ELECTROLYTE AND FLUID STUDIES DURING WATER DEPRIVATION AND STARVATION IN HUMAN SUBJECTS, AND THE EFFECT OF INGESTION OF FISH, OF CARBOHYDRATE, AND OF SALT SOLUTIONS [1,2]

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Human volunteers were deprived partially, or completely, of water and food for several days. Balances of water, of nitrogen, and of various electrolytes were measured, together with the concentrations of these same substances in serum. From these data, the partition of the total water loss between extracellular and intracellular phases was estimated.[3] The possible therapeutic values of water, various salt solutions, carbohydrate, and whole fish were assayed in certain experiments.

CHEMICAL METHODS

Samples of serum and defibrinated whole venous blood were collected anaerobically. Concentrations of sodium, potassium, and chloride in serum were determined by the methods of Hald (1, 2). Carbon dioxide content of serum or plasma was measured by the method of Van Slyke and Neill (3), heparinized plasma equilibrated with carbon dioxide at a partial pressure of 40 mm. Hg being used in Experiment I. Total and non-protein nitrogen of serum and of whole blood were measured by the Kjeldahl technic. Water content of serum and of cells was calculated from the respective concentrations of protein (4). Volume of cells in whole blood defibrinated over mercury (5) was measured by means of Daland microhematocrit tubes.

In urine, chloride was determined by the Volhard-Harvey titration (2), sodium by the method of Butler and Tuthill (6), potassium by the method of Hald (1), and total nitrogen by macro-Kjeldahl.

Several fillets of fish (haddock) were analyzed for nitrogen, water, chloride, sodium, and potassium. Average values were used in calculating metabolic balances. Per kgm. of whole fish, these were: nitrogen 28.4 grams; water, 818 grams; chloride, 26.1 m.eq.; sodium, 29.0 m.eq.; and potassium, 80.6 m.eq.

METHODS OF CALCULATION

The rationale of the methods for measurement of total water, and extracellular and intracellular phases has been fully discussed elsewhere (7). The same methods of calculation were used in these experiments with a few modifications. The initial extracellular volume, E_1, was taken to equal 20 per cent of the body weight, and changes in this volume were calculated from changes in the balance and concentration of chloride alone. Insensible weight loss, IL, was taken as the change in weight plus the weight of ingesta minus the weight of excreta and blood samples. As IL so measured in the sweating subjects included sweat, the usual relationship between insensible weight loss and total metabolism was altered. In the calculation of ΔW in these experiments, the average IL of the other 3 control nonsweating subjects was substituted for the observed IL. This procedure assumes that the average total caloric expenditure of the sweating subjects was the same as that of the control subjects, and is justified by their similarity in height, weight, and activity. The difference between the observed IL of the sweating subjects and the average of the controls was assumed to represent sweat which contained 30 m.eq. of chloride per liter (8); this was included in the chloride balance. The somewhat arbitrary character of this procedure makes the calculation of ΔW, ΔE, and ΔI_I in the sweating experiments less certain than in other experiments.

EXPERIMENTAL PROCEDURE

The volunteers were healthy males, active members of the Army of the United States. Each experimental period

[1] Lt. Col. D. B. Dill, Q.M.C., A.U.S., was responsible for the inception of this work. Capt. J. M. Quashnock, M.C., A.U.S., assisted in the management of the experiments and in the analysis of the data, as well as serving as a volunteer subject. Capt. Wilson, A.C., A.U.S., Lt. Holmes, Sn.C., A.U.S., Lt. Chovnick, A.C. A.U.S. Sgts. Tressler and Roberts, and Pvts. Perzanowski, Leyzorek and McHugh, all of the A.C., A.U.S., served as volunteer subjects. Mrs. T. Mintz did much of the work of chemical analysis, assisted by other members of the laboratory staffs at Wright Field and at Yale. Dr. A. J. Eisenman made all observations dealing with changes in blood cells. Miss Barbara Russell of the Yale University School of Nursing and Dr. S. C. Harvey of the Department of Surgery provided facilities for the care of the subjects. The work was carried out in connection with an Army Air Corps Contract.

[2] This article has been cleared for publication by the War Department Bureau of Public Relations. The opinions expressed are those of the authors and do not necessarily reflect official views of the War Department.

[3] Changes in the concentrations of lipids in serum and of ketones in whole blood were also followed. These will be reported in another paper (9).

TABLE I

Plan of experiments

Experiment	Period days	Food		Water			Other fluids
		None	Carbohydrate	None	Limited	Unlimited	
I, L	0 to 5	+			+		
F	0 to 5	+			+		
Q	0 to 4	+			+		
	4 to 5	+				+	
D	0 to 4	+			+		
	4 to 5	+					Dil. seawater[3]
P	0 to 5		+		+		
R	0 to 5		+		+		
W	0 to 5		+		+		
H	0 to 4		+		+		
	4 to 5		+				Dil. seawater[4]
IIA, Q[1]	0 to 3	+		+			
	3 to 4		+			+	
C[1]	0 to 3	+		+			
	3 to 4		+			+	
H	0 to 3	+		+			
	3 to 4		+			+	
T	0 to 3	+		+			
	3 to 4		+			+	

Experiment	Period days	Food			Water			Other fluids
		None	Carbohydrate	Fish	None	Limited	Unlimited	
IIA, R	0 to 3	+			+			
	3 to 4		+				+	
IIB, Q[1]	0 to 3		+	+				A. F. J.[2]
C[1]	0 to 3			+				A. F. J.[2]
H	0 to 3			+				A. F. J.[2]
T	0 to 3	+						A. F. J.[2]
R	0 to 3	+						0.6 per cent NaCl
III, H	0 to 2	+				+		
	2 to 6			+	+			
	6 to 7		+				+	
C	0 to 2	+				+		
	2 to 6	+			+			
	6 to 7		+				+	
T	0 to 2	+				+		
	2 to 4	+			+			
	4 to 5	+					+	
M	0 to 2	+				+		
	2 to 4			+	(+)			
	4 to 5	+					+	

[1] Exposure in hot room.
[2] Limited amounts of "artificial fish juice."
[3] Solution containing 1 part of seawater to 3.5 parts of fresh water.
[4] Solution containing 1 part of seawater to 5 parts of fresh water.

TABLE IIa

Balance of water, electrolytes, and nitrogen

Experiment I

Expt.	Period	Intake	Output[1]					Expt.	Period	Intake		Output				
		Oral	Urine							Oral		Urine				
		H_2O	Vol.	Na	Cl	K	N			H_2O	Carbohydrate	Vol.	Na	Cl	K	N
	days	*cc.*	*cc.*	*m.eq.*	*m.eq.*	*m.eq.*	*grams*		*days*	*cc.*	*grams*	*cc.*	*m.eq.*	*m.eq.*	*m.eq.*	*grams*
I, L	0 to 1	170	865	130	177	74	8.9	I, P	0 to 1	330	100	330	55	53	26	6.1
	1 to 2	375	428	60	59	30	9.0		1 to 2	500	100	180	16	12	7	4.2
	2 to 3	500	483	47	31	40	12.9		2 to 3	500	100	275	17	16	15	6.2
	3 to 4	500	468	18	16	32	12.9		3 to 4	500	100	155	2	0	7	3.7
	4 to 5	500	433	6	2	32	12.2		4 to 5	500	100	35	1	0	2	0.7
I, F	0 to 1	375	450	41	71	69	8.3	I, R	0 to 1	140	100	415	79	71	32	7.3
	1 to 2	500	480	39	32	31	10.9		1 to 2	320	100	258	31	43	12	5.3
	2 to 3	500	690	42	21	35	15.9		2 to 3	500	100	165	6	0	12	3.7
	3 to 4	500	680	20	15	35	12.0		3 to 4	500	100	151	3	4	8	3.3
	4 to 5	1000	795	26	11	60	13.4		4 to 5	500	100	238	4	4	21	5.6
I, Q	0 to 1	0	605	114	86	53	8.6	I, W	0 to 1	425	100	570	92	105	38	10.1
	1 to 2	0	403	62	69	28	7.2		1 to 2	500	100	415	51	54	23	8.4
	2 to 3	180	298	29	26	26	6.5		2 to 3	500	100	307	19	24	21	6.5
	3 to 4	225	361	54	46	27	7.3		3 to 4	500	100	312	19	20	20	7.2
	4 to 5	2080	630	38	22	34	9.9		4 to 5	500	100	295	12	12	28	7.4
I, D	0 to 1	150	720	111	157	76	6.5	I, H	0 to 1	290	100	720	206	213	59	11.7
	1 to 2	300	585	86	78	38	8.6		1 to 2	180	100	585	89	83	26	7.6
	2 to 3	325	535	42	26	42	10.9		2 to 3	500	100	535	50	52	25	10.1
	3 to 4	425	735	68	20	49	13.7		3 to 4	500	100	735	58	53	30	14.7
	4 to 5	2800[2]	945	111	69	71	13.9		4 to 5	2620[3]	100	945	63	74	100	18.4

[1] Blood taken for analyses and weights of stools, if any, were not recorded, and hence are not included in calculations.
[2] Diluted seawater containing 257 m.eq. of Na, 295 m.eq. of Cl, and 5 m.eq. of K.
[3] Diluted seawater containing 176 m.eq. of Na, 202 m.eq. of Cl, and no K.

TABLE IIb

Balances of water, electrolytes, and nitrogen

Experiments IIA, IIB, and III

Expt.	Period	Intake							Output[12]					
		Oral							Urine					Blood
		H_2O	Carbohydrate	Whole fish and/or substitute					Vol.	Na	Cl	K	N	Vol.
				Wt.	H_2O	Na	Cl	K	N						
	days	*cc.*	*grams*	*grams*	*cc.*	*m. eq.*	*m. eq.*	*m. eq.*	*grams*	*cc.*	*m. eq.*	*m. eq.*	*m. eq.*	*grams*	*cc.*
IIA, Q	0 to 3	45[1]								1430	261	255	157	27.3	75
	3 to 4	2265[2]	117							530	2	13	39	9.6	90
IIB, Q	0 to 3	120[3]	320	720	990[4]	41	34	78	21.8	1480	240	129	80	26.8	85
IIA, C	0 to 3	50[1]								1375	200	206	146	30.1	94
	3 to 4	2070[2]	82							530	8	20	41	12.4	87
IIB, C	0 to 3	118[5]	25	565	862[4]	36	30	66	17.4	1770	279	295	238	31.5	85
IIA, H	0 to 3	0								1715	305	243	157	31.0	78
	3 to 4	1920[6]	170							460	3	20	27	10.6	109
IIB, H	0 to 3	130[3]	25	808	1062[4]	43	36	85	24.4	3000	536	475	141	37.7	85
IIA, T	0 to 3	0								1378	165	176	118	25.0	65
	3 to 4	1580[6]	119							460	2	7	34	10.8	97
IIB, T	0 to 3	93[7]	19		1015[8]	51	38	51	3.3	2370	334	341	149	28.3	85
IIA, R	0 to 3	0								1645	284	269	97	24.7	65
	3 to 4	985	170							540	11	21	20	7.0	109
IIB, R	0 to 3	45[9]	23		1500[10]	154	154			2540	392	396	112	24.4	85
III, H	0 to 2	800								1020	176	169	84	16.5	80
	2 to 4	0		1584	1288	46	41	129	45.0	2115	135	109	158	46.6	95
	4 to 6	160[11]		1900	1555	56	50	153	54.0	2295	43	53	198	56.7	205
	6 to 7	4300[6]	25							650	2	8	33	16.0	125
III, C	0 to 2	800								965	62	60	64	18.0	80
	2 to 4	0								1030	79	64	84	27.5	100
	4 to 6	30								995	29	47	95	24.4	185
	6 to 7	3270[6]								450	3	9	32	11.4	125
III, T	0 to 2	800								910	68	93	96	15.2	80
	2 to 4	0								545	24	26	61	13.4	80
	4 to 5	2395								530	9	4	42	14.7	95
III, M	0 to 2	800								1810	234	263	164	20.4	80
	2 to 4	?		805	658	23	21	65	22.8	1645	128	73	118	37.7	90
	4 to 5	2400								660	13	26	46	17.4	85

[1] Injected intravenously containing 1 per cent NaSCN.
[2] Includes 50 cc. of 1 per cent NaSCN solution injected intravenously.
[3] Includes 80 cc. of lemon juice containing 2.7 m.eq. of K, and the rest as 50 per cent glucose injected intravenously.
[4] Includes 400 cc. of "artificial fish juice" containing 20 m.eq. of Na, 15 m.eq. of Cl, 20 m.eq. of K, and 1.4 grams of N.
[5] Includes 68 cc. of lemon juice containing 2.7 m.eq. of K, and 50 cc. of 50 per cent glucose injected intravenously.
[6] Includes 50 cc. of 50 per cent glucose injected intravenously.
[7] Includes 55 cc. of lemon juice containing 1.9 m.eq. of K, and 38 cc. of 50 per cent glucose injected intravenously.
[8] Consists entirely of "artificial fish juice."
[9] 50 per cent glucose injected intravenously.
[10] Consists entirely of 0.6 per cent NaCl solution.
[11] Includes 60 cc. lemon juice.
[12] Subjects passed no stools, with exception of H, who passed 128 grams during the first period of experiment IIA, 90 grams during experiment IIB, and 6 grams during the first period of experiment III.

was started at 7 a.m., at which time the subject voided and was weighed, stripped of clothing. A sample of venous blood was then taken. All urine was collected with thymol and sulfuric acid to prevent the loss of ammonia. Small stools were passed by several subjects on the first day; these were weighed and discarded. The scales on which the subjects were weighed in Experiments II and III were accurate to 10 grams. Those used in Experiment I were less accurate and the 2 or 3 individual weights which were obviously grossly in error are so indicated in the tables.

The first group of experiments (Experiment I) was performed at Wright Field in March, 1943, the specimens of blood and urine being shipped to New Haven for all analyses except those for carbon dioxide. The subjects were allowed the activity of their usual military duties. Experiments II and III were carried out at New Haven in June and September, 1943, respectively. Activity was permitted as desired and decreased in most of the subjects after the first 2 days. Subject C was more active than his associates in both experiments. In Experiment II, sweating was induced in 2 of the subjects by controlled heat in a special constant temperature room for several hours at a time.

In Experiments I and IIB, carbohydrate was administered in the form of sugar. In Experiment IIB, the subjects ate raw fillet of haddock on the first and third days; on the second day, the raw fish was so repellant and nauseating that they were unable to take any. In Experiment III, during the first 4 days, cooked fish was substituted in order to insure the ingestion of a considerable amount. The closed dish containing the fish was weighed before and after steaming for 15 minutes. Occasional slight weight losses were corrected by the addition of water. One subject (M) developed abdominal distress and was unable to continue. The other subject (H) taking the same fish experienced no such reaction, although the cooked fish became increasingly distasteful. On the fourth day, raw fish was substituted and eaten with no greater relish.

TABLE III

Body weights, and analytical data for serum and blood

Expt.	Time from start	Body weight	Serum					Blood		Red cell
			Na	Cl	HCO_3	K	Total protein	NPN	Hematocrit	Protein
	days	*kgm.*	*m. eq. per liter*	*m. eq. per liter*	*m. eq. per liter*	*m. eq. per liter*	*grams per cent*	*mgm. per cent*	*per cent cells*	*grams per cent cells*
I, L	0	85.0	138.1	101.1	20.1	4.04	6.79	29		
	2	81.4	138.0	99.1	18.9	3.45	7.32	42		
	5	78.2	130.5	98.3	18.5	4.17	7.53	42		
I, F	0	71.3	139.0	102.0	17.2	4.45	6.56	36		
	2	68.8	139.6	100.1	18.8	4.43	6.90	43		
	5	66.0	140.5	100.3	18.3	4.36	7.34	43		
I, Q	0	(73.6)†	134.0	97.5	20.1	4.64	7.01	32		
	2	(71.6)†	144.2	100.1	19.4	4.14	7.40	33		
	5	(71.5)†	130.2	100.3	19.3	4.21	7.61	31		
I, D	0	78.5	140.4	97.6	22.5	4.86	7.10	27		
	2	75.5	138.0	98.5	18.0	4.53	7.49	43		
	5	73.7	136.0	103.6	14.5	5.30	7.30	43*		
I, P	0	77.0	138.6	94.8	20.1	3.82	6.79	33		
	2	(76.1)†	142.8	99.7	19.5	3.52	7.48	40		
	5	72.7	136.2	97.3	19.8	4.36	7.41	44		
I, R	0	64.1	138.3	104.1	20.9	4.06	6.38	35		
	2	61.5	141.7	100.1	19.5	4.39	7.03	39		
	5	59.5	137.6	101.6	20.1	3.94	7.46	37		
I, W	0	70.0	138.0	96.9	19.5	3.66	6.63	32		
	2	67.3	134.7	99.2	18.5	4.65	7.28	34		
	5		138 1	98.3	20.5	4.37	7.10	36		
I, H	0	78.0	139.5	101.6	19.8	4.39	6.97	26		
	2	74.1	136.6	101.6	20.0	5.04	7.37	30		
	5	73.7	139.2	107.3	19.8	4.74	6.70	25		
IIA, Q	0	73.75	140.4	100.4	27.9	3.71	7.33	33	49.0	33.2
	3	68.25	143.3	99.8	24.1	5.36	8.09	34*	55.1	32.8
	4	69.10	137.4	95.2		3.62	8.17	33	52.1	31.3
IIB, Q	0	71.55	140.5	93.2	29.7	3.22	6.48	27	44.0	34.6
	3	67.83	145.9	103.3	31.4	3.56	7.98	40	47.1	34.7
IIA, C	0	72.16	142.0	100.4	26.8	3.16	6.38	40	56.2	33.3
	3	66.86	144.3	100.1	27.5	4.20	7.35	34	53.2	31.4
	4	67.65	142.7	95.7		3.50	7.38	28	51.5	31.8
IIB, C	0	71.47	141.8	103.5	26.7	3.87	6.52	31	45.4	35.1
	3	65.32	145.3	104.3	25.6	4.25	7.51	52	48.1	34.8
IIA, H	0	75.55	141.7	103.7	25.8	3.98	6.99	32	42.0	27.9
	3	71.00	144.8	101.4	23.4	5.14	7.74	40	50.0	27.3
	4	71.20	135.0	99.5		2.97	7.41	30	47.4	27.6
IIB, H	0	75.32	141.1	104.1	25.7	4.89	6.39	28	38.9	30.1
	3	69.51	141.5	100.5	24.8	4.65	7.84	41	47.5	30.0
IIA, T	0	76.98	143.6	98.2	29.1	3.67	7.32	28	51.5	34.0
	3	72.18	143.4	96.5	29.8	4.70	7.88	35	59.4	29.2
	4	72.29	137.7	94.9		3.90	7.63	33	52.3	33.5
IIB, T	0	76.08	137.7	101.2	27.8	3.86	6.68	27	47.4	33.6
	3	70.83	137.6	95.5	28.6	4.05	7.68	39	51.3	34.3
IIA, R	0	63.43	141.7	100.5	29.3	3.82	6.28	29	44.9	33.0
	3	59.59	139.1	97.1	25.2	3.95	6.93	38*	53.2	30.9
	4	59.31	138.0	96.8		3.90	7.05	28	52.2	31.3
IIB, R	0	62.94	140.8	104.1	27.4	4.15	6.22	26	42.5	33.6
	3	59.21	139.5	99.6	21.7	4.47	6.85	37*	45.3	34.4
III, H	0	75.26	144.1	101.5	26.2	4.91	7.12	28	39.0	26.0
	2	72.88	140.7	101.6	22.3	4.28	7.31	36*	41.1	28.6
	4	70.06	141.6	102.3	25.9	4.18	7.89	43	41.1	28.6
	6	68.14	151.1	104.7	28.1	4.10	8.42	53	41.9	27.7
	7	70.83	138.1	95.6	25.7	4.43	7.46	38	38.7	26.4
III, C	0	70.96	141.3	102.0	27.2	4.37	7.07	30	49.6	33.6
	2	68.86	141.6	98.0	25.9	4.36	7.31	41	55.2	32.6
	4	66.15	144.7	97.5	24.4	4.23	7.79	42*	53.8*	33.0
	6	63.53	147.4	101.6	25.5	4.55	7.70	45*	54.4*	31.4
	7	65.41	141.0	93.0	27.3	3.89	7.26	39*	51.2*	32.9
III, T	0	75.98	139.0	92.8	30.4	4.03	7.23	27	55.7	32.3
	2	73.29	142.6	95.6	30.2	4.34	7.49	32	57.1	32.3
	4	70.76	143.2	95.7	29.2	3.76	7.98	41	57.3	32.8
	5	71.73	137.7	91.2	26.8	4.40	7.76	39	56.7	32.1
III, M	0	75.36	141.0	103.6	26.6	4.22	7.11	30	51.4	32.7
	2	71.84	136.6	98.9	25.0	3.72	7.20	37	53.6	33.3
	4	70.91	140.8	95.9	25.5	4.03	7.51	37	56.4	33.2
	5	70.97	137.7	94.5	21.9	3.45	6.60	32*	52.0	33.1

* Blood ketone bodies greater than 15 mgm. per cent.

† The accuracy of these values is questionable.

TABLE IV

Insensible weight loss (IL) and changes in total body water (ΔW), in extracellular fluid (ΔE) and in intracellular fluid (ΔI_I and ΔI_{II})

Expt.	Period	IL	ΔW	ΔE	ΔI_I	ΔI_{II}	Expt.	Period	IL	ΔW	ΔE	ΔI_I	ΔI_{II}
	days	*kgm.*	*liters*	*liters*	*liters*	*liters*		*days*	*kgm.*	*liters*	*liters*	*liters*	*liters*
I, L	0 to 2	2.82	−2.85	−1.84	−1.01	−0.62	IIA, H	0 to 3	2.58	−3.73	−1.95	−1.78	−1.96
	2 to 5	3.27	−2.32	−0.33	−1.99	+1.30		3 to 4	1.46	+0.53	+0.07	+0.46	+2.18
I, F	0 to 2	2.42	−1.86	−0.70	−1.16	−0.88	IIB, H	0 to 3	3.88	−4.66	−3.47	−1.19	−0.69
	2 to 5	2.57	−2.11	−0.52	−1.59	−1.30							
I, Q	0 to 2	(0.96)*	−1.74	−1.82	+0.08	−2.78	IIA, T	0 to 3	3.32	−3.91	−1.45	−2.46	−0.87
	2 to 5	(1.26)*	+0.24	−0.88	+1.12	+2.41		3 to 4	1.09	+0.33	+0.15	+0.18	−1.17
							IIB, T	0 to 3	3.83	−4.21	−2.03	−2.18	−0.93
I, D	0 to 2	2.11	−2.44	−2.29	−0.15	−0.13							
	2 to 5	3.07	−0.98	+0.91	−1.89	−0.72	IIA, R	0 to 3	2.08	−3.28	−2.12	−1.16	−0.25
								3 to 4	0.49	−0.21	−0.17	−0.04	+0.25
I, P	0 to 2	(1.41)*	−0.64	−1.43	+0.79	−1.27							
	2 to 5	(4.72)*	−2.32	+0.23	−2.55	+1.30	IIB, R	0 to 3	2.57	−3.02	−1.71	−1.31	−0.93
I, R	0 to 2	2.57	−2.03	−0.57	−1.46	−1.07	III, H	0 to 2	2.04	−1.80	−1.55	−0.25	−0.03
	2 to 5	3.23	−1.31	−0.31	−1.00	+0.31		2 to 4	2.12	−2.50	−0.80	−1.70	−0.17
								4 to 6	1.38	−1.80	−0.48	−1.32	−2.40
I, W	0 to 2	2.91	−2.04	−1.80	−0.24	+0.17		6 to 7	0.81	+2.96	+1.14	+1.82	+2.83
	2 to 5			−0.46									
							III, C	0 to 2	1.82	−1.57	−0.05	−1.52	−0.45
I, H	0 to 2	3.23	−3.15	−2.64	−0.51	−0.10		2 to 4	1.54	−2.24	−0.62	−1.62	−1.35
	2 to 5	2.04	−0.02	−0.46	+0.44	−1.15		4 to 6	1.44	−2.13	−1.00	−1.13	−1.20
								6 to 7	0.79	+2.17	+1.07	+1.10	+1.12
IIA, Q	0 to 3	3.98	−4.78	−2.58	−2.20	−1.96							
	3 to 4	1.66	+1.23	+0.40	+0.83	+1.09	III, T	0 to 2	2.47	−1.99	−1.36	−0.63	−1.52
								2 to 4	1.88	−1.98	−0.33	−1.65	−0.57
IIB, Q	0 to 3	3.65	−2.65	−2.44	−0.21	−1.68		4 to 5	0.78	+1.23	+0.60	+0.63	+0.90
IIA, C	0 to 3	3.84	−4.58	−2.44	−2.14	−1.57	III, M	0 to 2	2.37	−2.85	−1.72	−1.13	+0.12
	3 to 4	1.44	+1.13	+0.30	+0.83	−0.04							
IIB, C	0 to 3	5.33	−5.21	−2.99	−2.22	−2.08							

* The accuracy of these values is questionable.

The experimental conditions imposed are summarized in Table I. Roman numerals refer to experiments, Experiment II being divided into 2 parts, A and B. The other letters refer to individual subjects.

RESULTS

Balance data are presented in Table II, the concentrations of various substances in serum and in blood in Table III. Table IV consists of the calculated total, extracellular, and intracellular water balances.

(*A*) *Changes in concentrations in serum and in whole blood*

Sodium of serum changed but little in the majority of the experiments. It increased 4 or more milliequivalents at some time during 7 out of 22 dehydration experiments, including the 2 in which the subjects perspired and the 2 in which water was withheld for 6 days. It decreased to a comparable extent in 2 others.

Chloride of serum increased 4 milliequivalents or more with dehydration in 4 instances and decreased to the same extent in 4 others.

Bicarbonate of serum was also usually little affected. In 3 cases, a slight reduction took place (I-D, IIA-R, IIB-R), associated with a marked rise of blood ketones. In Experiment III-C, on the other hand, bicarbonate was unaffected in spite of a comparable degree of ketonemia.

Potassium concentration in serum was usually virtually unchanged. It increased 1 milliequivalent or more only in Experiments I–W and in 4 of the 5 subjects of Experiment IIA.

Protein concentration in serum and *relative cell volume* in blood rose in all but 1 of the experiments in which dehydration occurred. This increase was not regularly progressive after the first 2 or 3 days, in spite of further dehydration.

Non-protein nitrogen concentration in blood

increased after 2 to 3 days of water restriction, with 1 exception. With further dehydration, the change was irregular. Ingestion of fish accentuated the rise.

(*B*) *Excretion of electrolytes and of nitrogen in urine*

Sodium and *chloride* continued to be excreted in considerable amounts during the first day or two after food and water were withdrawn. With each successive day thereafter, the excretion tended to diminish. Excretion of sodium tended to parallel that of chloride, but was not identical with it. No relationship was evident between urine volume and the excretion of these 2 electrolytes.

Potassium excretion remained at a high level throughout the experiments, although occasionally there was a slight decrease in the daily excretion of potassium after the initial period. On the whole, the ratio of potassium to nitrogen in the urine tended to exceed that found in skeletal muscle (10).

Nitrogen excretion continued at a high level throughout all experiments, and was correlated with urine volume (Figure 1). Three of the 4 subjects receiving carbohydrate in Experiment I had lower rates of protein metabolism than did the starving subjects, smaller amounts of nitrogen in the urine, and lower daily urine volumes.

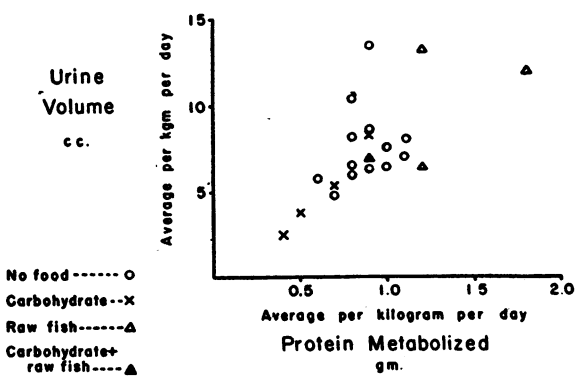

FIG. 1. URINE VOLUMES AND NITROGEN EXCRETION IN SUBJECTS PARTIALLY OR COMPLETELY DEPRIVED OF WATER.

Average daily volume of urine is correlated with the average daily amount of protein metabolized as measured by the nitrogen excreted in the urine. Subjects receiving carbohydrate tended to conserve body protein and so to have low urine volumes.

The concentrations of nitrogen in the urine were, however, about the same as those in the starving subjects.

(*C*) *Metabolism of foodstuffs*

Rate of *protein* metabolism varied from subject to subject. Those taking carbohydrate usually, but not always, had a lower rate of protein destruction than did those receiving no food. Subject H (Experiment III–H) had an abnormally high rate of protein metabolism while receiving large amounts of fish, and was unique in that he was for a time almost in nitrogen equilibrium. Nitrogen balance was negative in all others.

Carbohydrate metabolism in starving subjects must have been reduced early to a low level, since ketosis usually developed within 2 days.

Fat metabolism continued at a high level, since most of the total caloric expenditure must have come from this source.

(*D*) *Water metabolism*

(*1*) *Total water exchanges*

A considerable deficit of water developed in all experiments. Limited ingestion of water during starvation ameliorated but did not abolish this loss. The ingestion of salt in hypotonic solution during the initial period of starvation in 1 subject (Experiments IIA-R and IIB-R) did not mitigate the water loss. Later ingestion of hypotonic saline when dehydration was more advanced did result in some retention of water (Experiments I-H and I-D). Carbohydrate ingestion decreased the rate of water loss in 3 of the 4 experiments in which adequate data are available (I-P, I-R, and IIA-Q), mainly because there was a lower daily loss of water in the urine (Figure 1). The subject eating large quantities of fish (III-H) lost water just as rapidly as did the control (III-C) who took nothing (Figure 2).

Water was lost through urine, skin, and lungs, fecal loss being negligible. It decreased slightly in Experiment III-C after 6 days of complete starvation. Unusually large losses through the skin developed only after deliberate induction of sensible sweating in subjects Q and C of Experiments IIA and IIB. Because of the stability of the daily IL in non-sweating subjects, total rate of water loss from the body was modi-

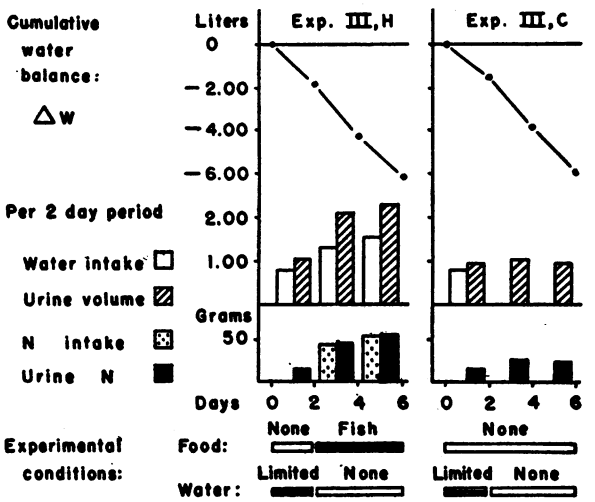

FIG. 2. INGESTION OF FISH BY A SUBJECT DEPRIVED OF WATER: FAILURE TO MITIGATE DEHYDRATION

Subject III-H ate fish while III-C served as a control. Water derived from the fish was not retained by subject III-H, so that both subjects lost water at approximately the same rate. Failure of water retention was apparently due to the greatly increased production of non-protein nitrogen, with consequent increase in the volume of urine used in its excretion.

fied only by some change in the relation of urinary volume to fluid intake, such as that following the ingestion of carbohydrate (Figure 1). If the ingestion of fluid was followed by an equal increase in the volume of the urine, as occurred after the ingestion of whole fish, no reduction in the rate of water loss resulted.

(2) *Partition between extracellular and intracellular phases*

Fluid was lost from both extracellular and intracellular phases. During the first 48 hours, extracellular loss usually predominated. This coincided with the period during which most sodium and chloride were lost in the urine. Later, the loss in terms of absolute amounts of fluid became predominantly intracellular, although in proportion to their respective initial magnitudes the losses from the 2 phases were about equal.

(3) *Rehydration experiments*

Experiments with rehydration in which water was offered *ad libitum* (final periods in all experiments of IIA and of III) indicate that the subjects retained only part of the water, even when considerable deficits of water were present. Almost always enough was retained to dilute the sodium of serum slightly below its initial concentration so that the body water became hypotonic. This was, of course, a consequence of the preceding salt loss. The 2 subjects who had perspired complained of abdominal cramps during rehydration. The water retained entered both phases.

(4) *Water of erythrocytes*

Using cell protein as an inverse measure of cell water (4), there is little correlation between water of erythrocytes (Table II) and change in total intracellular water (Table IV).

(E) *Reactions of subjects*

Thirst appeared early and regularly. After extended water deprivation, the thirst was quenched by the ingestion of an amount of water much less than that which had been lost. Lassitude was pronounced, and the subjects were often irritable and foolishly argumentative. These reactions were also present in the heavy fish eater (III-H), although starvation was much less and ketosis slight. The reaction to the ingestion of raw fish varied from distaste to nausea; no vomiting or diarrhea occurred.

DISCUSSION

Dehydration associated with starvation. Complete withdrawal of food and water results in dehydration through 2 mechanisms. In addition to the obvious negative water balance, there is a further loss of water associated with the starvation. Thus, in Benedict's experiment in which Levanzin lost in 3 days twice as much water as he ingested (13), and in some of our studies with dogs (12), fasting without water deprivation was accompanied by an increase in the negative water balance. This loss occurred through the maintenance of a large urine volume. It could not be cancelled by the ingestion of hypotonic saline (Experiment IIA-R). Sufficient electrolyte was excreted in the urine to prevent a rise, or to produce a decrease in the concentration of serum base. The concentrations of base and nitrogen in the urine were relatively low rather than maximal.

The mechanism of this initial diuresis is not clear. It does not appear to be the result of an increased production and excretion of ketone bodies. The diuresis appears quite early while ketosis is minimal. It then diminishes as ketosis increases. It is not the chief limiting factor in survival, since studies indicate that fasting animals allowed water *ad libitum* do not die of dehydration (14).

Effect of saline solutions in dehydration. Though it is known that concentrated salt solutions may provoke vomiting and diarrhea, the advisability of extending fresh water with sea water must be considered. Ladell (15) has shown that a small amount of the salt and water in a 62 per cent solution of sea water was retained during the first day by the dehydrated subject. Thereafter no further retention of salt was observed, and the negative water balance recurred. When the ingestion of the solution was discontinued, the salt and water retained initially were excreted. In our experiments with diluted sea water (I-H and I-D), a similar retention of water and salt occurred. Detailed analysis, however, of the combined dehydration and rehydration periods is not possible. Ladell believes that the reexpansion which occurs in the extracellular fluid volume is beneficial. Such solutions also permit, he states, the formation of the basal volume of urine with a decreased loss of body water. There is no proof, however, that any benefit accrues beyond that which could be obtained from the fresh water diluent alone. Moreover, the intake of diluted sea water is psychologically undesirable, since it would lead to the drinking of more concentrated solutions as the fresh water supply dwindled.

Effect of carbohydrate in dehydration. The anti-dehydrating effect of carbohydrate early in deprivation is in part the result of the water produced through its oxidation and in part the result of the protein-sparing effect. In Figure 1, the positive correlation between urine nitrogen and urine volume suggests that the amount of nitrogenous end-products is the chief limiting factor in the conservation of water through a decrease in the urine volume. Carbohydrate reduces the amount of nitrogen excreted.

The concentrations of blood ketones (9) indicate that carbohydrate ingestion is associated with an economy of body water before ketonemia becomes pronounced. Quantitative observations of urine ketones were not made. The decreased loss of water did not occur in the absence of the nitrogen-sparing effect, even though ketosis was inhibited (Experiment I-H). It is possible that with progressive ketosis, the excretion of ketone bodies assumes a greater rôle in the production of dehydration. During the early days of total deprivation, however, the nitrogenous end-products determine the volume of urine excreted.

Effect of ingested fish. Should fish be eaten by castaways with limited or non-existent water supplies? In Experiments IIIC and IIIH, subject H who ingested large amounts of fish without added water became dehydrated at exactly the same rate as the control (Figure 2). In these studies, only one species of fish was used and universal application of the results may not be valid. No difference could be detected between the effects of raw and cooked fish.

It would appear that fish eating did not ameliorate dehydration in man, since none of the water of the fish was retained, and the loss of the subject's own water was not curtailed. This can be attributed to the large volume of urine necessary for the excretion of the nitrogen of the fish protein. The sodium and chloride concentrations in the urine were very low and of no significance in increasing the urine volume. In the above experiments, the great similarity of the 2 curves of water loss may be fortuitous. The rate of dehydration might well vary with the species and composition of the fish. Furthermore, the ability of these 2 subjects to concentrate nitrogen in the urine might not be representative. These variables would increase or decrease the rate of water loss.

Since whole fish contained just enough water for the excretion of the metabolized nitrogen, the ingestion of fish by humans is definitely contraindicated under conditions of water deprivation. Dogs given dry protein became dehydrated much more rapidly than controls deprived of all intake (12). In contrast to humans, raw fish fillets without extra water maintained dogs in a vigorous state for at least 4 weeks (12). This difference between the human and dog subjects can be explained by the dog's greater ability to concentrate nitrogen, with conservation of some

of the water of the ingested fish. Unless the human subject can equal this ability to concentrate nitrogen, protein taken with insufficient water will be deleterious. Moreover, if the extrarenal water loss of the subject eating fish were increased by sweating, the same amount of water would still have to be sacrificed in the urine to excrete the nitrogen. Economy of water through the reduction of urine volume below that of the non-sweating subject is precluded. It seems likely, therefore, that men eating fish without additional water in tropical regions might on this account become more dehydrated than would those fasting without water.

With adequate water supplies to compensate for the dehydrating effect of protein, 2 clear advantages accrue to the fish eater. Ketosis is suppressed, and wastage of body protein is minimized.

SUMMARY AND CONCLUSIONS

1. Balances of water, nitrogen, and electrolytes have been studied during water deprivation, starvation, and the ingestion of various solutions and foodstuffs.

2. Fasting increased the negative water balance during water deprivation.

3. The loss of fluids and electrolytes occurred at first predominantly from the extracellular phase, and subsequently from the intracellular.

4. No clear advantage of hypotonic saline over fresh water could be demonstrated in the amelioration of dehydration.

5. Carbohydrate decreased the negative nitrogen balance, the ketone formation, the urine volume, and the dehydration of completely deprived subjects. Its water of oxidation was also made available to the body.

6. All of the water of ingested fish was used to excrete the protein metabolites and therefore failed to minimize dehydration.

7. Under conditions of limited water supply, ingestion of protein foods is definitely contraindicated. Carbohydrate is the foodstuff of choice.

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