THE VOLUME OF THE EXTRACELLULAR FLUIDS OF THE BODY [1]

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Changes in the volume of extracellular fluids of the body can be calculated from the exchanges of sodium (1) or of chloride (2), appropriate corrections being made when necessary for changes of concentration of these ions in the fluids (2). Such studies are technically difficult and time-consuming and yield no absolute values for volume of extracellular fluids. A diffusible, non-metabolized substance not normally present in the body but which, like sodium and chloride, is restricted to extracellular fluids would afford a convenient measure of the absolute volume of these fluids at any time. The experiments which follow represent an attempt to find such a substance.

Sucrose injected intravenously was tried first because it was known that this substance traverses capillary membranes with ease and yet does not enter red blood corpuscles. Later, the results of experiments of Crandall and Anderson (3) on the distribution of sulfocyanate suggested that this substance might be of use. Still later, the distribution of sulfate was studied when it was noted from the data of earlier experiments following the intravenous administration of Na_2SO_4 to dogs (4) that sulfate apparently distributes itself through only about 20 per cent of the body by weight.

EXPERIMENTAL SUBJECTS AND PLAN OF EXPERIMENTS

The subjects for the experiments were normal male laboratory workers, convalescent patients without evident abnormalities of hydration, and four patients with advanced renal failure without clinical evidence of edema. All experiments were started in the postabsorptive state, but in some instances small amounts of water, fruit juice and coffee were given during the experiments.

Sucrose, sodium sulfate and sodium sulfocyanate were injected intravenously, in doses of 15 to 30 grams for sucrose, 19 to 65 milliequivalents for sodium sulfate, and 0.8 to 1.8 grams for sodium sulfocyanate. Potassium sulfocyanate in doses of 1.25 to 1.75 grams has also been used *perorally.*

KSCN was given quantitatively *per os* as a 2.5 per cent solution. No significant changes in blood pressure were produced in either normal or hypertensive subjects. The substances for intravenous administration were weighed into a beaker, made up with freshly distilled water (approximately 25 cc. per gram for NaSCN and Na_2SO_4 and 5 cc. per gram for sucrose), and sterilized by boiling. Merck's reagent grade anhydrous Na_2SO_4 and commercial granulated sucrose required no preliminary desiccation, but NaSCN was dried to constant weight at 100° C. Injections were made at the rate of 10 cc. per minute. No toxic effects were noted, and diuresis was not provoked. The amount of solute left in the beaker and syringe was determined by analysis and correction made. Blood and urine samples were taken at varying intervals after the injections, and serum was separated from the blood after it was allowed to clot under oil.

ANALYTICAL METHODS

1. Sucrose. The iodometric titration of Shaffer and Somogyi (5) using "reagent 50" with 5 grams KI and 0.488 gram $KH(IO_3)_2$ per liter was used before and after hydrolysis.

For serum the Somogyi filtrate was used (6). Urine was merely diluted with water to contain between 15 and 30 mgm. of sucrose per 100 cc. Hydrolysis was effected by heating at 85 to 100° C. for two hours, in a 25 cc. volumetric flask covered with tinfoil, 20 cc. of serum filtrate or diluted urine plus 1.2 cc. 0.1 N HCl. After cooling, 0.1 N NaOH was added until the full blue color was obtained with bromcresol green. This usually required almost exactly 1.2 cc. of the alkali, and a drop in excess was found to be without effect on the subsequent reduction. The whole was made

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up to 25 cc., and 5 cc. aliquots were taken for the copper reduction. At the same time 4 cc. of untreated serum filtrate plus 1 cc. of water was used for the determination of glucose. Serum filtrate containing glucose without sucrose gave identical results before and after being subjected to the above hydrolysis.

From the analysis of solutions of sucrose containing 5 to 30 mgm. per 100 cc., a curve, which proved to be rectilinear, was constructed relating sucrose concentrations to thiosulfate. From this curve, serum sucrose was estimated from the difference between the titrations before and after hydrolysis. The accuracy of the sucrose determination is within ± 2 per cent for concentrations greater than 50 mgm. per 100 cc. of serum.

2. Sulfocyanate. Color was developed in a trichloroacetic acid filtrate of serum by the addition of the ferric nitrate reagent described by Crandall and Anderson (3). This is made by diluting 50 grams $Fe(NO_3)_3 \cdot 9H_2O$ and 25 cc. HNO_3 to a liter with water.

One cubic centimeter of serum was used for each of duplicate determinations. The precipitation of proteins was done in a round-bottomed tube (1.5 × 10.0 cm.), adding 20 per cent trichloroacetic acid drop by drop with vigorous shaking until a homogeneous mixture was obtained (usually after 6 or 8 drops have been added), after which the remainder of the 1 cc. of acid was added more rapidly. The tube was then stoppered, shaken vigorously, and centrifuged after standing at least 10 minutes. One cubic centimeter of the supernatant fluid was transferred to another tube in which color was developed with an equal volume of ferric nitrate reagent. Comparison with an aqueous standard solution of SCN plus reagent was made in a microcolorimeter. Omission of trichloroacetic acid from the standard was found to introduce no error. Since the color fades on standing, it must be developed in the standard and unknown at the same time and read within 10 minutes. In protein-free urine, no preliminary treatment is necessary, but SCN-free urine of the same color as the unknown was added to the standard and an equal amount of water to the unknown.

Duplicate determinations agree within ± 3 per cent, usually within ± 1 per cent. NaSCN added to serum and transudates in an amount equivalent to 10 mgm. per cent has been recovered repeatedly with an error of ± 1 per cent. Serum has been left in stoppered tubes at room temperature for 48 hours without demonstrable change in the sulfocyanate content.

3. Sulfate. The alkalimetric benzidine titration of Cope (7) as modified by Bourdillon (8) was used.

RESULTS

The volume of body fluid through which each solute is distributed is calculated by dividing the amount left in the body at the time of blood sampling by its concentration in the serum. The implied assumption that the concentration of the solute in the serum is the same as that in the other fluids through which it diffuses is of course incorrect, but for reasons to be discussed later only this rough method of calculation will be used at present. If the substance is present in the serum before the injection, as is true of SO_4 always and SCN occasionally when it has been used within the preceding week, the change of concentration in the serum is used. This has been found satisfactory in normal subjects given SCN repeatedly, and concentrations in the serum of 25 mgm. per cent have been attained without deleterious effect.

The significant data for the experiments with sucrose and the volumes of distribution calculated from the data are recorded in the first table. In general the calculated volume is significantly higher 2 hours after the injection than it is an hour earlier. The few studies in which determinations were done at one-half hour intervals indicate that diffusion is as complete one and one-half hours after the injection as it is one-half hour later. Studies after the third hour in normal subjects are impractical because of the rapidity of excretion of sucrose. In subjects with marked renal impairment without edema, however, it has been possible to show that no further distribution of sucrose occurs three and four hours after the injection. If only results obtained one and one-half or two hours after the injections are accepted, the average volume of distribution for Subject K is 17.2 per cent of the body weight; for Subject P, 20.1 per cent; for Subject L, 20.3 per cent; for Subject R, 26.0 per cent, and for Subject S, 28.0 per cent. The first

TABLE I

The volume of distribution of sucrose in normal man

Experiment number	Subject	Amount injected	Time after injection	Amount left in body	Concentration in serum	Volume of distribution of sucrose	
		grams	*hours*	*grams*	*mgm.*	*kgm.*	*per cent of body weight*
1	K	16.2	.5	11.6	112	10.4	16.3
			1.0	9.3	82	11.3	17.7
			1.5	7.6	73	10.4	16.3
2	K	21.1	1.0	12.3	117	10.5	16.4
			2.0	8.5	71	12.0	18.8
3	K	21.2	1.0	11.4	136	8.4	13.1
			1.5	8.9	86	10.4	16.3
			2.0	7.0	67	10.5	16.4
4	P	15.0	1.0	7.8	57	13.7	22.1
			2.0	5.1	41	12.4	20.1
5	L	20.7	1.0	12.2	85	14.3	17.0
			2.0	8.3	56	14.8	17.6
6	L	18.7	1.0	10.7	65	16.5	19.7
			2.0	7.5	43	17.4	20.7
7	L	17.4	1.0	11.0	67	16.4	19.5
			2.0	6.2	36	17.2	20.5
8	L	30.0	1.0	19.6	115	17.0	20.2
			2.0	14.3	76	18.8	22.5
			3.0	10.6	58	18.3	21.8
9	R	19.2	1.0	11.2	85	13.2	22.8
			2.0	8.1	53	15.3	26.4
10	R	19.9	1.0	12.9	108	11.9	20.5
			2.0	8.6	57	15.1	26.0
11	R	18.6	1.0	11.4	82	13.9	24.0
			2.0	7.9	53	14.9	25.7
12	S	18.0	1.0	10.5	62	16.9	29.2
			2	6.8	42	16.2	28.0

3 subjects were normal, young male physicians. Subject R was a rather undernourished elderly man with a moderate degree of arteriosclerosis who entered the hospital for treatment of Meniere's syndrome. Subject S was a young man recently recovered from an attack of catarrhal jaundice. The reproducibility of the results in the subjects in which more than one determination was made is so good that the variability for different subjects must be accepted as real. The series is too small to attempt to derive an average value for normal subjects.

The results of the experiments with SCN in normal subjects are recorded in Table II. All the subjects were young male physicians with

TABLE II

The volume of distribution of SCN in normal man

Experiment number	Subject	Amount given	Time after administration	Amount left in body	Concentration in serum	Volume of distribution of SCN	
		mgm.	*hours*	*mgm.*	*mgm.*	*kgm.*	*per cent of body weight*
1	L	1250	3.00	1244	6.4	19.4	23.1
			8.00	1219	6.4	19.1	22.8
			24.00	948	4.9	19.3	23.0
2	L	1240	10.00	1187	6.2	19.1	22.8
3	L	1250	5.00	1182	6.2	19.1	22.8
4	B	1250	10.00	1212	7.3	16.6	25.9
5	B	1750	10.00	1695	10.0	17.0	26.3
6	W	1250	10.00	1197	7.1	16.9	20.1
7	K	1250	2.00	1240	8.0	15.5	24.2
			3.00	1234	8.1	15.3	23.9
8	Pe	1500	10.00	1485	7.4	20.1	28.3
9	L	1800	1.00	1782	9.8	18.2	21.8
			2.00	1770	9.7	18.3	21.9
			3.00	1757	9.6	18.3	21.9
10	L	1238	.10	1237	8.9	13.9	16.6
			.60	1236	7.3	16.9	20.1
11	Sti	1254	1.50	1240	8.5	14.6	20.6
			2.75	1232	8.2	15.0	21.2

the exception of the last who was a young woman with fully compensated rheumatic heart disease, and the subject of Experiment 8 who had mild diabetes without evidence of any other abnormality. In the first 8 experiments KSCN was given by mouth, in most instances on the evening preceding the study. In the last 3 experiments NaSCN was injected intravenously. The distribution of SCN was apparently completed within 3 hours after the peroral administration of KSCN in Experiment 1, and within 1 hour after the intravenous administration of NaSCN in Experiment 9. In Experiment 10, the distribution was apparently incomplete in 35 minutes, judging from the relation of the value obtained at that time to other determinations on the same subject which agree remarkably well with one another, averaging 22.9 per cent of the body weight for the early experiments done with KSCN and 21.9 per cent for the experiment done 2 months later with NaSCN. In the third experiment the recorded concentration of KSCN in serum is actually the difference between the original level of 2.2 mgm. and the final one of 8.4 mgm. In all the other experiments, the serum was free from SCN at the start. The two determinations on Subject B, done at an interval of 6 months, give values of 25.9 and 26.3 per cent of the body

weight respectively. The body weight at the time of the second study exceeded the earlier one by 1 kgm. The calculated volumes for Subjects B and W, with body weights of 64 and 84 kgm. respectively, were almost identical. This is probably related to the fact that the former was quite sparsely covered with fat while the latter was moderately obese. The values for this small series, ranging from 20.1 to 28.3 per cent of the body weight, do not permit the deduction of any significant average.

TABLE III

The volume of distribution of SO_4 in normal man

Experiment number	Subject	Amount injected	Time after injection	Amount left in body	Concentration in serum	Volume of distribution of SO_4	
		m.eq.	*hours*	*m.eq.*	*m.eq.*	*kgm.*	*per cent of body weight*
1	L	47.3	.50	33	2.00	16.5	19.7
			2.25	18	0.96	18.7	22.3
2	L	41.8	.10	35	2.98	11.8	14.1
			.60	26	1.70	15.3	18.2
3	B	29.9	.25	23	1.98	11.6	17.8
			.75	17	1.22	13.9	21.4
			1.75	13	0.69	18.8	28.9
4	We	50.7	.50	40	4.28	9.3	17.2
			2.00	15	1.36	11.0	20.8

In the sulfate experiments, recorded in Table III, an endogenous excretion of 1 m.eq. per hour has been assumed (9). The recorded concentrations of sulfate in serum are actually the differences between the fasting levels and the levels at the times indicated. In Experiments 1, 3 and 4 where values are available 2 hours after the injections, the volumes of distribution are of the order of magnitude obtained with sucrose and SCN. To be more specific, Subject B shows a value of 28.9 per cent of the body weight as compared with 26.1 per cent with SCN; and Subject L, a value of 22.3 per cent as compared with averages of 22.4 per cent with SCN and 20.3 per cent with sucrose.

The results of some studies in which both sucrose and SCN were administered are given in Table IV. The results of Experiment 1 confirm the previous suggestion that while the distribution of sucrose is completed only during the second hour after injection in normal subjects, SCN is distributed more rapidly. The subject for Experiments 2 and 3 had advanced renal failure without edema. Between Experiments 2 and 3 salt intake was restricted for 3 days while water was given in large amounts. The body weight fell 0.6 kgm. and the base concentration in the serum fell more than 5 m.eq. Extracellular fluid was presumably sacrificed by transfer of water to the cells in order to lower their osmotic pressure to that of their environment as well as by absolute loss from the body indicated by the weight change. The values calculated from the distribution of sucrose and SCN parallel the expected fall in volume of the extracellular fluids. It was shown that when large amounts of Na_2SO_4 were injected intravenously into subjects who were given KSCN *per os* on the previous night, the concentrations of SCN and of Cl fell proportionately (8). Since excretion of these ions in the urine was negligible during the injections, this could only mean that Cl and SCN were distributed through approximately the same fraction of the body fluids. Since this fraction expands as the result of injection of a sodium salt, it is probably the extracellular fraction.

TABLE IV

Studies after the administration of both sucrose and SCN

Experiment number	Subject	Time after administration	Volume of distribution			
			Sucrose	SCN	Sucrose	SCN
		hours	*kgm.*	*kgm.*	*per cent of body weight*	*per cent of body weight*
1	L	1.00	17.0	18.1	20.2	21.6
		2.00	18.8	18.2	22.4	21.6
		3.00	18.3	18.4	21.8	21.9
2	D	1.00	17.5	20.7	35.3	41.8
		2.00	18.3	19.0	36.9	38.4
3	D	1.66	15.3	17.4	30.0	34.1

Preliminary studies on the distribution of the substances used between serum and blood cells and serum and transudates have been made. Previous work showing that neither inorganic sulfate nor sucrose added to blood *in vitro* permeates red blood cells has been confirmed. In one experiment when KSCN was added to oxalated whole blood *in vitro* in concentration of 20 mgm. per 100 cc. without precaution against loss of CO_2, the concentration in the plasma was found to be 23.8 mgm. per 100 cc. The concentration in cells, then, must have been somewhat lower than in plasma. No more exact knowledge concerning

the distribution of SCN between serum and cells is available at present. The ratio of sulfate in transudates to sulfate in serum has been found to be approximately unity (8). On two occasions serum and transudates obtained from patients after the injection of sucrose contained sucrose in approximately the same concentration. Exact agreement was not expected because the rapidity with which sucrose is excreted prevented the allowance of a sufficient interval between the injection and the study to insure the attainment of diffusion equilibrium. Studies made 12 to 64 hours after the administration of SCN to patients with transudates show an average concentration in serum ten per cent higher than that in transudates. With two exceptions, the concentration in serum exceeds that in fluid by between 7 and 14 per cent, with an average of 10 per cent. In the exceptions, the excesses were 5 and 21 per cent respectively. Two patients in the series who were deeply jaundiced gave ratios similar to those for the rest. That the difference between SCN concentration in serum and fluids can not be attributed to insufficient time for complete diffusion has been shown by the fact that the difference was the same in repeated determinations on the same individual made from 12 to 64 hours after giving the SCN, and also by the fact that in one instance the concentration of SCN in ascitic fluid and serum taken from this patient remained unchanged after equilibration for 48 hours across a cellophane membrane. That the observed differences are not due to analytical error has been shown by the quantitative recovery from SCN-free serum and transudates of added SCN in amounts equivalent to 10 mgm. per cent. Sucrose and SCN gain access to spinal fluid in traces only (3, 10). This is probably another evidence that spinal fluid is a highly specialized fluid not comparable to transudates and need not deduct from the value of these substances in measuring extracellular fluids.

Sucrose has been quantitatively recovered from the urine within 24 hours after intravenous injection in normal subjects on 3 occasions. Within 5 days of the administration of 1250 mgm. of KSCN *per os* to a normal subject, 1196 mgm. were recovered from the urine, the excretion on the fifth day being 56 mgm. This is in accord with the finding of Pollak (11) that SCN given to animals either *per os* or parenterally can be recovered quantitatively from the urine. In the six and one-half hours following the injection of 47.3 m.eq. of SO_4 into a normal subject 51.7 m.eq. of inorganic SO_4 appeared in the urine. Allowing 1 m.eq. per hour for endogenous production, this indicates satisfactory quantitative recovery.

DISCUSSION

Sucrose, SCN and inorganic SO_4 are apparently distributed through approximately 20 per cent of the weight of normal man. This portion, then, must differ from the remainder of the water of the body. That it probably represents extracellular fluids seems probable from the fact that it varies in size with procedures calculated to change the volume of the extracellular fluids. An entirely extracellular distribution for sucrose and inorganic SO_4 can be accepted with little reservation since these substances do not enter blood cells although they pass freely into transudates. The fact that the distribution of SCN in the body follows so closely that of these substances under varying conditions and in different subjects is presumptive evidence that SCN too remains entirely without the cells if the red corpuscles of the blood are excepted. Additional evidence to support this contention is presented in Table V in which analyses from Corper (12) of SCN in blood and tissues of dogs 24 to 72 hours after the injection of NaSCN are compared with analyses from Cameron and Walton (13) of Cl in blood and tissues of dogs. Chloride in the blood of dogs has been assumed at 300 mgm. per 100 cc. The concentrations of SCN, like those of Cl, vary with the vascularity of the organ, and the ratios of SCN

TABLE V

Comparison of tissue analyses and blood analyses for Cl (Cameron and Walton) and for SCN (Corper)

	Cl		SCN	
	Grams per kgm.	Tissue / blood	Grams per kgm.	Tissue / blood
Blood	3.00		0.64	
Lung	2.30	0.77	0.52	0.81
Kidney	2.51	0.84	0.34	0.53
Heart	1.19	0.40	0.39	0.61
Liver	1.36	0.45	0.27	0.42
Muscle	0.67	0.22	0.08	0.13

in tissues to SCN in blood are of the same order of magnitude as the corresponding ratios for Cl. If it is admittted that Cl need enter no cells other than blood cells, then the same may be said of SCN.

Of the three substances employed SCN is distributed through the body most rapidly, sucrose least rapidly. The excretion of SCN is many times slower than that of either SO_4 or sucrose. The rapidity of excretion of the latter two together with their relatively slow distribution make their use impractical in patients with excessive transudation, particularly into the serous cavities, unless renal function is much impaired. On the contrary SCN is excreted so slowly that sufficient time may be allowed between the administration of the substance and the study of its distribution to insure complete diffusion through the largest accumulations of fluids. The occurrence of any appreciable gradient between serum and extravascular fluids with such slow excretion is inconceivable. SCN has the further advantages that it may be given by mouth as a K salt thus avoiding the administration of Na to edematous patients, and presumably, since K is not retained in the serum, having no effect on total base or volume of extracellular fluids. The determination may be done with sufficient accuracy on small amounts of serum containing less than 1 m.eq. of SCN per liter, and if repeated determinations are necessary within 24 hours sufficient SCN remains in the body to obviate the administration of any more of the substance. Sucrose has the advantage that, being a non-electrolyte, it probably attains the same concentration in the water of serum and extravascular extracellular fluids. It has the disadvantages, however, that the analyses are time consuming and require concentrations in the serum of a magnitude which may change the volume of extracellular fluids appreciably. Furthermore, its rapid excretion in concentrated solution introduces possible error attendant upon the presence of considerable amounts of sucrose in the renal pelves and possibly in incompletely emptied urinary bladders which in the calculation would be attributed to the extracellular fluids. For SO_4, the same disadvantages obtain with the additional factors that the exact distribution of this ion between serum and transudates is still uncertain and that in order to obtain concentrations in the serum high enough for accurate measurement, considerable amounts of a Na salt must be given.

For practical purposes as a measure of the volume of extracellular fluids, then, SO_4 may be eliminated from consideration for the present. Sucrose is suitable for subjects with impaired renal function and, in the absence of abnormal transudates, for subjects with normal renal function. For general application, SCN affords the greatest number of advantages. In the light of our present knowledge the most accurate representation of extracellular fluid volume from the distribution of SCN would be as follows:

$$\frac{\text{Amount retained} - \text{Amount in blood}}{\text{Concentration in transudates}} + \text{Serum volume.}$$

Since SCN is present in red blood cells in approximately the same concentration as in serum, the amount of SCN in blood is roughly the product of blood volume and concentration in serum. This is of course only roughly true, as has been pointed out before. In the one experiment in which the relationship was studied, the concentration in cells was slightly lower than that in serum. If the actual concentration of SCN in transudates is not available, it may be estimated as 100/110 of the concentration in serum or determined directly by ultrafiltration of serum. For sucrose, since its concentration in the water of all extracellular fluids is probably uniform, the amount retained in the body divided by the concentration of sucrose in the water of serum should give the volume of extracellular fluids directly without consideration of blood or serum volumes.

TABLE VI

Calculations of volume of extracellular fluid for Experiment 1, Table IV

Hours after injection	Sucrose			SCN					Volume of distribution	
	Left in body	Concentration in water of serum	Volume of extracellular fluids	Left in body	Concentration		Amount in blood	Volume of extracellular fluids	Sucrose	SCN
					In serum	In transudates				
	grams	*grams per liter*	*liters*	*mgm.*	*mgm. per liter*	*mgm. per liter*	*mgm.*	*liters*	*liters*	*liters*
1	19.6	1.23	15.9	1782	98	88	784	16.3	17.0	18.1
2	14.3	0.82	17.4	1770	97	87	776	16.4	18.8	18.2
3	10.6	0.62	17.1	1757	96	86	768	16.5	18.3	18.4

These calculations for volume of extracellular fluids have been applied to Experiment 1 of Table IV, in which sucrose and sulfocyanate were injected simultaneously. The subject, one of the authors, weighing 84 kgm., was assumed to have 8 liters of blood with 5 liters of serum. The data for and the results of the calculations are presented in Table VI, and the " volumes of distribution " of these substances as previously calculated by dividing the amount retained by the concentration in the serum are given for comparison. Volume of extracellular fluid calculated from SCN and sucrose are in good agreement. While the differences between these values and the " volumes of distribution " are not striking, these differences will vary widely with the changes in the relation of blood volume to total extracellular fluid volume which occur in disease. Any accurate calculation of extracellular fluid volume from the distribution of SCN must ultimately take account of the differences in the concentration of the substance in blood and extravascular fluids. Sucrose has the advantage that this differentiation presumably does not exist.

The distribution of SCN between serum and transudates is contrary to that of other anions and is at direct variance with the Donnan theory if all the SCN is diffusible. It seems probable that some of the SCN in the serum is restrained in some manner, possibly in combination with proteins. The combination of anions with protein at body reaction has been demonstrated for CO_2 and hemoglobin (14). The diffusion of SCN from serum is being subjected to further study.

Crandall and Anderson (3) showed that SCN enters all the gastro-intestinal secretions, attaining concentrations of the same order of magnitude as it does in serum. Sucrose does not enter the gastro-intestinal tract. In the present studies, done in the postabsorptive state and in the absence of digestive disturbances, the amount of SCN in the gastro-intestinal tract must be very small. It may prove possible with sufficient refinement of the methods to determine the amount of fluid present in the gastro-intestinal tract in disease by simultaneous studies with SCN and sucrose.

In experiments on 4 subjects with advanced renal insufficiency without edema (one of which is recorded in Table IV) the calculated volume for extracellular fluid was extremely high, making up 30 to 43 per cent of the body weight. The consistently high values obtained in these subjects probably indicate an extreme degree of cellular wastage with replacement by interstitial fluid.

SUMMARY AND CONCLUSIONS

Sucrose, SCN and inorganic SO_4, are distributed through approximately the same fraction of the body fluids.

This fraction varies in magnitude with measures planned to vary the extracellular fluid volume and probably is composed of the extracellular fluids only.

It makes up approximately 20 per cent of the weight of normal subjects, although there is considerable individual variability. Extremely high values have been found in cases of terminal nephritis without edema, probably indicating marked cellular wastage.

SCN is distributed more rapidly than SO_4 or sucrose.

The speed of excretion of SO_4 and sucrose interferes with their practical application to the measurement of extracellular fluid volume. Sucrose has the advantage, however, that being a non-electrolyte, it is probably present in the same concentration in the water of serum and that of extravascular extracellular fluids.

SCN has numerous advantages. It enters red blood cells, however, and is present in serum partly in bound form. In order to use it as a practical method of measuring volume of extracellular fluids, the concentration of SCN in transudates or ultrafiltrate of serum must be known. It has been shown that the concentration in transudates is approximately 100/110 that in serum. Until more accurate information is available, a tentative method for the calculation of extracellular fluid volume from data obtained after the administration of SCN is:

$$\frac{\text{Amount retained in body} - (\text{concentration in serum} \times \text{blood volume})}{100/110 \times \text{concentration in serum}} + \text{Serum volume.}$$

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