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Research Article

ALKALINE TIDES[1]

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Diurnal variations in urinary acidity have been described and investigated extensively since Bence Jones (1) first reported the excretion of alkaline urine after meals. This post-meal alkaline tide and the period of spontaneous alkalinity which begins in the early morning hours, the so-called morning alkaline tide, have received especial attention, and several hypotheses have been advanced to account for them. The subject has been reviewed recently by Brunton (2). The reported observations have been nearly all of serial determinations of acid concentration in the urine or of urinary pH, data which permit no estimation of the amount of alkali excreted or retained per unit time. The few papers which present quantitative data of acid excretion have used methods which to us seem faulty or inaccurate, or in the investigation of the morning alkaline tide have paid no attention to variations in urinary volumes or to exercise and change of posture, factors which may have a striking effect on the curve of acid excretion. We have therefore investigated the spontaneous morning alkaline tide as it occurs in the normal resting subject without food or water, and then have studied some of the effects produced by exercise, by variation in fluid intake, and by the ingestion of food.

METHODS

Two normal subjects with normal gastric acidity were studied. They were awakened by alarm at 6 a.m. and remained in bed during the periods of observation. Half-hourly specimens of urine were obtained, and determinations of volume, titratable acidity and ammonia were made.

Titration acidity of the urine was determined by a modification of the "total acid minus CO_2" method of Albright, Bauer, and Aub (3). Five or ten cc. samples of urine were placed in large pyrex tubes, 0.5 cc. of a water solution of phenolsulphonphthalein (40 mgm. per 100 cc.) was added, and sufficient tenth normal sulphuric acid accurately measured from a calibrated 2 cc. burette to acidify the urine. Carbon dioxide was then removed by rapid aeration for twenty minutes and volumes made up to 20 cc., making the concentration of indicator 1 mgm. per 100 cc. Titration to pH 7.35 was done with N/50 NaOH containing the same concentration of indicator. Subtraction of the NaOH used from five times the volume of N/10 acid added gives the fixed acid or alkali in terms of fiftieth normal.

This method of titration was used because its results, in terms of free acid or alkali excreted per unit time, measure the quantity of free base (alkali reserve) gained or lost to the body. A simple example illustrates this point. A liter of glomerular filtrate excreted at pH 7.35 and titrated without loss of CO_2 would yield a result of zero. Yet its excretion would represent a loss of about 22 mM. of body alkali, the figure which is obtained by the "total acid minus CO_2" method.

Ammonia was determined by the method of Van Slyke and Cullen (9).

RESULTS

The normal morning alkaline tide. With the subject at rest, without water or food, a curve of excretion of free fixed acid or alkali was obtained which may be regarded as basal for the individual under the conditions of the experiment. After a period of about two hours during which there was a fairly constant rate of acid excretion, deviation of the curve in the direction of alkalinity began and continued to a maximum output of free alkali at five to five and a half hours after waking. Data for the morning hours on Subject A are given in Table I and Figure 1. In the graphs, only the free acid or alkali excreted per unit time is plotted. Graphs of acid plus am-

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monia are similar in form. In the experiments on Subject B in which observations were continued throughout the day (Figure 5), it is seen that the period of spontaneous alkali excretion may continue until late in the afternoon, the initial morning level of acid excretion not being reached until 9 p.m. The remarkable constancy of the rate of excretion of free acid during the first half hour after waking deserves remark. The extreme variation in eighty observations on the two subjects under a variety of experimental conditions was 1.0 mM. per hour.

TABLE I

Mean values of urinary volumes, free fixed alkali, and ammonia in Subject A. Seven experiments in each group

Time	No water			250 cc. of water per hour			250 cc. of water per hour		
	No food			No food			Breakfast at 6:15 a.m.		
	Volume rate	Alkali	Ammonia	Volume rate	Alkali	Ammonia	Volume rate	Alkali	Ammonia
	cc. per hour	*m. eq. per hour*	*m. eq. per hour*	*cc. per hour*	*m. eq. per hour*	*m. eq. per hour*	*cc. per hour*	*m. eq. per hour*	*m. eq. per hour*
11 p.m. to 6 a.m.	51	−1.6	1.7	43	−1.6	1.9	46	−1.5	1.6
6–6:30	31	−1.7	1.9	41	−1.8	2.0	32	−1.8	1.6
6:30–7	31	−1.7	1.9	98	−1.7	2.2	86	−1.8	2.2
7–7:30	35	−1.7	1.8	251	−1.0	2.0	137	−2.2	2.8
7:30–8	35	−1.6	1.9	305	−0.4	1.6	301	−1.8	2.5
8–8:30	39	−1.2	1.3	294	0.6	1.2	211	−1.4	1.9
8:30–9	45	−0.7	1.2	237	2.1	0.9	164	0.9	1.3
9–9:30	47	0.3	0.8	250	4.2	0.8	283	5.0	0.8
9:30–10	59	2.0	0.6	311	4.9	0.8	345	6.9	0.7
10–10:30	64	2.9	0.5	328	5.6	0.7	310	6.7	0.7
10:30–11	64	3.5	0.4	343	5.5	0.8	350	7.4	0.7
11–11:30	72	4.3	0.4	274	5.0	0.6	262	5.7	0.7
11:30–12	61	3.2	0.4	268	5.2	0.6	339	5.3	0.7
12–12:30	59	2.9	0.4	285	4.8	0.6	287	4.0	0.7
12:30–1							281	2.8	0.7

Effects of water diuresis. In the experiments in which no water or food was taken, increase in the excretion of alkali was always accompanied by an increase in the rate of urine secretion. When diuresis was produced by drinking water, the period of diminishing acid excretion began about an hour earlier than when no water was taken, and the later portion of the morning curve was somewhat higher than the low-volume curve (Figure 1). A few high-volume data on Subject B are shown in Figure 4 and are seen to lie within the same range as those on Subject A.

Effects of exercise. Strenuous exercise on the previous day resulted in almost complete obliteration of the morning alkaline tide (Figure 3). A

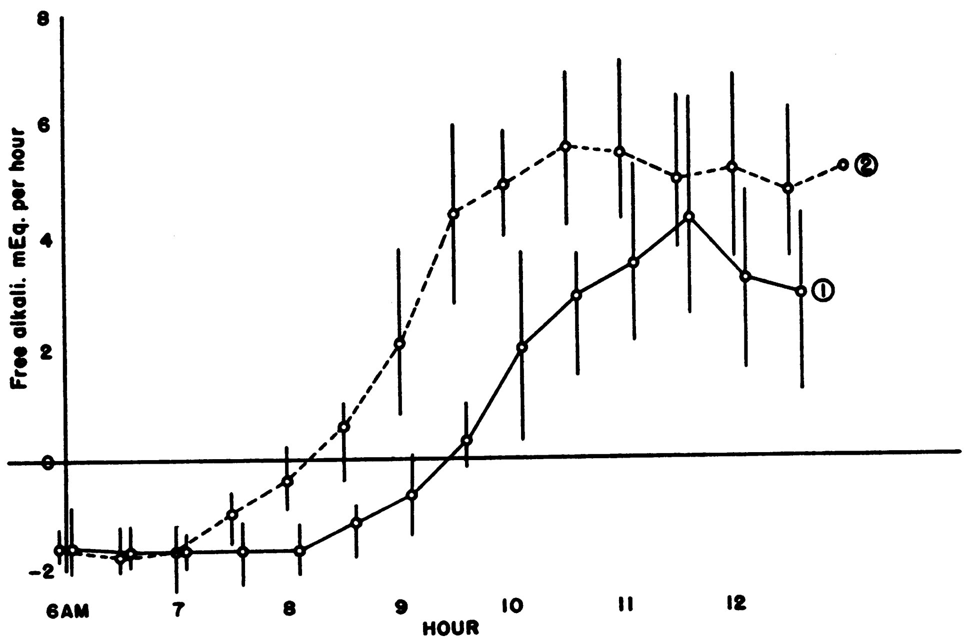

FIG. 1. EFFECT OF WATER DIURESIS ON MORNING ALKALI EXCRETION. SUBJECT A.
CURVE 1. NO FOOD. NO WATER.
CURVE 2. NO FOOD. WATER 250 CC. PER HOUR.

Mean values from seven experiments are plotted in each curve. Range of data is shown by vertical lines.

short period of very mild exercise diminished the alkali excretion temporarily (Figure 4). If the subject on arising walked quietly to the laboratory, a distance of one block, and worked there throughout the morning, the tide was practically obliterated (Figure 3). These deviations in the direction of acidity were not accompanied by a diminution in volume output of urine.

of egg, coffee, toast and grapefruit at different hours on different days (Figure 4). Delay in the rise of the curve after a breakfast has been eaten may be due to smaller volumes (Table I), but this cannot explain the greater acidity, since the graphs of Figure 1 show that with considerably smaller volumes at this period there is no increased excretion of acid.

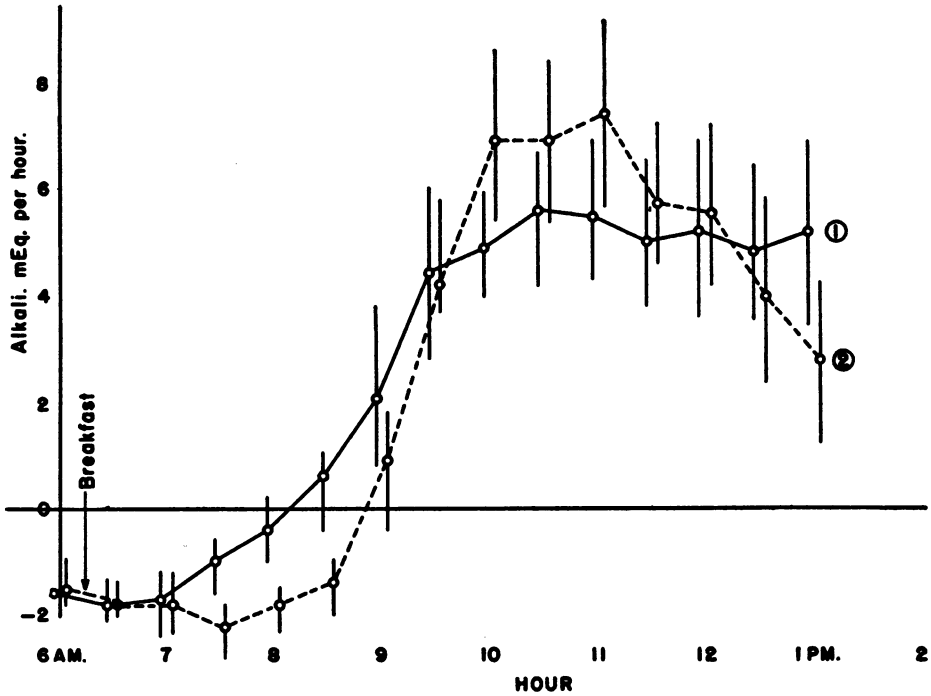

FIG. 2. EFFECT OF BREAKFAST ON MORNING ALKALI OUTPUT. SUBJECT A.
CURVE 1. NO FOOD. WATER 250 CC. PER HOUR.
CURVE 2. BREAKFAST AT 6:10. WATER 250 CC. PER HOUR.
Mean values from seven experiments are plotted. Range of data is indicated by vertical lines.

Effects of eating. In six experiments on Subject A a breakfast consisting of dry wheat cereal, cream and sugar was taken immediately after waking. In this series, water was taken every half hour, and comparison is therefore made with the high-volume curve without breakfast (Figure 2). A period of increased acid excretion began about one and one-half hours after waking and continued for an hour, after which the alkaline deviation began, the curve being steeper and rising somewhat higher than that of the control series. This increased excretion of acid following breakfast was seen in all six experiments, and was noted also in Subject B, who took a breakfast

When orange juice or small doses of soda were taken late in the evening, there was a marked increase in the morning alkali excretion, although the acidity of the intervening night urine was not appreciably affected. Two such curves are shown in Figure 3.

DISCUSSION

Our data are of interest as quantitative measures of the morning alkaline tide in normal individuals under approximately basal conditions; and the effects of certain departures from these conditions may throw some light on the cause and possible significance of alkaline tides.

Alkaline tides have been accounted for by all the principal physiological processes which produce alkali, and which might take place at the times the tides occur. The hypothesis that secretion of gastric acid will acount for increased alkalinity of the urine after meals fails when it is observed that during the period of maximal gastric secretion there is increased excretion of acid in the urine. This brief acid tide immediately after eating has been described also by Campbell and Webster (4) and by Jansen and Karbaum (5).

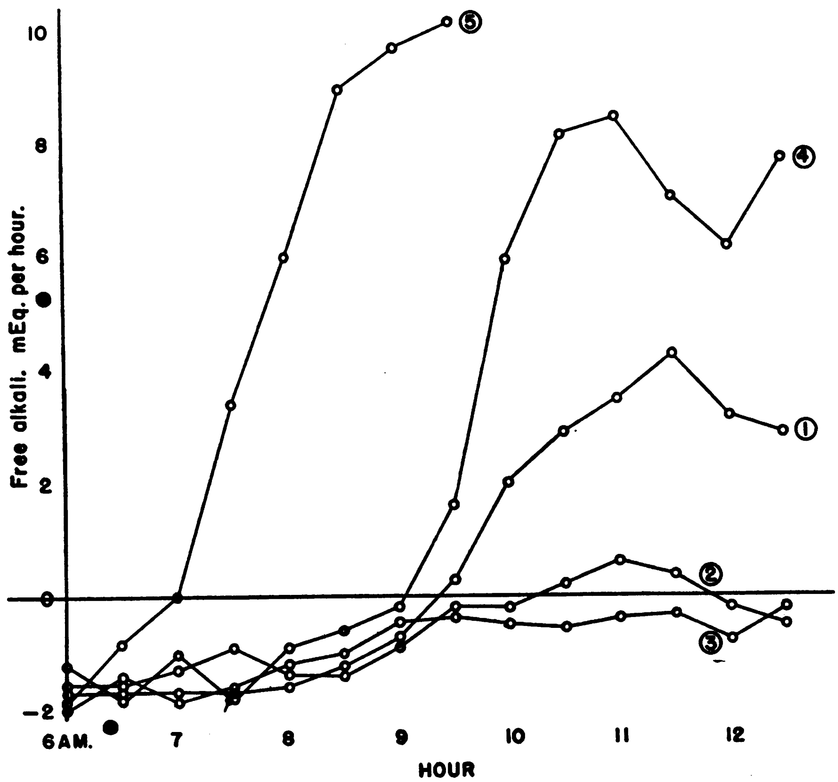

FIG. 3. EFFECTS OF EXERCISE AND OF INGESTION OF ALKALI ON THE MORNING OUTPUT OF ALKALI. SUBJECT A.

1. Mean basal curve.
2. Subject at quiet work in the laboratory.
3. Heavy exercise the day before.
4. One liter of orange juice at 10 p.m. the night before.
5. Three grams of soda at 10 p.m. the night before.

Diuresis, which has been held responsible for increased alkali excretion through failure of the kidney to retrieve bicarbonate is also an inadequate explanation, since a highly acid urine may be excreted with high volume output. Variations in urinary volume, however, have an undeniable influence on the output of alkali. In our low-volume series, it will be noted that with increasing alkali output there was an increase in urinary volumes. This is seen in the mean values of Table I and was noted in each of the individual experiments of that group. And when the volumes were greatly increased by water ingestion, without otherwise changing the conditions of the experiment, the large volumes contained a significantly greater amount of alkali than did the small volumes of corresponding time periods in the low-volume series (Figure 1). This might be considered evidence favoring the diuresis hypothesis. But considering the two curves as a whole it is apparent that the high-volume curve differs from the low-volume curve mainly in being displaced to the left. The alkali excretion under diuresis begins sooner and reaches its maximum sooner. In its later portion it lies slightly higher, but whether significantly so cannot be determined from our present data. We conclude that diuresis may be a factor in the production of a more rapid and perhaps slightly greater tide, but that it is not the primary cause of the tide.

which occur after eating, concluded that since the alkali reserve of the systemic blood does not increase during the secretion of gastric acid, the increased blood alkali resulting from gastric secretion must be stored temporarily in an "Alkalidepot," and that the later mobilization of this alkali for use in the alkaline intestinal secretions results in alkalinity of blood and urine.

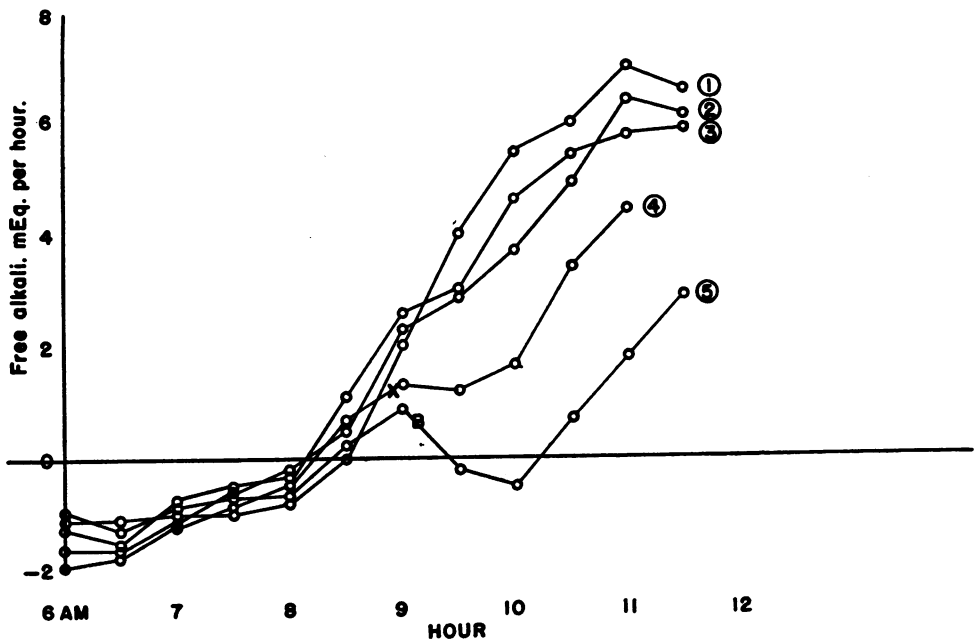

FIG. 4. EFFECTS OF MILD EXERCISE AND OF BREAKFAST ON MORNING ALKALI EXCRETION. SUBJECT B.

1, 2, 3. Normal curves.
4. At *X* the subject (150 pounds) stepped on and off a chair (17 inches) ten times in about 30 seconds.
5. Breakfast at *B*.

Diminished sensitivity of the respiratory center at night with return to a state of greater irritability on waking in the morning is an attractive hypothesis to account for the morning alkalinity of the urine. Cullen and Earle (6) have reported, however, that the observed changes in blood pH and bicarbonate do not support this view. The observation that the spontaneous morning alkaline tide may continue throughout the entire day would also speak against respiratory adjustment as a prominent factor in the production of the tide.

Jansen and Karbaum (5), investigating the changes in blood bicarbonate and carbon dioxide

It seems to us that the existence of temporary accumulations of alkali, presumably in the liver, with increased or decreased discharge into the blood in response to certain influences, would perhaps best explain certain characteristics of the alkaline tides. Experimentally, Beckmann (7) has reported that the injection of soda solution into the portal vein in dogs produces no immediate rise in the bicarbonate of the arterial blood. The increased morning alkaline tide after a normally acid night and early morning urine, which we have found when soda or orange juice is taken the evening before, would be adequately accounted for by this mechanism. The sharp and immediate inhibition of the daytime alkaline tide by very slight exercise and by taking food, events which would not be expected to have any immediate influence on the acid-base equilibrium, suggests also that the alkali excretion is an incidental matter possibly subject to reflex influences rather than the result of necessary physiological processes taking place at the moment.

distortion of the normal diurnal alkaline tide. Two items of evidence on this point are of interest. Figure 5 shows two all-day curves from Subject B under nearly identical conditions, except that on one day the subject had no food, while on the other he was given a breakfast at 6:30 a.m. After the breakfast he shows an alkaline tide which rises higher than the spontaneous diurnal tide, and which has a much shorter duration. But the total output of alkali on the two days is approximately the same. The breakfast appears merely to have brought about a more rapid excretion of the same supply of alkali. The other evidence is the observation of numerous investigators that when three meals are taken during the day there is a marked alkaline tide after breakfast, a smaller tide after the noon meal, and a very small tide or none at all after dinner in the evening, as though the supply of alkali were depleted by that time.

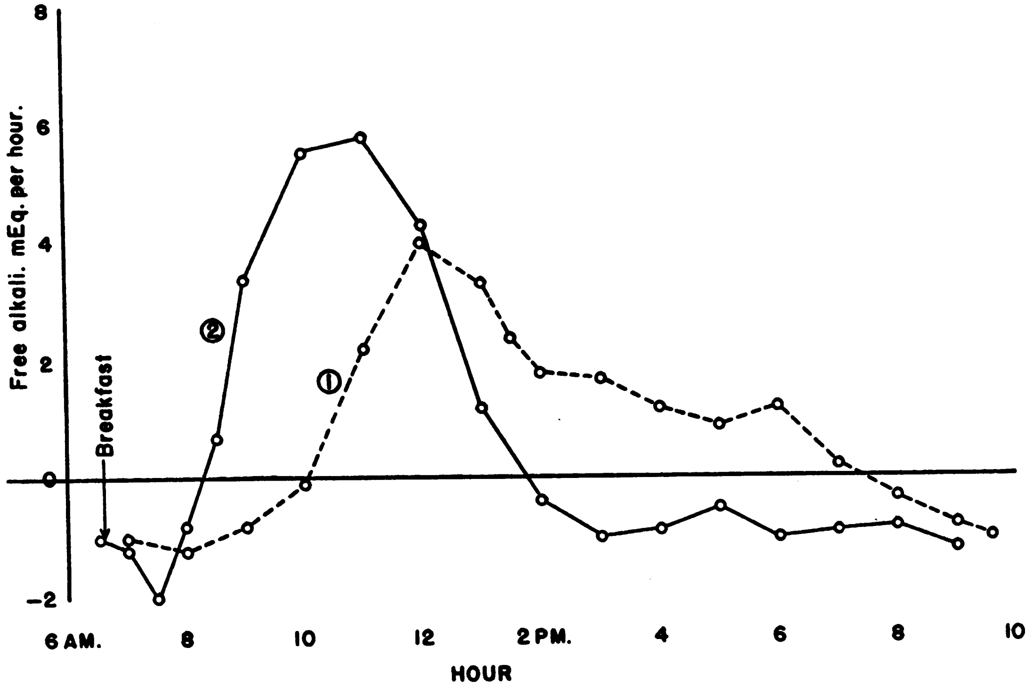

FIG. 5. ALL-DAY GRAPHS OF ALKALI EXCRETION. SUBJECT B.
1. No food or fluid taken.
2. Breakfast at 6:30.

In this connection the investigations of Forsgren (8) on the diurnal cycle of the liver are of interest. He has presented evidence that the liver stores up certain substances at night (assimilatory phase) and discharges them into the blood in the daytime (dissimilatory phase). Since a considerable part of the exogenous supply of body alkali first appears as such in the liver, and since the daytime alkaline tide coincides in time with the daytime dissimilatory phase of liver activity, it seems not unreasonable to suspect a nocturnal accumulation of alkali in the liver, release of which in the daytime would contribute to the morning alkaline tide. Indeed it may be wondered whether the alkaline tide after meals represents an accession of alkali from a new source, or whether it may not be merely a

SUMMARY

1. Quantitative measurements of the so-called morning alkaline tide in two normal resting subjects are reported.

2. In the undisturbed subject the spontaneous alkaline tide persisted throughout the day.

3. The morning alkaline tide appeared earlier under water diuresis, and was temporarily inhibited by light exercise and by the ingestion of food. Soda or orange juice taken the night before produced a larger morning alkaline tide, with little effect on acid excretion during the intervening night period.

4. The origin of alkaline tides is discussed, and it is suggested that varying discharge into the blood stream of alkali held in the liver may contribute to diurnal variations in the excretion of free acid and alkali.

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