makes its analysis difficult; appropriately prepared extracts of freeze-dried material, however, can be examined accurately by paper chromatography as here illustrated. The lipid pattern disclosed indicates that the CSF cannot be a simple plasma transudate; the disproportionately high content of ethanolamine phosphatide might imply contributions by the choroid plexuses or ependymal cells. The origin of the cardiolipin-like plasmalogen is similarly unknown and especially puzzling because cardiolipin is generally believed to be exclusively a mitochondrial lipid.

Summary. Freeze-dried chloroform-methanol extracted samples of human cerebrospinal fluid (CSF) were examined for various lipids by means of paper chromatography. Phosphatidyl ethanolamine and ethanolamine plasmalogen were characteristically high as compared with blood plasma. Sphingomyelin, phosphatidyl choline and a small amount of choline plasmalogen were also present. The neutral lipids were composed of triglycerides, cholesterol and cholesterol ester. A plasmalogen resembling cardiolipin was present in low concentration. The cerebrosides were not detected.

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Effects of Vasoactive Drugs on Serum Electrolytes in Hypertensive and Normotensive Humans.* (27812)

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Previous studies have suggested that extracellular sodium decreases during acute rises in blood pressure and increases as pressure falls acutely(1-4). Inverse movements of potassium of lesser amounts usually accompany these sodium movements. It was concluded that sodium transfer systems are the primary determinants of smooth muscle tone(3,4). However, experimental data have been neither consistent nor conclusive. In addition, drugs, such as epinephrine and epinephrine-like substances, which were used in some studies, have extravascular metabolic effects as well as effects on vasomotor tone(5,6).

The present study reviews the acute effects of drugs, which primarily affect vasomotor tone, on the distribution of electrolytes in man. Patients with "essential" hypertension and normotensive subjects were studied to determine whether the effects of vasoactive drugs upon electrolyte distributions are influenced by initial blood pressure levels.

Materials and methods. The subjects of this study were divided into 4 groups (Tables I-IV). Groups A and C include 10 and 7 patients, respectively, with chronic arterial (essential) hypertension (blood pressures, 140/90 mm Hg or higher), and Groups B and D include 7 and 4 subjects, respectively, with normal blood pressures. Antihypertensive therapy was avoided for 2 weeks prior to these studies. The patients with normal blood pressures were convalescent hospital subjects believed to have normal hearts, lungs, and kidneys.

The patients were in the postabsorptive state and were not given premedication. A cardiac catheter was passed into the right atrium from a peripheral vein. Control data were obtained during an initial period of 60

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minutes. Peripheral (brachial) artery pressures were measured by a single observer by the auscultatory method. Three systemic (brachial) arterial blood samples were collected at intervals for determinations of serum sodium, potassium, and chloride concentrations. Blood was allowed to pour gently from an indwelling arterial needle into dry, chemically clean test tubes. The tubes were tightly stoppered, and the bloods allowed to clot for 1 hour. The serums were then separated by centrifugation. Serum sodium and potassium concentrations were measured in duplicate with a lithium internal-standard flame photometer.† Serum chloride concentration was measured in duplicate by the method of Schales and Schales(7). Duplicate measurements of serum sodium, potassium, and chloride were required to agree within 2.0, 0.2, and 2.0 meq/l, respectively. In any given subject, serum sodium and chloride concentrations in the 3 control samples did not vary by more than 2.0 to 3.0 meq/l, and potassium concentrations did not vary by more than 0.2 to 0.3 meq/l.

After the control data were obtained, one of 2 drugs was injected over a period of 30 seconds into the right atrium through the catheter. The subject was not aware of drug injections. In Groups A and B, trimethaphan‡ was injected. Trimethaphan is primarily a ganglion blocking agent, whose onset and duration of activity are approximately 1-3 minutes and 10-20 minutes, respectively (8,9). The drug was dissolved in 5% dextrose in water in a concentration of 1.0 mg/ml. The injected dose was 0.10 mg/kg body weight. In Groups C and D, phenylephrine was injected in a dosage of 0.5 mg. Phenylephrine has primarily peripheral vasoconstrictor properties, whose onset and duration of actions after intravenous administration are similar to those of trimethaphan.

After these drugs were injected, blood pressures (auscultatory) were measured every 30 seconds during the initial 5 minutes, and, then, at intervals until they returned to control values. Systemic (brachial) arterial blood samples were collected at the times when maximal changes in blood pressure occurred. In some patients, samples were collected before the maximal pressure responses, and, in some, after these times, when pressures were returning toward control levels. It was, thus, planned that samples would be obtained at representative phases of the blood pressure

† Baird-Atomic, Inc., Cambridge, Mass.

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TABLE I. Arterial Pressures and Serum Electrolytes before and after Trimethaphan Administration. Hypertensive patients (Group A).

	Patient			Pressure (mm Hg) Systemic artery		Serum electrolytes (meq/l)		
	Sex	Age (yr)	Time (min)	Systolic	Diastolic	Na	K	Cl
1.	♂	25	Control	200	150	137	4.3	108
			1	157	120	"	4.1	107
			3	162	87	"	4.2	"
			9	187	146	"	"	109
2.	♀	30	Control	140	95	137	3.7	102
			1	114	68	139	3.6	104
			3	100	58	137	3.5	103
			4	104	80	139	3.6	105
3.	♀	40	Control	200	150	137	3.2	102
			2	180	130	"	"	100
			3	182	132	"	"	102
			4	195	150	139	"	100
4.	♂	40	Control	158	125	135	4.8	100
			2	134	106	132	"	"
			6	130	"	135	"	99
5.	♂	42	Control	180	118	142	4.3	103
			1	160	100	141	"	102
			2	128	92	143	"	106
6.	♀	44	Control	180	112	138	4.0	102
			1	129	85	"	"	101
			3	127	90	"	"	103
			7	130	95	136	3.9	"
7.	♀	47	Control	195	107	133	3.8	97
			2	115	75	131	"	"
			3	125	95	135	3.9	98
			10	175	100	134	4.0	97
8.	♂	48	Control	193	138	140	4.6	101
			1	122	82	138	4.5	"
			2	100	76	"	"	102
			3	92	72	139	"	100
9.	♂	50	Control	190	125	143	3.7	103
			1	170	110	142	"	102
			2	130	90	140	3.6	"
			3	118	88	"	3.7	104
10.	♂	55	Control	140	95	134	4.2	98
			1	110	80	"	4.1	99
			2	"	"	"	4.3	"

Avg control values are listed for each subject. Following these data, values are listed according to the times (column "Time") after drug administration.

changes. These samples were analyzed for sodium, potassium, and chloride concentrations by the methods described above. Changes in serum electrolytes were considered to be significant only if these changes exceeded the differences which existed between control samples (*vide supra*).

Results. Tables I to IV list the values for blood pressures and serum electrolytes. Since there was a minimal variation in these parameters during control periods, average values are tabulated for these periods. Following these data, serum electrolytes are listed according to the times following drug injections when arterial blood samples were collected. Blood pressures at these times are listed in corresponding lines.

There were no consistent or significant changes in serum potassium, sodium, and chloride concentrations during the vasodepressor or pressor reactions following administration of trimethaphan or phenylephrine, respectively, in these subjects.

TABLE II. Arterial Pressures and Serum Electrolytes before and after Trimethaphan Administration. Normal subjects (Group B).

	Patient			Pressure (mm Hg) Systemic artery		Serum electrolytes (meq/l)		
	Sex	Age (yr)	Time (min)	Systolic	Diastolic	Na	K	Cl
1.	♂	22	Control	125	84	133	4.2	97
			1	114	75	132	"	95
			2	"	"	133	"	98
2.	♂	24	Control	110	70	138	3.5	101
			2	105	56	"	"	102
3.	♀	30	Control	124	87	134	4.3	100
			2	94	66	132	"	"
			3	106	76	131	4.2	103
			4	—	—	135	4.3	"
4.	♂	46	Control	130	80	135	4.8	94
			2	112	"	132	4.4	93
			4	120	82	135	4.5	95
			5	116	80	"	"	"
5.	♂	47	Control	125	85	143	4.7	102
			1	85	60	139	4.4	97
6.	♀	50	Control	128	80	137	4.6	95
			1	110	65	136	"	94
			2	73	55	"	"	96
7.	♂	22	Control	124	76	137	4.1	104
			2	110	70	136	4.0	"
			7	99	64	"	"	103
			8	106	69	"	4.2	104

See footnote, Table I.

TABLE III. Arterial Pressures and Serum Electrolytes before and after Phenylephrine Administration. Hypertensive patients (Group C).

	Patient			Pressure (mm Hg) Systemic artery		Serum electrolytes (meq/l)		
	Sex	Age (yr)	Time (min)	Systolic	Diastolic	Na	K	Cl
1.	♂	21	Control	150	104	139	3.8	99
			1	180	124	138	3.7	100
			2	188	134	"	4.0	101
			7	156	113	137	3.5	102
2.	♂	29	Control	143	94	135	4.1	105
			1	162	125	"	4.3	106
			3	"	100	"	4.1	105
			8	145	95	136	4.3	103
3.	♂	35	Control	178	122	132	3.6	101
			2	240	130	131	3.7	100
			5	222	123	132	3.4	"
			9	183	120	131	"	101
4.	♀	45	Control	150	90	140	4.0	103
			1	182	113	141	4.2	101
			2	180	111	"	4.4	104
			8	150	90	140	4.3	"
5.	♀	45	Control	143	100	139	5.0	102
			1	220	150	"	"	103
			3	192	117	137	4.7	102
			6	172	106	138	4.8	"
6.	♀	47	Control	160	115	136	4.0	103
			1	213	120	134	3.8	102
			2	226	130	135	4.0	104
			4	222	120	136	3.8	101
7.	♀	47	Control	190	110	134	4.2	106
			2	270	137	135	4.3	105

See footnote, Table I.

Discussion. Muirhead and co-workers(1) found marked decreases in plasma sodium (average–14 meq/l) and increases in plasma potassium (average +3.2 meq/l) during intravenous infusions of norepinephrine in anesthetized dogs. Robertson and Peyser(2) found that serum sodium and chloride each fell an average of 8 meq/l and serum potassium rose an average of 7.9 meq/l in anesthetized cats 5 minutes following injections of 500 μg/kg of l-epinephrine. Others have noted immediate increases in serum potassium by as much as 50%, followed by a sharp drop to subnormal levels, after intravenous administration of epinephrine to cats, dogs, and man(5,10,11). Friedman and co-workers studied the effects of norepinephrine, angiotonin, and pitressin on distribution of electrolytes in bilaterally nephrectomized rats and dogs, and found that electrolyte shifts

TABLE IV. Arterial Pressures and Serum Electrolytes before and after Phenylephrine Administration. Normal subjects (Group D).

	Patient			Pressure (mm Hg) Systemic artery		Serum electrolytes (meq/l)		
	Sex	Age (yr)	Time (min)	Systolic	Diastolic	Na	K	Cl
1.	♂	25	Control	123	85	135	4.0	103
			3	190	120	"	4.1	"
			6	150	100	136	4.0	"
			8	120	80	"	"	104
2.	♀	26	Control	138	86	130	4.3	101
			1	156	110	129	"	"
			2	176	130	133	—	104
			6	154	94	131	4.1	102
3.	♂	36	Control	120	70	136	4.8	103
			2	142	96	134	5.1	"
			10	122	74	"	4.9	"
4.	♀	46	Control	137	80	138	4.5	104
			1	220	110	139	4.7	105
			4	165	90	140	4.6	103
			8	160	84	139	"	104

See footnote, Table I.

(movement of sodium out of extracellular space and movement of potassium into extracellular space) occurred during acute increases in blood pressure(3,4). Other studies (12-15), however, as well as the present study, have indicated that there are no significant changes in serum electrolytes during drug-induced changes in blood pressure.

These differences in results may be related to differences in properties of various vasoactive substances. Extravascular effects of some drugs influence tissue and plasma electrolyte compositions independently of changes in vasomotor tone, thereby obscuring whatever changes may occur within vessel walls and in their local environments. D'Silva(5,6) demonstrated in the cat that the source of increased extracellular potassium following injections of adrenalin and adrenalin-like substances appears to be, almost exclusively, the liver. The possibility exists that other vasoactive drugs may also affect electrolyte compositions of extravascular structures.

It appears that changes in electrolytes within vessel walls and in their local environments can best be evaluated by direct analyses of vascular tissues during a variety of vasomotor activities. Tobian and Fox(13) demonstrated that femoral arteries of dogs which received infusions of norepinephrine for 30 minutes lost potassium and gained sodium. Daniel and co-workers(12) found only a decrease in potassium content in the rat aorta immediately after injection of l-norepinephrine. Daniel and Dawkins(15) demonstrated increased potassium in aortas of rats with renal hypertension and spontaneously-occurring hypertension; in the latter rats, aortic sodium content decreased. These differences in electrolyte contents of aortas may be related to different forms of hypertension, species differences, and differences in duration of the hypertensive states. This important aspect of the problem of vasomotor tone and blood pressure regulation requires further study.

Summary. Trimethaphan was injected intravenously into 10 hypertensive and 7 normal subjects, and phenylephrine was injected intravenously into 7 hypertensive and 4 normal subjects. Blood pressures (auscultatory) and serum sodium, potassium, and chloride were measured before and at frequent intervals after administration of these drugs. No significant changes in serum electrolytes occurred following administration of trimethaphan or phenylephrine. These data, in conjunction with those of others, suggest that serum electrolytes may not accurately reflect alterations in electrolyte compositions of vascular structures during drug-induced changes in vasomotor activity. Vasoactive drugs may affect electrolyte compositions of extravascular structures, and, thus, influence serum electrolytes. Serum values, therefore, have little significance. Electrolyte changes within vessel walls and in their local environments may best be evaluated by direct analyses of vascular tissues.

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Action of Steroids on Lysergic Acid Diethylamide (LSD) Metabolism.* (27813)

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We have previously reported that natural steroids affect LSD action in trained rats(1), human volunteer subjects(2) and in a brain function, the optically evoked primary cortical potential of rabbits(3). In addition, prednisone, a synthetic steroid, is an effective antagonist of some phases of the LSD reaction in humans, according to Abramson and Sklarofsky(4). In order to learn more about LSD-steroid interaction, we have studied the metabolism of LSD *in vitro*.

Methods. Male Holtzman rats weighing 200-250 g were sacrificed by decapitation and 2-3 g of liver removed. To each liver sample 4 volumes of chilled isotonic KCl solution were added and the liver homogenized in a Potter-Elvehjem apparatus. A supernatant fraction containing microsomes and soluble fraction was prepared by centrifugation at 10,000 *g* for 15 minutes(5). Fractions from 200 mg of liver were incubated in a Dubnoff metabolic incubator at 37°C for 2 hours in a medium containing 35 μmol fumarate, 16 μmol glucose-6-phosphate, 1 unit glucose-6-phosphate dehydrogenase, 3.7 μmol TPN, 20 μmol $MgCl_2$, 0.32 μmol LSD and 660 μmol phosphate buffer pH 7.9 to make a final volume of 3 ml. Free steroids were suspended in a suitable vehicle† and added to the flasks to make final concentrations of 1×10^{-3} M and 1×10^{-7} M. Estimations of LSD remaining in the flasks after incubation were made according to the method of Axelrod *et al.*(5).

Results. Additions of LSD to the liver fraction and medium followed immediately by extraction and estimation of the recovered LSD resulted in 100% recovery of the LSD. Possible effects of the steroid suspending vehicle were assessed by comparison of LSD utilization in complete systems with and without addition of vehicle. No differences in LSD utilization between the two were noted.

Inhibition of LSD metabolism by a representative steroid, progesterone, at increasing dilutions is shown in Fig. 1. After demonstrating the inhibitory property of progesterone in detail, other steroids were tested at 2 dose levels. These results are shown in Table I. The degree of inhibition was found to be greatest for the adrenal cortical hormones and least for Dehydroepiandrosterone.

In addition to the use of liver homogenates, several experiments were performed using liver slices and brain slices. Liver slices me-

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† Suspending vehicle Special Formula No. 17874 (SV No. 17874) which consists of an aqueous solution of sodium chloride (0.9%) polysorbate 80 (0.4%), carboxymethylcellulose (0.5%) and benzyl alcohol (0.9%).