TABLE I.
Means and Standard Deviations for 5 Measurements of 3 Tracings by 2 Methods.

	Differential analyzer		Disc planimeter	
	Mean Sq. in.	Stand. dev.* Sq. in.	Mean Sq. in.	Stand. dev. Sq. in.
	Tracing No. 1			
Albumin	1.302	.002	1.288	.048
$Alpha_1$	.106	.005	.113	.014
$Alpha_2$	.228	.008	.227	.005
Beta	.310	.005	.313	.007
Phi	.204	.004	.202	.005
Gamma	.407	.009	.401	.008
Delta	.362	.014	.361	.007
Total area	2.918	.045	2.905	.066
	Tracing No. 2			
Albumin	1.244	.006	1.237	.010
$Alpha_1$	.162	.005	.168	.006
$Alpha_2$	.291	.002	.295	.008
Beta	.386	.002	.384	.010
Phi	.223	.002	.223	.002
Gamma	.480	.005	.484	.006
Delta	.406	.007	.404	.008
Total area	3.190	.028	3.194	.028
	Tracing No. 3			
Albumin	1.576	.006	1.526	.052
$Alpha_1$	.179	.004	.180	.008
$Alpha_2$	.243	.003	.248	.007
Beta	.393	.002	.395	.005
Phi	.160	.003	.163	.010
Gamma	.298	.006	.313	.016
Delta	.398	.005	.408	.009
Total area	3.248	.020	3.233	.062

*Standard deviation $S = \sqrt{\frac{\Sigma(x_1 - \bar{x})^2}{n-1}}$.

greater precision than those obtained with the planimeter, and that the greatest actual differences arise in measurements of the largest areas, namely those of the albumin peak, and of the total area of the pattern. Considering percentage deviations from the mean, the maximum deviation for the set of 120 measurements on the differential analyzer was 7.3%, with 88% of the deviations below 2%, and 31% below 0.5%. The same set of measurements by means of the planimeter yielded a maximum deviation from the mean of 22.1%, with 61% of the values below 2.0% and 21% below 0.5%.

In addition to obtaining more accurate results, use of the differential analyzer will save a great deal of time, especially when comparatively large numbers of tracings can be run at one time. While it takes approximately 2 hours to set up the mechanism for the operation, the time required for measurement of a tracing is only 10 minutes. Use of the planimeter requires approximately 1 hour per tracing, since the lack of precision made it necessary to measure each tracing at least twice.

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Simultaneous Bilateral Determinations of Cerebral Blood Flow and Arterial-Cerebral Venous Oxygen and Glucose Differences.* (17977)

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The validity of the nitrous oxide procedure for measuring cerebral blood flow depends upon the assumption that blood obtained from one internal jugular bulb is representative of mixed cerebral venous blood. Since the brain is actually a heterogeneous organ, comprised of a wide variety of cell types, and with different rates of metabolism in its various parts, the nitrous oxide technic at best yields an average value for the blood flow through and the metabolism of these different areas. Unless the blood draining these parts is reasonably well mixed, or at least consistently distributed, it is manifestly impossible to reach valid conclusions concerning

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either local or whole brain metabolism by sampling blood from one internal jugular bulb. These studies were undertaken because a difference of opinion concerning the mixing and distribution of cerebral venous blood is apparent in the literature(1-5) and as a preliminary to further observations on the circulatory dynamics of the brain. The nitrous oxide technic, as devised by Kety and Schmidt(1) and as modified in this laboratory(6) was used to measure cerebral blood flow and metabolism in 18 simultaneous bilateral observations in 12 subjects.

Method. The subjects chosen represented several disease states, since it was felt that the validity of the method could be tested better in this way than with normal subjects alone. Three of the patients (A.C., A.P., and J.S., Table I) had clinical evidence of unilateral cerebral disease. The nitrous oxide technic has been described elsewhere (1); the modification in use in this laboratory consists of drawing simultaneous, integrated samples from artery and vein throughout the 10 minute period of nitrous oxide inhalation(6). In every instance samples taken for blood flow determination and oxygen and glucose contents were drawn simultaneously from the artery and right and left internal jugular bulbs. Blood oxygen content was measured by the spectrophotometric method of Hickam and Frayser(7); blood glucose content was measured by Nelson's modification of Somogyi's method(8). Samples for blood oxygen content were drawn before and after each blood flow determination so that each arterial-cerebral oxygen difference is an average of two determinations. Two samples for blood glucose content were drawn from the artery and both jugular bulbs before and after each blood flow determination so that each arteriovenous glucose difference is an average of 4 determinations. Mean arterial pressures used to calculate cerebral vascular resistance were measured by the auscultatory method.

Results. The data are presented in detail in Table I. The p values were calculated by comparing the differences between the right and left determinations in the individual subjects. It is apparent that there is no significant difference between the two sides in any of the measured cerebral metabolic values. The deviations are all within the experimental error of these determinations as performed in this laboratory. The 3 patients with unilateral cerebral disease did not differ from the remainder of the subjects in this respect.

Comment. The prevailing disagreement concerning the percentage of subjects in whom longitudinal and straight sinus blood mix completely in the torcular(9-12) does not particularly bear on the problem of the validity of the nitrous oxide procedure. It is agreed that if this were the only mechanism whereby blood from the various parts of the brain were mixed, the nitrous oxide technic would be invalid in a considerable percentage of cases. Anatomical studies reported by Shenkin, Harmel, and Kety(13) indicate adequate opportunity for cortical-subcortical mixing of blood draining from the various histologic areas of the brain. The studies reported here support those observations and indicate that regardless of the anatomical variations in different individuals, the calculated cerebral blood flows and oxygen and glucose contents of simultaneously drawn

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TABLE I.
Bilateral, Simultaneously Determined, Cerebral Metabolic Values.

Patient	Age	Remarks	Cerebral blood flow, ml/min./100 g brain R.	L.	Arterial-cerebral venous O_2 diff. vol. % R.	L.	Arterial-cerebral ven. glu. diff. mg % R.	L.	Cerebral oxygen consump. ml O_2/min. 100 g brain R.	L.	Cerebral glucose consump. mg glucose/min./100 g brain R.	L.	Cerebral vascular resist. R.	L.
E.	47	Cerebral vascular dis.												
		Before stellate block	51	50	6.4	6.5	—	—	3.2	3.2	—	—	2.84	2.90
		After stellate block (rt.)	48	47	6.8	7.1	10	13	3.2	3.3	4.8	6.1	2.96	3.02
O.	63	Cerebral vascular dis.												
		Before stellate block	44	45	5.2	5.7	—	—	2.3	2.6	—	—	2.50	2.45
		After stellate block (rt.)	37	32	6.7	6.9	9	7	2.5	2.2	3.3	2.2	2.78	3.22
C.P.	35	Subarachnoid hemorrhage	40	35	6.3	7.1	—	—	2.5	2.5	—	—	2.20	2.51
A.C.	37	Mitral stenosis. Embolism to cortical branch of rt. middle cerebral artery	32	35	7.7	7.7	8	8	2.5	2.7	2.6	2.8	3.02	2.77
A.P.	57	Embolism to branch of left middle cerebral artery before stellate block	—	—	5.4	5.3	10	12	—	—	—	—	—	—
		After stellate block (left)	—	—	5.9	5.2	11	11	—	—	—	—	—	—
C.S.	29	Coarctation of aorta	43	45	8.0	7.3	8	8	3.4	3.3	3.4	3.6	3.05	3.19
J.W.	42	Rheumatoid arthritis serial detm's. (1)	39	41	—	—	11	13	—	—	4.3	5.3	2.05	1.95
		(2)	50	51	—	—	12	14	—	—	6.0	7.1	—	—
		(3)	43	47	—	—	12	11	—	—	5.2	5.2	—	—
J.S.	37	Berry aneurysm, left int. carotid artery. Before ligation	71	73	4.4	4.4	10	11	3.1	3.2	7.0	7.8	1.39	1.36
		After ligation of left int. carotid artery	—	—	4.9	4.9	7	5	—	—	—	—	—	—
R.	36	Hysteria. Serial detm's (1)	66	57	5.1	5.6	12	12	3.3	3.2	7.9	6.8	—	—
		(2)	57	52	5.3	6.3	13	12	3.1	3.3	7.4	6.2	—	—
		(3)	56	51	6.9	6.7	10	9	3.8	3.4	5.6	4.6	—	—
W.	30	Tic doloreux, before stellate block	75	70	6.5	6.6	13	14	4.9	4.8	9.7	9.7	1.27	1.36
		After stellate block (left)	60	53	6.3	6.3	11	12	3.8	3.4	6.6	6.4	1.59	1.79
S.	68	Simple depression	39	41	7.0	7.0	12	11	2.7	2.9	4.9	4.7	2.30	2.20
E.	22	Myasthenia gravis	77	69	5.6	5.2	9	8	4.3	3.6	6.7	5.5	1.20	1.30
		Mean	51.6	49.7	6.13	6.21	10.4	10.6	3.24	3.17	5.69	5.60	2.24	2.31
		p values	>0.05		>0.3		>0.6		>0.3		>0.5		>0.2	

$t = \frac{\text{Mean diff.}}{\text{Std. error of mean diff.}}$. R = Right. L = Left.

samples from the right and left internal jugular bulbs do not differ appreciably on the two sides in subjects at rest. These data also suggest that adequate mixing of blood from the two cerebral hemispheres may occur in the presence of unilateral cerebral disease. They are not in agreement with the findings reported by Ferris and his colleagues(2); this discrepancy remains unresolved. These data would also cast doubt on the assumption that accurate differential values for metabolism of the cortex and lower portions of the brain can be adduced from bilateral internal jugular bulb samples(5,14).

Summary and conclusions. 1. The values for cerebral blood flows, arterial-cerebral venous oxygen and glucose differences were not significantly different on the two sides in 18 simultaneous bilateral observations in 12 subjects. 2. Three subjects with unilateral cerebral disease also had similar values on the two sides. 3. The assumption that blood obtained from one internal jugular bulb is representative of mixed cerebral venous blood appears to be correct.

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Diurnal Variations of Renal Function in Congestive Heart Failure. (17978)

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Employing a constant intravenous infusion technic, Sirota, Baldwin and Villarreal(1) have examined the diurnal variations of renal function in normal subjects. These studies reveal a significant decrease in urine flow during sleep, resulting primarily from increased tubular reabsorption of water, with only a slight and questionably significant decrease in glomerular filtration rate from 12 midnight to 4 a.m. The renal plasma flow did not vary significantly throughout the 24 hour period. The present report is concerned with similar studies in patients with congestive heart failure.

Methods. Simultaneous endogenous creatinine chromogen, inulin and p-aminohippurate clearances were determined during 4 to 6 hour periods throughout 24 hours in 10 male subjects in congestive heart failure. In 6 subjects sodium excretion was also followed. In 5 subjects cardiac failure was associated with rheumatic heart disease, in 4 with arteriosclerosis, and in 1 with cor pulmonale. Six of these patients at the time of study had persistent or increasing peripheral edema in spite of complete bed rest, low salt diet and complete digitalization. Of the other 4. 2 were edema-free and 2 were undergoing diuresis, spontaneous in 1 case and in the other as a result of digitalization. With the exception of 1 individual (E.), mercurial diuretics were withheld for a minimum of 5 days prior to study. The test substances were administered by means of a constant delivery pump at an approximate rate of 0.3 cc/min. Five per cent glucose in distilled water was used as the diluent.§ Analytical methods and details of technic in continuous 24 hour clearance studies have been reported previously(1).

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§ PAH dissolved in 5% glucose solution forms a reaction production in which the p-amino group is covered. This product apparently has a low clearance, as indicated in the low extraction ratios of PAH-glucose mixtures(2). For this reason all data on C_{PAH} are deleted from the report.