation of body organs (*e.g.*, 1,2) and possible existence of "autoantibodies" to human organs have been reported(3,4,5,6). Gadjusek(7) searched for "autoimmune" antibodies in sera of patients with various diseases and found positive complement fixation reactions in 3% tested with liver antigens and

in 10% tested with kidney antigens. Yeh, *et al.*,* have differentiated by precipitin test in human sera circulating protein from various organs of the body. Wide variations in quantity circulating were found. It might be hypothesized that in neurological disease, brain antigens may circulate in the serum. In the present study the possible presence of antibodies to human brain in sera and spinal fluid of various hospital populations and evidence concerning presence or absence of circulating brain antigens in sera and spinal fluids of these populations were investigated by means of precipitin formation. The results reported here constitute only a beginning in this type of study.

Materials and methods. Preparation of antigen. A portion of frontal lobe of brain from a 70-year-old male, 5 hours after death, was stored at −20°C. A 12 g portion, composed of grey and white matter, was homogenized in cold acetone, centrifuged, the acetone removed, and the residue resuspended in 150 cc of saline. *Immunization of rabbits with human brain.* Intraperitoneal injections were given twice weekly to white, male rabbits (5-7 lbs) starting with 1 cc of homogenate and increasing the dose by 1 cc a week until 5 cc were given in final fifth week. Before mixing with antiserum the same antigen homogenate was cleared by centrifuging at 4°C at 3000 rpm for 15 minutes. Sera obtained by cardiac puncture of 8 immunized rabbits were pooled. A precipitate was observed at 1024-fold dilution of this antiserum when the latter was mixed with antigen solution. Serum was obtained from (1) a group of 128 patients from the general medical and surgical service,† not having any known neuropsychiatric disorder. (2) A random group of 46 patients from neuropsychiatric wards, with various acute and chronic mental disorders, of which 2 were acute schizophrenia. (3) Group of 29 patients with schizophrenia, severe type. (4) Group of 41 patients with paresis, but negative serology. Sera from third group were collected before ataractic drug therapy and for 6 consecutive weeks after drug administration. Cerebrospinal fluid was obtained from 10 patients, 2 of which had neuropsychiatric illness and 2 had multiple sclerosis. Using adequate controls, microprecipitin tests were set up by mixing 0.2 cc of antiserum and 0.2 cc of brain antigen, human serum (diluted 1:4), or spinal fluid, incubating 1 hr. at 37°C, storing 18 hrs. at 4°C, centrifuging, and examining for precipitate.

TABLE I. Precipitin Formation with Human Serum *vs* Brain Antigen.

Type of patient	No. in series	No. positive	Highest dilution of serum giving a precipitin
Medical & surgical	128	3	16, 32, 8
Random	45	0	0
Schizophrenic	29	1	8
Paretic	41	1	80

Results. When serial dilutions of human serum were mixed with human brain solution (Table I), 3 individuals out of 128 general medical and surgical cases and 2 patients out of 115 neuropsychiatric cases gave a positive precipitin reaction, in dilutions of human sera ranging from 8 to 160 fold. A precipitate still resulted with sera drawn twice or thrice from these positively reacting patients, whose diagnoses were schizophrenia (1 case), paresis, (1 case), mild arthritis, (1 case), alcoholism (2 cases).

When various dilutions of antibrain rabbit serum were mixed with sera of human subjects, a precipitation resulted in one out of 45 random neuropsychiatric patients (2%), in 3 instances out of 29 severe schizophrenic patients (10.4%) and in 13 instances out of 41 paresis patients (31.7%), (Table II).

TABLE II. Precipitin Formation with Antibrain Rabbit Serum and Human Serum.

Type of patient	No. in series	No. positive	Highest dilution of antiserum giving a precipitin
Medical and surgical	128	0	0
Random NP	45	1	640
Schizophrenic	29	3	320, 320, 5120
Paretic	41	13	160 (2 cases) 320 (4 ") 640 (2 ") 1280 (3 ") 2560 (2 ")

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† Furnished through courtesy of Dr. J. L. Garey, Chief, Clinical Labs.

TABLE III. Reactions of Cerebrospinal Fluid.

Type of patient	No. in series	Spinal fluid mixed with human brain antigen — No. giving precipitin	Antibrain serum mixed with CSF — No. giving precipitin	Highest dilution of antiserum giving a precipitin
Non-neuropsychiatric	6	0	6	8 (2 cases) 16 (4 ")
Random neuropsychiatric	2	0	2	8, 16
Multiple sclerotic	2	0	2	8, 32

The sera from all severe schizophrenic patients were secured before ataractic drug or placebo treatment and each week for 6 consecutive weeks thereafter. Sera from 3 of these patients gave a positive precipitin reaction for all 7 specimens of each case. A wide range of antiserum dilutions was tried and led to clear precipitates from 80-fold to 5120-fold (Table II).

The sera of 13 of 41 paretic patients showed a strongly positive reaction at various antiserum dilutions; 6 sera tested a week later remained positive.

Of 10 spinal fluids tested, none reacted with precipitin formation when mixed with brain antigen, but all gave a definite precipitin when mixed with antibrain serum (Table III), regardless of disease state of patient.

Conclusions. Rabbit antiserum to a saline soluble component of human brain, when mixed with spinal fluids and with sera from patients with various illnesses, gave a precipitate with all spinal fluids and with 17 out of 244 human sera. These positively reacting sera were from 4 schizophrenic and 13 paretic patients. On the other hand, human brain antigen mixed with human serum gave a precipitate in 5 out of 244 cases. The 5 sera were from one arthritic, one paretic, one chronic schizophrenic and 2 alcoholic patients. The few sera reacting positively show that this is not a general flocculation phenomenon, but whether immune systems actually related to brain are being tested here, is the subject of further study. The relatively high number of paretic patients giving a positive reaction with antibrain serum may have a bearing upon this. These results may provide a lead for further investigation of brain disease.

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Reactions of Stuart Factor and Factor VII with Brain and Factor V. (24856)

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Several workers have shown that a potent prothrombin conversion factor forms on incubation of factor V (labile factor, Ac Globulin, proaccelerin) with serum and brain extract (1-4). This product can be sedimented by high speed centrifugation(1) and will, for convenience, be referred to as "extrinsic thromboplastin." The factor in serum which takes part in formation of this product was believed to be factor VII (stable factor, proconvertin, SPCA). The one-stage prothrombin time is prolonged in congenital deficiency of Stuart factor (SF) as well as congenital deficiency of factor VII so that it now appears

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