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Research Article

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Finally, in the 12 hydrated subjects supine recumbency reduced C_{H_2O} and V from a mean of 11.6 and 14.5 to 6.2 and 8.2 ml/100 ml of GFR. In eight of these experiments urine osmolality fell or did not change. Simultaneously, C_{urea}/C_{inulin} fell from 0.64 […]

Effect of Hypotonic Expansion on Sodium, Water, and Urea Excretion in Late Pregnancy: the Influence of Posture on These Results

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ABSTRACT Mineralocorticoid-treated, normotensive third trimester subjects positioned in lateral recumbency were studied before and during the infusion of 300 mEq of hypotonic saline. Urinary sodium excretion increased in all subjects from a mean value of 199 to 416 μEq/min. In 12 maximally hydrated subjects free water clearance (C_{H_2O}) and urine flow (V) increased from means of 7.54 and 9.50 to 11.6 and 14.5 ml/100 ml of glomerular filtrate (GFR) Also the ratio of urea to inulin clearance (C_{urea}/C_{inulin}) increased from 0.59 to 0.64. The changes in the renal handling of water and urea suggest that fractional sodium reabsorption decreased at proximal nephron sites.

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Finally, in the 12 hydrated subjects supine recumbency reduced C_{H_2O} and V from a mean of 11.6 and 14.5 to 6.2 and 8.2 ml/100 ml of GFR. In eight of these experiments urine osmolality fell or did not change. Simultaneously, C_{urea}/C_{inulin} fell from 0.64 to 0.57. These data suggest that the antinatriuresis, which occurred when the volume-expanded subjects were positioned in supine recumbency, was accompanied by a decrease in the fractional reabsorption of sodium at proximal nephron sites.

INTRODUCTION

Potent factors which affect the tubular reabsorption of sodium may be important determinants of renal sodium excretion (1, 2). For instance, the natriuresis which follows volume loading of the dog is largely due to a prompt decrease in the tubular reabsorption of sodium which is independent of mineralocorticoid activity (3–6). In this same species production of experimental salt retention is accompanied by ablation of the tubular natriuretic response (7, 8). These tubular natriuretic factors may be operative in normal man and of importance in the sodium homeostasis of patients with chronic renal disease (9, 10). They have not been investigated in pregnant subjects. A protocol was therefore designed with special reference to the pertinence of the newer concepts of tubular sodium handling to pregnancy.

Changes in the renal clearance of sodium, water, and urea induced by hypotonic saline expansion were measured in mineralocorticoid-treated third trimester subjects. The women were initially positioned in lateral recumbency, but after the volume load they assumed a supine posture. Since changing from a lateral to a supine position in late pregnancy reduces the glomerular filtration rate (GFR) (11), it was possible to reduce filtered

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sodium below levels measured before saline loading and then to analyze the effects of such reductions on urinary sodium excretion. Furthermore, subjects were studied while undergoing a maximal water diuresis, and during such conditions changes in per cent of urine flow or in free water generation per unit of GFR or variations in the ratio of urea to inulin clearance may be inversely related to changes in the reabsorption of filtrate in the proximal tubule (12–14). Also, maintenance of hydration was used to eliminate any effects of antidiuretic hormone on the sodium excretion of the pregnant subjects (15, 16).

These studies demonstrated that volume expansion of lateral recumbent, third trimester pregnant women resulted in increases in both filtered and excreted sodium, and that this natriuresis was accompanied by a decrement in the fractional reabsorption of proximal filtrate. On the contrary, supine recumbency was antinatriuretic despite considerable volume loading and even when the filtered sodium remained above control values. Finally, the data suggested that when expanded lateral recumbent subjects assumed a supine decubitus position there was an increment in the fractional reabsorption of sodium in the proximal tubule.

METHODS

15 studies were performed on normotensive women in their third trimester of pregnancy. All subjects were volunteers who gave informed consent. They were studied in the Perinatal Research Center. Their ages ranged from 18 to 28 yr of age and their parity from 0 to 5. They had no evidence of renal or cardiovascular disease. One subject (O.S.) eventually delivered twins. No attempt was made to control dietary salt before the experiment, and on entry to the hospital the subjects received unrestricted diets.

Eight of the volunteers were prehydrated with approximately 1500 ml of water 8–10 hr before the experiment, and all subjects were studied after an overnight fast. All studies were conducted early in the morning with the subject in bed. Approximately 2 hr before the experiment each subject received 10 mg of deoxycorticosterone acetate intramuscularly, then drank water (20 ml/kg of body weight) over a period of 30–45 min. She was then catheterized with an indwelling triple lumen Foley catheter and assumed a lateral recumbent position. After she received appropriate priming doses, an intravenous infusion containing sustaining amounts of inulin and *p*-aminohippurate (PAH) in isotonic saline was maintained at a rate of approximately 0.5 ml/min throughout the study by a constant infusion pump. As diuresis ensued it was maintained by oral supplements of water calculated to replace urinary loss.

When urine flow was stable three to six successive collections were made. Each collection was of 10–20 min duration and was terminated by washing the bladder rapidly with 100–150 ml of sterile distilled water and 50–150 ml of air.

After completion of control collections, the patient remained in the lateral recumbent position, and an infusion of 0.5 N saline was commenced. 4 liters was infused over a period of 2 hr. Collection periods were resumed at the start of the 2nd hr and continued until a total of 300 mEq of sodium had been infused. (These collections were made in 13 of the 15 studies.) In some instances in which very high urine flows were recorded during hypotonic loading, the subjects received further oral supplements of water in amounts calculated to maintain the original positive water balance.

After the infusion the subject assumed a supine position, and 15–30 min later an additional three to six collections were made. During each of these three phases of the study two to three specimens of heparinized blood were obtained, and the plasma promptly separated. All specimens were analyzed for inulin, *p*-aminohippuric acid, urea, sodium, potassium, chloride, and osmolality. In addition, total plasma solids were recorded on one or more blood specimens during each group of collection periods.

After the study, the obstetrical care of each patient was managed by one of the authors (P.W.) Urine cultures were obtained at subsequent prenatal visits and in the puerperium. With one exception, all subjects remained free of urinary tract infection. Patient G.W., who was recatheterized during labor for urinary retention, contracted a postpartum infection. She was successfully treated, and her urine was sterile 4 months after delivery.

Inulin was determined by the method of Roe, Epstein, and Goldstein (17). The concentrations of plasma and urine *p*-aminohippuric acid were measured on the AutoAnalyzer by the method of Smith and associates (18), and urea was determined by the analyzer modification of the carbaminodiacetyl reaction described by Skeggs (19). Sodium and potassium were measured by a flame photometer with an internal lithium standard. Osmolality was determined by measurement of freezing point depression.[1]

RESULTS

The protocols of two experiments are given in Tables I and II. The results of all 15 studies are summarized in Table III. Subjects were originally divided into two groups, those prehydrated the evening before the study and those who were not. Since no significant differences were noted between the groups, their results are considered together.

Sodium metabolism

Lateral recumbency. In 13 experiments subjects positioned in lateral recumbency were studied before and during expansion with hypotonic saline. In these studies filtered sodium averaged 17.7 mEq/min before and rose to 19.9 mEq/min during expansion. Simultaneously, urinary sodium excretion which averaged 199 μEq/min during the control collections rose to 416 μEq/min. The amplitude of this natriuresis varied considerably among

[1] There is a theoretical objection to measuring osmolality of urines diluted by bladder washout. The error is due to the fact that the dissociation of salts like NaCl is related to their concentration. Our subjects studied during water diuresis had urines of low osmolality. Therefore, the effects of washouts on the osmotic coefficients are minimal and virtually without effect upon the results. This fact has been verified in our laboratories where the addition of equal volumes of distilled water to 17 dilute urines (range 39–139 mOsm/kg) reduced their osmolalities 50.6% (SD 1.2).

TABLE I

Effects of Hypotonic Saline Infusion and Assumption of a Supine Position in Subject D. C.

Time	AF	V	C_{inulin}	C_{PAH}	P_{Na}	F_{Na}	$U_{Na}V$	U_KV	$\frac{C_{osm}}{GFR} \times 100$	$\frac{C_{H_2O}}{GFR} \times 100$	C_{urea}/C_{inulin}	FF
min	*ml/min*	*ml/min*	*ml/min*	*ml/min*	*mEq/liter*	*mEq/min*	*μEq/min*	*μEq/min*	*ml/min*	*ml/min*		
−110	Patient received 10 mg of deoxycorticosterone acetate, i.m. After ingesting 20 ml of water per kg of body weight, she assumed a lateral recumbent position. As diuresis ensued, supplements of water equal to the urine output were given orally.											
0	Priming dose: 250 mg of inulin, 500 mg of PAH. Infusion I started 45 mg/min of inulin: 20 mg/min of PAH in saline at 0.5 ml/min.											
48–59	29.7	15.4	129	652	136	17.5	356	59.4	2.74	9.22	0.635	0.198
59–69	28.8	14.5	136	640	(136)	18.5	341	54.7	1.98	8.70	0.573	0.212
69–90	29.1	14.7	149	669	136	19.0	345	56.0	2.42	8.34	0.581	0.211
91	0.5 N saline started at 33.5 ml/min until 4 liters has been given.											
144–154	44.0	28.2	143	671	135	19.3	900	70.4	4.42	15.4	0.643	0.209
154–163	44.0	26.4	150	670	(135)	20.3	780	70.4	3.82	13.7	0.629	0.224
163–172	42.7	26.5	146	642	(135)	19.7	782	59.7	3.55	14.6	0.614	0.228
172–182	41.8	26.4	154	672	134	20.6	745	62.7	3.90	13.3	0.570	0.229
192	Patient assumed a supine position.											
204–218	22.4	11.3	138	676	134	18.5	197	65.0	1.42	6.93	0.491	0.202
218–245	22.8	11.4	146	687	137	19.9	185	68.9	1.40	6.41	0.399	0.211
245–269	23.0	10.2	149	715	134	20.2	192	71.1	1.51	5.28	0.378	0.209

Abbreviations as follows: AF = apparent urine flow including washout; V = actual urine flow; C_{inulin} = clearance of inulin; C_{PAH} = the clearance of *p*-aminohippurate; P_{Na} = plasma sodium; F_{Na} = filtered sodium; $U_{Na}V$ = sodium excretion; U_KV = potassium excretion; $\frac{C_{osm}}{GFR} \times 100$ = fractional osmolar clearance; $\frac{C_{H_2O}}{GFR} \times 100$ = fractional free water clearance; C_{urea}/C_{inulin}, urea to inulin clearance ratio; FF = filtration fraction; ( ) = interpolated value.

the volunteers, the increases in sodium excretion ranging from a modest rise of 50 μEq/min (subject G.W.) to a substantial increase of 700 μEq/min (subject P.K.). In 10 of the 13 studies urinary sodium excretion had already risen by the start of the 2nd hr, and its rate of excretion varied little during successive collection periods (cf. Table I). In the other three experiments the natriuresis continued to increase during the 2nd hr of expansion (cf Table II). In these latter studies urine flow, too, rose slowly during the collection periods. However, the increase from the first to the last collection period did not exceed 10%.

Thus, the renal response to expansion of lateral recumbent subjects was an increase in both filtered and excreted sodium. Furthermore, and of importance to the design of this protocol, is the fact that the magnitude of the volume infused was sufficient to evoke a natriuresis before the time when the subject was requested to assume a supine position.

Supine recumbency. 15 subjects positioned in lateral recumbency were expanded with hypotonic saline. After the saline load they changed to the supine recumbent position. In these experiments, the results obtained during supine recumbency were compared to those obtained during the lateral recumbent control periods. The filtered load averaged 18 mEq/min during control collections, and the mean value for urinary sodium excretion was 219 μEq/min. After assumption of a supine position the filtered load of sodium averaged 16.3 mEq/min, and sodium excretion averaged 179 μEq/min. Filtered sodium fell to below control values in 11 studies (range of decrement 0.3–5.8 mEq/min).

The results of all 15 experiments are shown in Fig. 1. The graph depicts the net changes in filtered and excreted sodium. Regardless of the direction of the change in filtered load, these expanded subjects did not have a significant sodium diuresis. The only exception was subject P.K. In this case a modest natriuresis occurred despite an apparent decrease in the filtered load of sodium. In this experiment, however, a very substantial sodium diuresis was in progress when the patient assumed a supine posture. With institution of this maneuver sodium excretion actually fell more than 500 μEq/min; but the fall did not totally erase the natriuresis in

TABLE II

Effects of Hypotonic Saline Infusion and Assumption of a Supine Position in Subject B. H.

Time	AF	V	C_{inulin}	C_{PAH}	P_{Na}	F_{Na}	$U_{Na}V$	U_KV	$\frac{C_{osm}}{GFR} \times 100$	$\frac{C_{H_2O}}{GFR} \times 100$	$\frac{C_{urea}}{C_{inulin}}$	FF
min	*ml/min*	*ml/min*	*ml/min*	*ml/min*	*mEq/liter*	*mEq/min*	*μEq/min*	*μEq/min*	*ml/min*	*ml/min*		
−105	Patient received 10 mg of deoxycorticosterone acetate, i.m. Then this subject, who had received 1500 ml of water at 11 p.m. the preceding evening, ingested 20 ml of water/kg of body weight and assumed a lateral recumbent position. As diuresis ensued, supplements of water equal to urine output were given orally.											
0	Priming dose: 250 mg of inulin, 500 mg of PAH. Infusion I started: 45 mg/min of inulin: 20 mg/min of PAH in saline at 0.5 ml/min.											
80–93	22.4	11	138	826	134	18.5	118	126	2.19	5.77	0.622	0.166
93–108	19.6		136	781	(135)	18.4	117	120	1.98	5.87	0.606	0.175
		10.7										
108–122	22.9		136	708	136	18.5	137	102	2.00	5.86	0.576	0.195
123	0.5 N saline started at 33.5 ml/min until 4 liters has been given.											
174–194	33.5	21.4	142	890	135	19.2	237	72.5	2.06	13.1	0.697	0.169
194–204	31.8		146	913	(136)	19.9	286	68.5	2.20	13.3	0.713	0.160
		22.7										
204–214	44.9		146	873	137	20.0	326	77.2	2.20	13.3	0.713	0.167
219	Patient assumed a supine recumbent position.											
242–257	24.9	14.9	136	814	137	18.6	180	75.7	2.72	8.99	0.584	0.167
257–273	24.4	14.6	139	861	137	19.0	210	83.6	2.48	8.00	0.597	0.161
273–313	24.6	13.5	131	839	136	17.8	168	77.5	2.37	8.47	0.580	0.156

Abbreviations as in Table I.

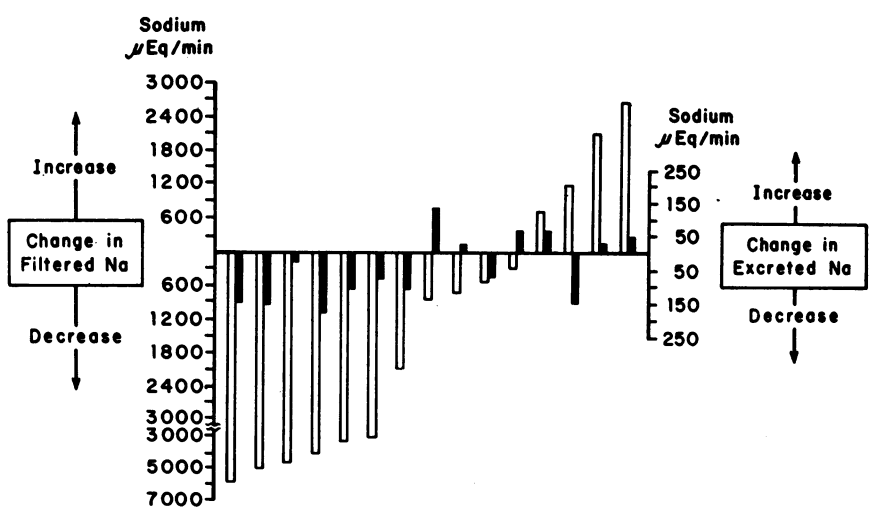

FIGURE 1 Summary of 15 experiments in which subjects positioned in lateral recumbency were infused with hypotonic saline and then assumed a supine posture. Each bar represents the difference between the supine and the control periods in one experiment. The white bars represent changes in filtered sodium, the black bars, changes in excreted sodium.

TABLE III

Summary of Experiments

	Group	C_{inulin}	P_{Na}	F_{Na}	$U_{Na}V$	$U_{K}V$	FF	$\frac{C_{urea}}{C_{inulin}}$	$\frac{V}{GRF} \times 100$	$\frac{C_{osm}}{GFR} \times 100$	$\frac{C_{H_2O}}{GFR} \times 100$	U_{osm}
		ml/min	*mEq/liter*	*mEq/min*	*μEq/min*	*μEq/min*			*ml/min*	*ml/min*	*ml/min*	*mOsm/kg*
B. H.	Control	137	135	18.5	124	116	0.178	0.60	7.95	2.06	5.83	72
68 kg	Loading	145	135	19.6	282	73	0.161	0.70	14.9	2.15	13.2	43
P 1	Supine	134	136	18.2	186	79	0.160	0.59	10.7	1.86	8.49	50
P. R.	Control	170	128	21.8	108	45	0.168	0.51	6.94	1.38	5.19	52
89 kg	Loading	179	133	23.8	178	49	0.167	0.57	10.4	1.68	8.84	37
P 1	Supine	161	131	21.1	127	68	0.141	0.56	8.32	1.18	7.15	38
M. W.	Control	138	134	18.5	175	37	0.260	0.51	10.7	0.97	9.78	25
63.2 kg	Loading	170	137	23.3	506	59	0.262	0.57	17.4	2.79	15.2	31
P 1	Supine	142	135	19.2	239	75	0.231	0.55	8.73	1.62	6.68	49
P. S.	Control	105	136	14.3	134	56	0.219	0.72	12.3	1.47	10.8	33
52.9 kg	Loading	107	132	14.1	204	36	0.231	0.66	15.6	1.15	14.0	31
P 1	Supine	80	135	10.8	67	32	0.191	0.57	9.76	1.23	8.40	35
C. H.	Control	145	136	19.7	342	43	0.325	0.64	11.9	2.47	9.42	61
57.5 kg	Loading	141	135	19.1	461	47	0.316	0.75	15.7	2.56	13.4	50
P 0	Supine	109	135	14.7	184	56	0.297	0.74	3.62	1.63	1.96	135
J. M.	Control	115	133	15.3	179	58	0.263	0.66	8.67	2.05	6.57	64
66.7 kg	Loading	158	128	20.2	372	51	0.310	0.61	10.0	1.97	8.06	59
P 1	Supine	113	131	14.8	101	63	0.262	0.52	7.15	2.13	4.96	81
M. L.	Control	70.2	128	8.99	221	54	0.214	0.63	10.3	3.25	7.19	52
41 kg	Loading	78.0	127	9.91	486	55	0.217	0.69	20.0	7.51	13.1	50
P 4	Supine	53.3	128	6.82	105	52	0.156	0.72	13.1	3.18	9.95	47
O. S.	Control	160	135	21.6	142	36	0.241	0.37	8.44	1.63	6.74	88
65 kg	Loading	186	130	24.2	264	40	0.237	0.46	10.9	2.11	8.82	91
P 5	Supine	144	127	18.3	83	44	0.214	0.34	8.88	1.67	6.97	64
B. T.	Control	131	133	17.4	134	106	0.216	0.67	7.21	1.97	5.24	78
113 kg	Loading	146	135	19.7	257	119	0.253	0.71	10.4	2.07	8.29	62
P 4	Supine	147	136	20.0	186	111	0.209	0.68	9.11	2.18	6.94	65
B. B.	Control	104	134	13.9	210	66	0.282	0.56	8.63	2.42	5.85	78
52.8 kg	Loading	124	135	16.7	402	71	0.296	0.71	11.6	2.44	9.10	54
P 1	Supine	52	136	8.15	77	30	0.304	0.49	4.02	1.16	3.09	80
D. C.	Control	135	136	18.3	342	57	0.215	0.58	10.7	2.27	8.75	59
62.6 kg	Loading	149	135	20.1	777	65	0.223	0.61	18.1	4.17	14.3	62
P 0	Supine	144	135	19.5	191	68	0.207	0.38	7.64	1.44	6.20	53
P. K.	Control	137	133	18.3	312	65	0.207	0.62	11.3	2.31	9.08	59
62 kg	Loading	164	130	21.3	1013	77	0.221	0.65	18.7	5.34	13.3	79
P 1	Supine	131	134	17.5	445	82	0.216	0.59	7.35	3.15	3.65	124
G. W.	Control	166	142	23.6	168	45	0.256	—	—	—	—	—
113 kg	Loading	161	139	22.4	207	53	0.256	—	—	—	—	—
P 1	Supine	146	141	20.6	151	59	0.216	—	—	—	—	—

Control = mean of three or more stable periods before hypotonic loading of lateral recumbent subject; loading = three or more stable periods during the 2nd hr of hypotonic saline loading; supine = three or more stable periods after assumption of a supine position; P = parity; U_{osm} = urine osmolality. (Measured osmolality multiplied by the quotient of AF/V.) Other abbreviations as in Table I.

TABLE III—(*Continued*)

	Group	C_{inulin}	P_{Na}	F_{Na}	$U_{Na}V$	U_KV	FF	$\frac{C_{urea}}{C_{inulin}}$	$\frac{V}{GFR} \times 100$	$\frac{C_{osm}}{GFR} \times 100$	$\frac{C_{H_2O}}{GFR} \times 100$	U_{osm}
		ml/min	*mEq/liter*	*mEq/min*	*μEq/min*	*μEq/min*			*ml/min*	*ml/min*	*ml/min*	*mOsm/kg*
G. Z.	Control	152	133	20.2	359	70	0.234	—	—	—	—	—
65.5 kg	Supine	123	131	16.1	176	55	0.210	—	—	—	—	—
P 1												
H. K.	Control	125	132	16.5	336	44	0.203	—	—	—	—	—
56.5 kg	Supine	141	131	18.5	368	61	0.174	—	—	—	—	—
P 0												

progress. Furthermore, in four subjects no natriuresis occurred despite the recording of filtered loads of sodium above their control values, and in two of these patients (H.K. and B.T.) the increase in filtered sodium was 2 and 2.6 mEq/min, respectively.

Thus, in supine recumbency no decrease in fractional tubular sodium reabsorption could be demonstrated when the filtered load was reduced. Contrarily, this position consistently blunted the natriuresis apparent in lateral recumbency, and this blunting of the natriuresis occurred even if the filtered load of sodium remained substantially above control.

Plasma sodium. Plasma sodium remained stable in all experiments, with two exceptions. In the experiments on J.M. and O.S. decreases of 5 and 7 mEq/liter occurred. The average plasma sodium in each group was: control, 134 mEq/liter; loading in lateral recumbency, 133 mEq/liter; and supine recumbency, 133 mEq/liter.

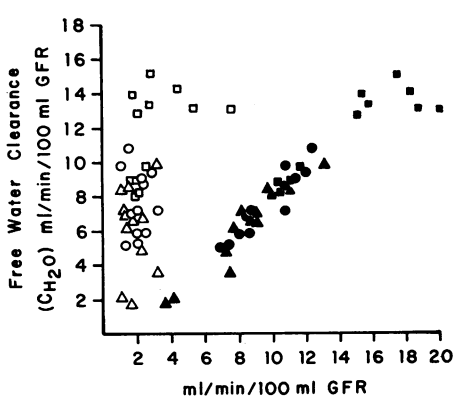

FIGURE 2 The fractional clearance of solute-free water plotted against fractional osmolar clearance (open symbols) and against fractional urine flow (closed symbols). Circles represent control measurements, squares are the results measured during expansion of subjects positioned in lateral recumbency, and triangles the results measured when the women assumed a supine posture.

Potassium excretion. The mean values for potassium excretion were similar in each phase of the study. They are 60, 61, and 62 μEq/min during the control, loading, and supine collection periods, respectively. The values during the individual studies are recorded in Table III. There was considerable variation among the different phases of individual experiments, but no specific patterns were noted.

Water metabolism and urea clearances

12 studies were conducted during which maximal water diuresis was maintained throughout the experiment. In these experiments osmolar and free water clear-

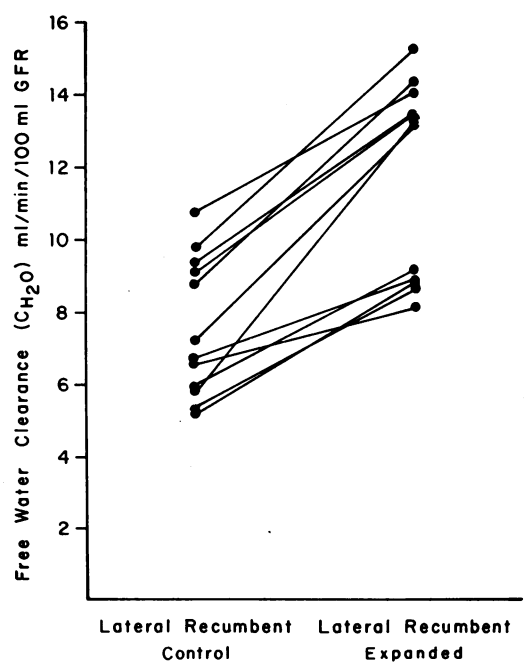

FIGURE 3 The effect of an intravenous infusion of hypotonic saline on the fractional free water clearance of pregnant women positioned in lateral recumbency.

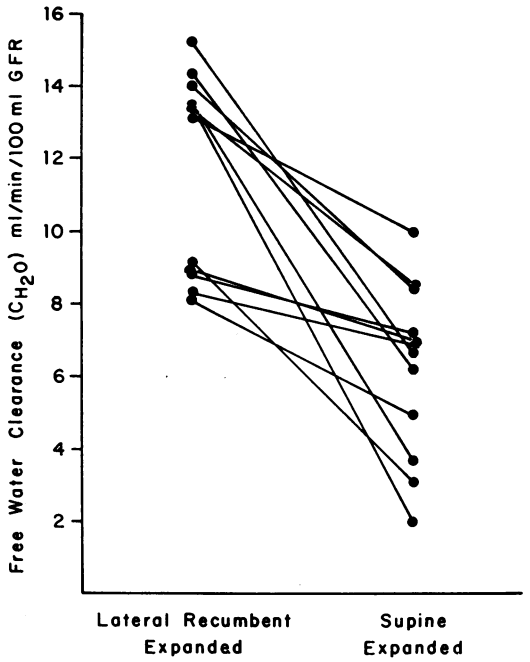

FIGURE 4 The effect of changing from a lateral to a supine posture on the fractional free water clearance of volume-loaded pregnant women.

ances were measured, and the clearances of urea and inulin were compared (Table III). During these studies changes in urine flow per 100 ml of GFR (V%) were linearly related to changes in free water clearance per 100 ml of GFR (C_{H_2O}%). This becomes apparent when free water clearance (C_{H_2O}) is plotted as a function of osmolar clearance (C_{osm}) and urine flow (V) (Fig. 2). During any phase of the experiment per cent of changes in C_{osm} were minimal. This is borne out by the observation that the average change of C_{osm} during a given study was only 1.34 ml/100 ml of GFR. Therefore any change in V was accompanied by a quantitatively similar change in C_{H_2O}.

Water metabolism in lateral recumbency. C_{H_2O}/100 ml of GFR rose in every experiment when subjects were expanded while positioned in lateral recumbency (Fig. 3). Thus, there was a rise in mean C_{H_2O} from 7.54 to 11.6 ml/100 ml of GFR. Similarly, V increased from a mean of 9.60 to 14.5 ml/100 ml of GFR.

The effect of supine recumbency. The change that occurred when the lateral recumbent expanded subjects assumed a supine position is illustrated in Fig. 4. C_{H_2O} fell in every instance from a mean of 11.6 to 6.2 ml/min/100 ml of GFR. Simultaneously, V fell from 14.5 to 8.2 ml/min/100 ml of GFR. Urine osmolalities (U_{osm}) are recorded in Table III. Despite the fall in both C_{H_2O}% and V% the osmolality remained the same or decreased in 7 of the 12 experiments. In two subjects, however (P.K. and C.H.), U_{osm} rose to 124 and 135 mOsm/kg, respectively.

Urea clearances. Changes in the ratio of urea to inulin clearances (C_{urea}/C_{inulin}) are recorded in Table III. During the control periods C_{urea}/C_{inulin} averaged 0.59. During saline loading of lateral recumbent subjects this ratio increased in 10 of the 12 studies and averaged 0.64 (increment 0.03–0.15). In the supine position C_{urea}/C_{inulin} averaged 0.57. In 11 of the 12 experiments the ratio fell when the subject assumed a supine position (decrement 0.01–0.23).

DISCUSSION

These experiments extend observations concerning the natriuretic response to volume expansion of pregnant women (20–23), as the changes in V%, C_{H_2O}%, and C_{urea}/C_{inulin} suggest that during hypotonic saline loading of lateral recumbent subjects, fractional sodium reabsorption decreased in the proximal nephron. This study also underscores the importance of posture as a determinant of sodium excretion in late pregnancy, for supine recumbency was antinatriuretic despite considerable volume loading. Finally, when the expanded subject changed from lying on her side to lying on her back, the data suggest that the decrement in sodium excretion was accompanied by an increase in the fractional reabsorption of proximal filtrate.

12 subjects were studied during a state of maximal hydration. Under these conditions data relative to water and urea excretion may reflect changes in the reabsorptive activities of different loci of the nephron. For instance, Ecknoyan, Suki, Rector, and Seldin have demonstrated that during maximal water diuresis increases in C_{H_2O}% and V%, induced by hypotonic saline loading, are indicative of an increase in the reabsorption and delivery of filtrate (sodium) to the distal diluting sites (12). In our experiments expansion of lateral recumbent pregnant subjects consistently resulted in increments of both V% and C_{H_2O}%. Also, Goldstein, Lenz, and Levitt suggest that during maximal water diuresis changes in the ratio of C_{urea}/C_{inulin} relate inversely to changes in proximal tubular reabsorption (13). This ratio increased in 10 of the 12 studies. Therefore, the increases in C_{H_2O}% and V%, and the increments in C_{urea}/C_{inulin} suggest that during the hypotonic saline infusion of lateral decubitus subjects, there was a decrement in the reabsorption of proximal filtrate.[2]

[2] There are theoretical objections to the use of C_{H_2O}, V%, and C_{urea}/C_{inulin} in the way described above. These objections are discussed and countered by the various authors (12, 14). Pertinent to this study is the following: to date, all supportive evidence for the use of V% and C_{H_2O}% as indices of distally delivered and reabsorbed fractions of filtered sodium has been obtained during animal protocols. Secondly, use of C_{urea}/C_{inulin} as an index of proximal tubular

When the expanded subjects assumed a supine posture V% and C_{H_2O}% decreased in every experiment. In 11 of 12 studies a decrement in C_{urea}/C_{inulin} occurred. These data per se may not be used as an index of proximal reabsorptive changes, unless one can eliminate the following possibility. The postural maneuver, by eliciting the secretion of small amounts of antidiuretic hormone, or by decreasing the GFR, might have caused an increase in the back diffusion of solute-free water at distal nephron sites (24, 25). Such back diffusion, irrespective of cause, should increase the osmolality of the final urine, and U_{osm} did in fact increase in five instances. In the remaining seven experiments, however, U_{osm} decreased or did not change, and the decrements of C_{H_2O}%, V%, and C_{urea}/C_{inulin} in these latter studies suggest that supine recumbency increased the fractional reabsorption of proximal filtrate.

Infusion of subjects positioned in lateral recumbency led to a saline diuresis in addition to the decrement in the fractional reabsorption of proximal filtrate. Then supine recumbency dramatically ablated the natriuresis, and simultaneously the fractional reabsorption of sodium increased in the proximal part of the nephron. Such observations, however, must not be construed as evidence that there is a causal relationship between these changes in proximal tubular reabsorption and the sodium content of the final urine. Micropuncture studies, which demonstrate that large variations in proximal tubular rebasorption may occur without any quantitative changes in urinary sodium excretion, suggest that the regulation of distal tubular reabsorption may be important determinants of renal sodium homeostasis (26–28). Although in our protocol the linear relationship between C_{H_2O}% and V% indicates that during hypotonic loading most of the increment of sodium delivered to the diluting site was in fact reabsorbed, we have no other information relevant to the dynamics of distal reabsorptive mechanisms.

Auld, Lalone, and Levinsky have given hypotonic saline to maximally hydrated, nonpregnant humans both before and after mineralocorticoid-induced chronic extracellular volume expansion (9). The results in their normal subjects are similar to those in our pregnant subjects in that saline loading results in increments of both V% and C_{H_2O}%. However, the response in their chronically expanded subjects was different in that hypotonic loading evoked an exaggerated natriuresis but little change in C_{H_2O}%, a result interpreted by others as evidence that hypervolemia inhibits sodium reabsorption in the ascending loop of Henle (12). Since gravidity is associated with an increment in extracellular volume and in the production of aldosterone (29, 30), it is of note that our pregnant subjects responded to hypotonic saline infusion in a manner similar to that of normal man and different from that seen in an experimentally induced hypervolemic state.

Another aspect of this protocol concerns further characterizations of the importance of posture to sodium excretion during pregnancy. Previous studies had shown that assumption of a supine posture results in an immediate decrement in urinary sodium excretion (11, 31). Our data extend this observation by demonstrating that supine recumbency is antinatriuretic despite considerable volume loading and even when the GFR remained above lateral recumbent control values.

In a number of the experiments, supine recumbency reduced the GFR considerably below control values. When saline-loaded, mineralocorticoid-treated dogs manifested similar reductions in their filtered sodium, urinary sodium excretion remained considerably above control values, thus demonstrating the presence of tubular natriuretic factors (3–7, 32). In this study reduction of the filtered load by assumption of a supine position did not demonstrate any natriuretic factors. The maneuver blunted natriuresis even when the filtered load of sodium remained up to 2.6 mEq/min above that recorded during lateral recumbent control periods. Recently, by requesting subjects to assume a supine position during the 2 hr of hypotonic loading, we have studied two subjects in whom urinary sodium excretion decreased, although the filtered load increased more than 5 mEq/min above lateral recumbent control values.[3]

Thus, the antinatriuresis of supine recumbency is present regardless of the direction of the change in filtered load (Fig. 1), and in those subjects whose GFR are above control values there is a net increase in the tubular reabsorption of sodium. Furthermore, it appears that this increase is not related to any change in endogenous mineralocorticoid activity, as the subjects were given large doses of deoxycorticosterone acetate.

In attempting to explain the supine antinatriuresis of late pregnancy a number of mechanisms have been suggested. The decrease in filtered sodium has been mentioned as a causal factor (33), but in this study volume expansion before changing position resulted in a number of instances in which supine recumbency was antinatriuretic despite an increased filtered load. The increase in caval pressure induced by supine recumbency has also been implicated (31, 34–36), since in man congestion of the inferior vena cava induced by an inflatable balloon consistently reduced urinary sodium excretion (37). We have no data to support or deny this sug-

reabsorption involves two assumptions, also unproven in man: that tubular reabsorption of urea is passive, and that during water diuresis the distal nephron is impermeable to this molecule.

[3] Lindheimer, M. D., and P. V. Weston. Unpublished observations.

gestion. It is of interest, though, that in the dog acute constriction of the inferior vena cava does not inhibit a natriuretic response to saline loading (7), while in this study supine recumbency caused a considerable decrement in sodium excretion. Also, an increased filtration fraction has been noted in many situations in which sodium reabsorption increases (38). In one study a small increment in the filtration fraction was noted when pregnant women changed from a lateral to a supine position (31). In another study renal function tests were done with pregnant women on their backs one day and on their sides the preceding or following day, and changes in filtration fraction were equivocal (11). In our study, in which a volume load was given before the postural maneuver, the filtration fraction decreased in 13 of 15 experiments.

The mechanism of how supine recumbency causes antinatriuresis cannot be determined from these experiments, as a number of factors implicated in the renal sodium metabolism of pregnant subjects were not controlled in the present study. Humoral agents, such as progesterone, angiotensin, and estrogen may affect renal salt handling (39–42). Physical factors also must be considered. These include changes in ureteral pressure (43–45) and in uterine blood flow induced by supine recumbency. The latter is of interest since the uterine-placental circulation has been likened to an arteriovenous shunt (45–47). Also, postural changes may affect the autonomic nervous system (48–50). Future investigations will have to take factors such as these into account.

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