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CIRCADIAN RHYTHMS OF URINARY EXCRETION: THE RELATIONSHIP BETWEEN THE AMOUNT EXCRETED AND THE CIRCADIAN CHANGES

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SUMMARY

1. The circadian rhythms of urinary excretion of water, sodium, chloride, potassium, urate, calcium and phosphate have been studied in several groups of volunteers.

2. These rhythms have been measured: under nychthemeral and constant routine regimens; while subjects were in an Isolation Unit or allowed free egress into society; with spontaneous changes in dietary intake; or after potassium-loading.

3. A direct relationship between 24 h mean rate of excretion and range of excretion was found in all circumstances and for all variables; this relationship was found also when the mesor and amplitude of the cosine curve best describing each 24 h of data were considered.

4. These relationships derive from the observation that, with increases in 24 h mean rates of excretion, nocturnal rates increased less than diurnal rates.

5. This differential sensitivity as between the night and day times has both endogenous and exogenous components.

6. It is suggested that circadian rhythms of urinary excretion result at least partially from this differential sensitivity of the kidney to homeostatic control mechanisms.

INTRODUCTION

The nychthemeral (i.e. over a period of 24 h) rhythms of urinary excretion of many substances in the urine have often been described, both with and without statistical analyses (Bartter, Chan & Simpson, 1979; Conroy & Mills, 1970; Halberg, Reinhardt, Bartter, Delea, Gordon, Reinberg, Ghata, Halhuber, Hofmann, Gunther, Knapp, Pena & Garcia-Sainz, 1969; Mills, 1966; Minors, Mills & Waterhouse, 1976; Wesson, 1964). Under many other circumstances – after time-zone transitions, during shift work and on non-24 h days, reviewed by Minors & Waterhouse (1981) – the circadian rhythms of urinary excretion have given information regarding endogenous and exogenous factors in producing a particular rhythm. However, when the mechanisms by which these rhythms originate have been considered (Conroy & Mills, 1970; Mills, 1966, 1973; Moore-Ede, Brennan & Ball, 1975), it seems that no single cause (plasma concentration, glomerular filtration rate, hormonal influence) can readily account for any rhythm under all circumstances.

Furthermore, the kidneys play a vital role in the control of body fluid composition, having to conserve substances at some times and to remove them at others. As a result of this, the daily mean rate of urinary excretion of many substances can vary over a wide range. It has been observed, both by considering the rate of excretion of a substance during the course of a nychthemeron (Goldsmith, Siemsen, Mason & Forland, 1965; Mann, 1972; Mann, Stiller & Korz, 1976; Wesson, 1964) and by fitting cosine curves to such data (Lewis & Lobban, 1956; Mills & Waterhouse, 1973), that there is a direct relationship between the mean rate of excretion over the course of the 24 h (or the mesor of a fitted cosine curve) and the difference between maximum and minimum rates (or twice the amplitude of a fitted cosine curve). Indeed this relationship is tacit in the use of the 'relative amplitude' (defined as the ratio of amplitude to mesor) to describe a circadian rhythm of urinary excretion (Lewis & Lobban, 1956; Sollberger, 1955).

TABLE 1. Details of subjects

Group	Number	Age	Where studied	No. of nychthemera	Conditions	n
A	20 F, 26 M	18–22	Isolation unit A1	1–3	Nychthmeral	88
			Isolation unit A2	1	Constant routine	46
B	4 M	19, 20	Isolation unit	11	Nychthemeral	44
C	1 F, 3 M	18–31	Society	7–13	Nychthemeral	45
D	4 M	18–20	Society	9	Nychthemeral, K^+-loaded and depleted	36

F, female; M, male; n, number of subject-days.

METHODS

Four groups of presumed healthy subjects have been studied, some details of whom are given in Table 1. Groups A and B were investigated in an Isolation Unit, fully described by Elliott, Mills, Minors & Waterhouse (1972). This unit provided a constant ambient temperature and humidity. Subjects were asked to adopt standard times for sleep in darkness (24.00–08.00 h) and eating meals (08.30, 13.00, 18.30 h). The exact composition of meals and snacks was left to the subjects but this was determined in broad terms by the type of food provided. Group A was studied under two conditions: first, in nychthemeral conditions for 1–3 d (group A1) and afterwards during a constant routine (group A2), details of which have been given elsewhere (Mills, Minors & Waterhouse, 1978*a*). In principle, during the constant routine, subjects stayed awake and sedentary in constant conditions for 24 h (starting at 04.00 h) and took an identical snack each hour, the composition of which resulted in a normal 24 h intake of sodium (200 mmol), chloride (200 mmol) and potassium (80 mmol). Groups C and D were asked to adhere to similar times of meals, retiring and rising, but, by virtue of being allowed free access to society, lived in an environment which was considerably more variable than that of groups A and B. Nevertheless, the subjects of these groups (C and D) were asked to refrain from undue exercise on the days under study. Group D lived for the first half of the experiment on a potassium-restricted diet (average daily intake 50 mmol) and for the second 5 days on the same diet supplemented by potassium chloride (average daily intake 150 mmol).

In all experiments, subjects gave timed samples of urine about every 2 h (hourly on the constant routines) while awake and a sample on waking. The volume of each was measured and an aliquot refrigerated for later analysis. Analysis of sodium, chloride, potassium, creatinine, calcium, phosphate and urate was performed by Auto Analyzer II. The rate of excretion of each constituent

was calculated for each sample and where necessary correction for bladder-emptying errors was made (Longson & Mills, 1953).

The statistical and methematical analyses will be described in the Results section where appropriate. At this stage it is pointed out that when correlation co-efficients were calculated, all days from all subjects were treated independently. Thus, if four subjects each contributed 10 d data, forty datum points would contribute to the calculation of the correlation co-efficient.

For the present purposes, the nychthemeron was defined as the period of 24 h from 04.00 to 04.00 with night spanning 24.00–08.00 h. Inspection of subjects' record cards indicated that during nychthemeral conditions only insubstantial periods of waking took place at 'night' and that there was negligible sleep during the day.

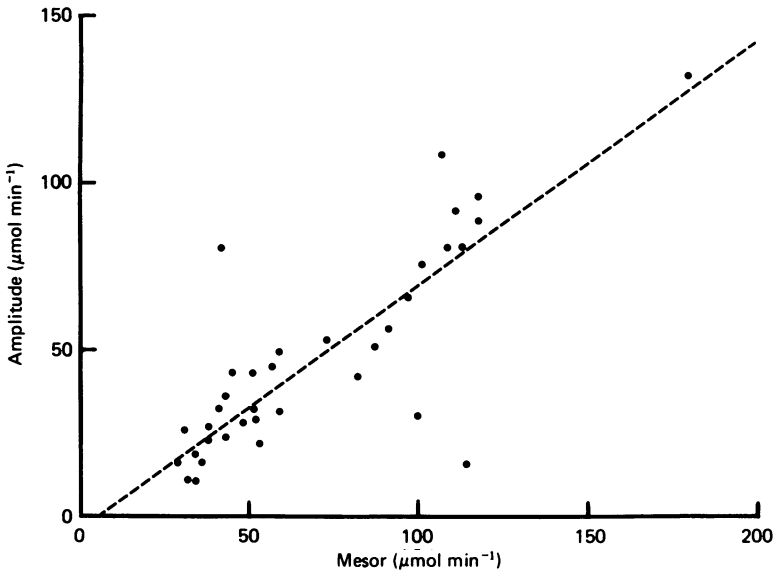

Fig. 1. The regression of amplitude upon mesor for urinary potassium excretion of group D. Each point is derived from the 24 h cosine curve fitted to a single nychthemeron. Four subjects, nine nychthemera each.

RESULTS

Nychthemeral conditions

The relationship between within-day variation in excretory rates and mean 24 h excretion.

For each constituent, a 24 h cosine curve was fitted to the data from each nychthemeron for each subject by the method of Fort & Mills (1970). From each curve were extracted the parameters mesor and amplitude (with a cosine curve, the amplitude is defined as the difference between mesor and peak). For each group, a linear regression analysis of amplitude upon mesor was then performed for each constituent upon all data points. An example is shown in Fig. 1. Parameters m (gradient) and c (intercept upon amplitude axis) are shown in Table 2 for each constituent. In a similar way, for each constituent, the 24 h mean excretory rate and range of excretory rates (difference between maximum and minimum values) were calculated for each subject and nychthemeron. Then, as before, a linear regression

TABLE 2. Parameters m (gradient) and c (intercept upon amplitude or range of excretion axis) for linear regression analyses performed upon all groups and constituents

	Regression of amplitude upon mesor										Regression of range of excretion upon 24 h mean rate of excretion									
	m					c					m					c				
	A1	B	C	D	A2	A1	B	C	D	A2	A1	B	C	D	A2	A1	B	C	D	A2
Flow	0·79 ±0·06	0·67 ±0·13	0·72 ±0·09	1·13 ±0·08	0·57 ±0·12	0	0	0	0	0	2·03 ±0·21	2·73 ±0·43	3·71 ±0·34	3·55 ±0·29	2·79 ±0·40	0	0	0	0	0
Sodium	0·46 ±0·07	0·53 ±0·09	0·75 ±0·09	1·05 ±0·14	0·30 ±0·06	0	0	0	0	0	1·05 ±0·16	1·05 ±0·23	1·45 ±0·28	2·00 ±0·33	1·11 ±0·13	0	0	0	0	0
Potassium	0·71 ±0·07	1·12 ±0·08	0·73 ±0·08	0·72 ±0·08	0·60 ±0·10	0	−53, −8*	0	0	0	1·45 ±0·20	2·83 ±0·23	1·48 ±0·21	1·84 ±0·14	1·43 ±0·21	0	−139, −14*	0	0	0
Chloride	0·49 ±0·07	0·59 ±0·10	0·67 ±0·09	0·87 ±0·14	0·36 ±0·07	0	0	0	0	0	1·12 ±0·13	1·20 ±0·25	1·21 ±0·22	1·51 ±0·32	1·36 ±0·15	0	0	0	0	0
Phosphate	0·23 ±0·06	0·45 ±0·12	n.s.	n.s.	0·27 ±0·08	0	0	n.s.	n.s.	0	1·06 ±0·15	1·49 ±0·30	0·71 ±0·27	n.s.	0·57 ±0·19	0	0	0	n.s.	0
Calcium	0·23 ±0·06	0·38 ±0·07	0·25 ±0·10	0·28 ±0·05	n.s.	0	0	0	0	n.s.	0·59 ±0·14	0·85 ±0·18	0·74 ±0·20	0·85 ±0·12	0·81 ±0·19	0	0	0	0	0
Urate	0·29 ±0·07	0·42 ±0·06	0·28 ±0·12	0·68 ±0·12	0·32 ±0·08	0	0	0	0	0	0·73 ±0·17	0·81 ±0·18	n.s.	1·21 ±0·20	1·00 ±0·18	0	0	n.s.	0	0

Values are means±S.E. of mean. A1, B, C, D, A2 refer to the different groups. 0, intercept not significantly different from zero ($P > 0·05$); *, 95% confidence interval (μmol min^{-1}); n.s., correlation co-efficient not significantly different from zero.

analysis of range upon 24 h mean was performed. These parameters also are shown in Table 2.

A number of points emerge from this Table, for both linear regression analyses. (1) A direct relationship between the two parameters was found in all groups and for all constituents (with the partial exception of phosphate excretion which will be considered in the Discussion). (2) For any constituent the gradient of the line for the regression of range of excretion upon mean rate of excretion was greater than that for the regression of amplitude upon mesor. (3) Although some significant differences between groups for parameter m were found for a particular constituent, when the different constituents were ranked in descending order of m, then the groups behaved similarly (Table 3) with the ranks for flow and potassium highest, and those for calcium, urate and phosphate lowest. Friedman's two-way analysis of variance performed upon the ranking of the m values from the regressions of the amplitudes upon the mesors gave no significant difference between the groups ($P > 0{\cdot}95$) and a significant difference between the constituents ($P < 0{\cdot}005$). A very similar ranking and statistical result was obtained when the m values from the regressions of the ranges of excretion upon the mean rates of excretion were considered. (4) The parameter c rarely differed significantly from zero ($P > 0{\cdot}05$).

TABLE 3. Ranking of m values for the linear regression of amplitude upon mesor for all groups and constituents

	Group			
	A1	B	C	D
Flow	1	2	3	1
Sodium	4	4	1	2
Potassium	2	1	2	4
Chloride	3	3	4	3
Phosphate	6·5	5	7	7
Calcium	6·5	7	6	6
Urate	5	6	5	5

The relationship between diurnal and nocturnal excretory rates

The direct relationships found above between mean nychthemeral excretory rates and circadian variations in excretion of a substance could, in principle, derive from the following possibilities. As mean nychthemeral excretory rate increased: (1) the increase could be confined to the diurnal period, nocturnal values falling; (2) the increase could be confined to the diurnal period, nocturnal values remaining unchanged; (3) the increase could occur throughout the nychthemeron with nocturnal increases being substantially less than those diurnally. These possibilities can be distinguished by comparing, for each constituent, the relationship between nychthemeral (04.00–04.00 h) and nocturnal (24.00–08.00 h) rates of excretion. An example of this comparison is illustrated in Fig. 2 and the results of the linear regression analyses for all constituents and groups are shown in Table 4.

A number of points emerge from this Table. (1) Increases in the nychthemeral rate of excretion are associated with significant ($P < 0{\cdot}05$) nocturnal increases; this result

disproves the first two possibilities (above). (2) With the exception of phosphate, all values for m are significantly less than unity ($P < 0{\cdot}05$) that is, the nocturnal is less than the nychthemeral increase. (3) Although, for any constituent, different values of m are found in different groups, when these values are ranked as before, then the groups behave similarly. Also the ranking is the *inverse* of that in Table 3 with calcium, urate and phosphate now highest and potassium and flow lowest. (4) With the partial exception of flow (see Discussion), most values for parameter c do not differ significantly from zero ($P > 0{\cdot}05$).

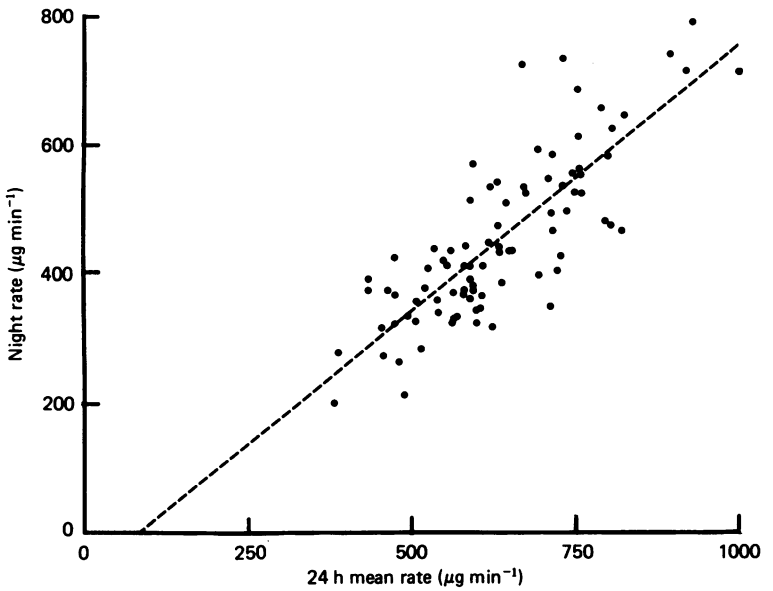

Fig. 2. The regression of nocturnal (24.00–08.00 h) upon 24 h mean excretory rate (04.00–04.00 h) for urinary urate of group A1. Forty-six subjects, one to three nychthemera each.

Constant routine conditions

Data from these experiments (group A2) are included in Tables 2 and 4. In these conditions there are no differences as far as the subjects' behaviour is concerned between night and day; nevertheless, for the purposes of the analysis, 'nocturnal', 'nychthemeral', etc. refer to the same clock hours as before. The comments that applied to the nychthemeral conditions apply to the constant routine data. (1) For all constituents there are direct relationships between the 24 h mean excretory rate and the range and between mesor and amplitude (when a cosine curve is fitted to each nychthemeron). (2) Parameter m is greater when the regression of 24 h range upon mean rather than that of amplitude upon the mesor is considered. (3) The ranks for parameter m of different constituents are similar to those of group A1 in Table 3. (4) For all constituents there are significant ($P < 0{\cdot}05$) relationships between 24 h mean rate of excretion and nocturnal excretion. For phosphate, calcium and urate,

TABLE 4. Parameters m (gradient) and c (intercept upon nocturnal excretory rate axis) for linear regression analysis of nocturnal excretory rate upon 24 h mean excretory rate performed upon all groups and constituents

	Regression of nocturnal excretory rate upon 24 h mean excretory rate									
	m					c				
	A1	B	C	D	A2	A1	B	C	D	A2
Flow	0·45 ± 0·06	0·66 ± 0·12	0·13 ± 0·05	0·23 ± 0·04	0·55 ± 0·12	0	0	0·18, 0·78*	0·10, 0·49*	0
Sodium	0·69 ± 0·07	0·65 ± 0·07	0·38 ± 0·09	0·26 ± 0·09	0·75 ± 0·06	0	0	0	0	0
Potassium	0·47 ± 0·05	n.s.	0·31 ± 0·06	0·48 ± 0·05	0·54 ± 0·07	0	n.s.	0	0	0
Chloride	0·65 ± 0·06	0·57 ± 0·07	0·34 ± 0·09	0·37 ± 0·08	0·75 ± 0·06	0	0	0	0	0
Phosphate	1·01 ± 0·06†	0·64 ± 0·09	0·75 ± 0·16†	1·21 ± 0·25†	0·96 ± 0·09†	0	1·6, 21·2*	0	0	0
Calcium	0·88 ± 0·06	0·85 ± 0·06	0·70 ± 0·09	0·77 ± 0·04	1·02 ± 0·08†	0	0	0	0	0
Urate	0·82 ± 0·06	0·62 ± 0·05	0·60 ± 0·10	0·46 ± 0·09	0·93 ± 0·06†	0	0	0	0	0

0, n.s., as defined for Table 2; *, 95% confidence limits (μg min^{-1} for phosphate, ml min^{-1} for flow); †, not significantly different from unity ($P > 0·05$).

parameter m is statistically indistinguishable from unity; for the other constituents, values are less than unity, that is, nocturnal increases are less than nychthemeral. (5) The ranking of m values in Table 4 tended to be the inverse of that found for m values in both linear regression analyses of Table 2. (6) For no regression lines were there values of c significantly different from zero ($P > 0{\cdot}05$).

DISCUSSION

The present study has shown that, for healthy subjects, when the urinary excretory data from a number of nychthemera and subjects are described by best-fitting cosine curves, then a direct relationship exists between the mesors and the amplitudes of these curves. This confirms the results of others (Lewis & Lobban, 1956; Mills & Waterhouse, 1973). The finding is not a spurious result of the cosine–curve fitting technique since the same data could be used to show a direct relationship between the 24 h mean rate of excretion and the circadian range of excretion (Table 2). Such a result has been found before with urinary data (Goldsmith *et al.* 1965; Mann, 1972; Mann *et al.* 1976; Wesson, 1964), with other variables, for example reaction time (Mann, Rutenfranz & Wever, 1972), and in other species (Aschoff & von Saint Paul, 1973; Sollberger, 1955). Interestingly, in Fig. 2 of the renal study of Mann *et al.* (1976), values of the ratio (range of oscillation/mean of oscillation) for sodium and potassium were approximately 1·25 and 1·7 respectively, values close to those of m in our Table 2.

Inspection of Table 2 indicates that the parameter m of the regression lines has a larger mean and standard error when the range and 24 h mean are considered rather than the amplitude and mesor. This is to be expected, first, since the amplitude of a cosine curve is only one half the difference between the maximum and minimum values of the cosine curve and, secondly, because the range depends upon only two values whereas the amplitude of the cosine curve is computed from all data. It is noteworthy also that for sodium, chloride and potassium, variables with considerable endogenous components (Minors & Waterhouse, 1981), the range of excretion is approximately twice the amplitude of the cosine curve, whereas, for the other variables with larger exogenous components a value in excess of double is often found. Nevertheless, the rankings of parameter m by either analysis are very similar and comment on the possible significance of these rankings will be made later.

The regression of nocturnal rate of excretion upon 24 h mean rate of excretion (Table 4) indicates that the kidney is, on average, less able to excrete substances during the night than during the rest of the nychthemeron. In fact, the comparison of nocturnal with total 24 h excretion, as here, underestimates the relative amounts of material excreted diurnally rather than nocturnally. For example, if the average value for parameter m is 0·6, it can be simply shown that the diurnal rate is 2 times the nocturnal rate of excretion, that is four-fifths of the load is excreted diurnally. The inverse relationship between the ranks of m in Tables 2 and 4 has already been mentioned. This is not unexpected. Thus, if there is a marked nocturnal–diurnal difference in the ability of the kidneys to deal with an excess of material, this will manifest itself as a marked diurnal increase, that is, there will be a large circadian range or amplitude of excretion. By contrast, if the kidneys show little circadian

variation in their ability to get rid of excess material, then the maximum–minimum difference will be slight.

This greater sensitivity of renal reflex mechanisms during the day-time as compared with the night-time has been observed in humans before. Thus Vagnucci, Shapiro & McDonald (1969) found that the saliuresis following recumbency was far less marked at 04.00 than at 19.00 and a similar conclusion has been drawn by Kass, Sulzman, Fuller & Moore-Ede (1980) as a result of their studies upon central vascular expansion in a primate. Such a differential sensitivity of a system involved in homeostatic control processes has been observed also in non-renal systems, for example: chemoreceptor reflex responses to carbon dioxide (Bulow, 1963); cardiovascular responses to postural changes and to exercise (Klein & Wegmann, 1980); and thermoregulatory responses to thermal loads (Aschoff & Heise, 1972).

As has already been described, this differential sensitivity can be invoked to account for the relationship between mesor and amplitude and between 24 h mean and range that we have found. Furthermore, since the value of the parameter *c* was indistinguishable from zero, whether one considered the regressions of range upon 24 h mean, amplitude upon mesor (Table 2) or nocturnal rate of excretion upon 24 h mean rate of excretion (Table 4), then it is possible that these relationships hold throughout wide ranges of excretion. If this is so, then the normal circadian rhythm observed in nychthemeral circumstances can be speculated to be, at least in part, a result of this phenomenon of increased diurnal sensitivity. At this stage it should be pointed out that an alternative explanation has been put forward (Wever, 1963). This explanation is based upon the observations that the internal clock behaves as a pendulum oscillator and that theory predicts that such an oscillator will manifest a direct relationship between mean and amplitude of oscillation. Such a view has been elaborated upon in connexion with renal function by Mann *et al.* (1976). At the moment a decision in favour of either view cannot be taken and it might well transpire that the two views are in no way incompatible.

The factors which mediate these nychthemeral changes in sensitivity are not known (but for some discussion of this see Minors & Waterhouse, 1981) but the nychthemeral conditions under which experiments A1, B, C and D were performed might well play a role (Aschoff, 1978). Thus, during the night sleep took place (and this is known to decrease the rate of excretion of a number of substances: Mills, Minors & Waterhouse, 1978*b*) and during the day-time meals were taken. However, the position is complicated since these exogenous influences are not equally strong for all constituents. Thus, whether the changes after non-24 h days (Mills, Minors & Waterhouse, 1977; Simpson, Lobban & Halberg, 1970), time-zone shifts (Aschoff, Hoffmann, Pohl & Wever, 1975; Elliott *et al.* 1972) or shift work (Chaumont, Laporte, Nicolai & Reinberg, 1979; Vieux, Ghata, Laporte, Migraine, Nicolai & Reinberg, 1979) are considered, some constituents (for example, flow, calcium and urate) have large, others (potassium) small, and others (sodium, chloride) moderate exogenous components. For these reasons, the constant routine experiments were performed in which exogenous rhythmicity was minimized.

The results from these constant routine experiments lead to a number of conclusions. (1) The differential sensitivity between night and day has an endogenous component since it persists in conditions in which nocturnal–diurnal differences have

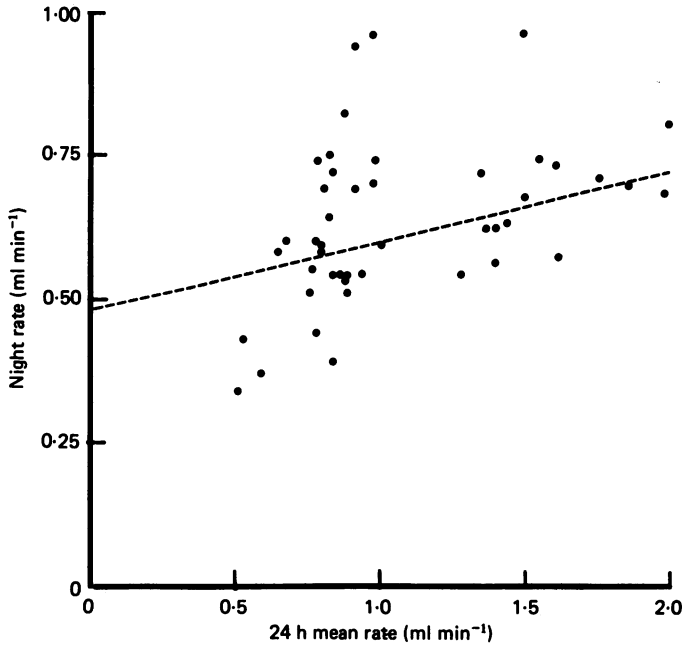

Fig. 3. The regression of nocturnal upon 24 h mean excretory rate for urinary flow of group C. Four subjects, seven to thirteen nychthemera each.

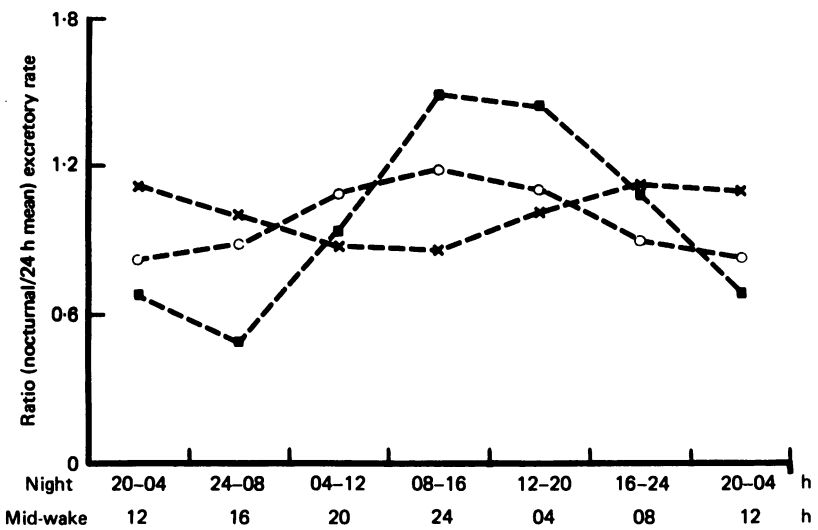

Fig. 4. Potassium (■), urate (○), and phosphate, X, data from group A2 during constant routine. Relationship between 'nocturnal'/24 h mean excretory rate (ordinate) for different times of 'night' and 'mid-waking' (abscissa). For more details, see text.

been minimized. (2) The ratio (nocturnal/24 h mean rate) tends to be higher on the constant routine when compared with nychthemeral conditions (compare groups A1 and A2 in Table 4). A simple explanation is that the constant routines remove the 'masking', exogenous effects of sleep and meal-times observed in nychthemeral conditions (Aschoff, 1978; Mills *et al.* 1978*b*); thus nocturnal values are less depressed and the effect of meals is not confined to the day time. (3) The ratio (nocturnal/24 h mean rate) rises for calcium and urate until it is not significantly different from unity. This suggests that the endogenous component of differential sensitivity is weak in these two constituents.

Considered together, the nychthemeral and constant routine data imply that there are both endogenous and exogenous components to the observed differential sensitivity. It can be further speculated that the relative size of these components depends not only upon the constituent under consideration but also upon details of the regimen; these factors might account for the different values for m between different groups (Tables 2 and 4).

In some respects the results for urinary flow are anomalous. Thus it is generally accepted as having a high exogenous component (Lewis & Lobban, 1957; Mills *et al.* 1977; Simpson *et al.* 1970) and yet it is ranked very differently from calcium and urate (Table 3). A contributing factor might be that, under nychthemeral conditions, increases in 24 h mean excretion will result from increased diurnal uptake and, because the renal response to water intake is so rapid, this will result in an increased diurnal output. Thus the amplitude and range will be raised markedly and the ratio (nocturnal/24 h mean rate) will be lowered. Such an argument would not apply to, for example, potassium since the renal response to 'loading' is far slower (Bia & De Fronzo, 1981). Some evidence in favour of this explanation can be found in Fig. 3 in which it can be seen that at high 24 h mean excretory rates, the ratio (nocturnal/24 h mean rate), tends to rise less steeply producing a 'dog-leg' effect. A mathematical result of this is that the regression line fitted to all the data takes on a slightly lesser (underestimated) slope with a positive value for parameter c (see Table 4, groups C and D). More formally, in groups C and D there was a significant fall in the value of the ratio (nocturnal/24 h mean rate) with increasing values of the 24 h mean rate. However, this cannot be the whole explanation since the anomalously low value of m persists in constant routine conditions (Table 4); the reason for this is unknown.

Inspection of Tables 2 and 4 indicates that phosphate also behaves differently from the other constituents. Phosphate shows a rate of nocturnal excretion which approximately equals the 24 h mean rate in both nychthemeral and constant routine conditions (Table 4); this will account for low values for parameter m in Table 2. A partial explanation may be that the acrophase of the cosine curve best describing the rhythm of phosphate excretion is not in the middle of the period of wakefulness, as for the other constituents considered here, but just before 'night' (Halberg *et al.* 1959; Minors *et al.* 1976). The effect of this is demonstrated in Fig. 4 for phosphate (group acrophase 18.24) and, as a comparison, potassium (group acrophase 12.54) and urate (group acrophase 11.18). The constant routine data have been used since these alone consist of equally spaced data points. This Figure shows the ratio (nocturnal/24 h mean rate) where 'nocturnal' has been defined in six different ways, always consisting of eight adjacent hours but starting at 24.00 (normal), 04.00, 08.00, 12.00,

16.00 and 20.00 h. It can be seen that when 'night' spans the acrophase then the ratio is about maximum, but, when the time of 'mid-wakefulness' and the acrophase coincide, then ratio is at or near its minimum. Interestingly, the range of values for the ratio for urate and phosphate is similar but that for potassium is considerably higher. This might again indicate the stronger endogenous component for potassium in contrast to that for phosphate or urate.

Teleologically, the advantages of having a decreased reflex sensitivity during the night (when intake is negligible and output due to postural changes would tend to be high) are obvious enough, but it is interesting to speculate to what extent the hypothesis and speculations above would apply in conditions when renal circadian rhythms are altered (Aslanian, Assatrian, Bagdassarian, Kurginian & Shukhian, 1978; Hillier, Knapp & Cove-Smith, 1980; Wesson, 1979, 1980). Thus the inverted rhythms associated with cardiac failure have been attributed to inappropriate renal responses to postural changes (Conroy & Mills, 1970). To what extent might these changes be reflexions of abnormal differential renal sensitivity?

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