

*Original Article*

## Seasonal variations in serum sodium levels and other biochemical parameters among peritoneal dialysis patients

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### Abstract

**Background.** Although modest seasonal variations in blood biochemical composition have been reported in end-stage renal disease patients treated with haemodialysis, there have been no adequate explanations. The current study aimed to explore whether these phenomena are present in peritoneal dialysis patients and to discuss these variations.

**Methods.** This was a retrospective study with an enrollment of 44 anuric PD patients. Serum biochemical parameters, peritoneal function, dialysis adequacy, peritoneal ultrafiltration volume and body weight were analysed in relation to climate variables for a study period of 2 years.

**Results.** PD patients exhibited cyclic variations in blood biochemical concentrations. Monthly mean outdoor temperature was inversely correlated with serum concentrations of sodium ( $r = -0.712$ ,  $P < 0.001$ ), potassium ( $r = -0.697$ ,  $P < 0.001$ ), bicarbonate ( $r = -0.642$ ,  $P < 0.001$ ), BUN ( $r = -0.654$ ,  $P < 0.001$ ), albumin ( $r = -0.496$ ,  $P = 0.012$ ), peritoneal ultrafiltration volume ( $r = -0.723$ ,  $P = 0.001$ ) and body weight ( $r = -0.623$ ,  $P < 0.001$ ). Serum chloride and creatinine concentrations were not correlated with temperature or other climate variables.

**Conclusions.** PD patients showed seasonal variations in serum electrolyte concentration and peritoneal ultrafiltration volume. Monthly outdoor mean temperature was inversely correlated with serum electrolytes and ultrafiltration volume. A likely explanation is loss of these electrolytes through perspiration. Neglect of this annual cycle in PD patients may lead to

biases in interpretation of clinical study and individual laboratory data.

**Keywords:** electrolyte; end-stage renal disease; peritoneal dialysis; perspiration; seasonal variation; ultrafiltration

### Introduction

In the general population, seasonal variations have been demonstrated in calcium metabolism [1,2], affective disorder rate [3], cardiovascular disease risk [4,5] as well as numerous infectious [6,7] and rheumatologic diseases [8,9]. In end-stage renal disease (ESRD) patients, blood pressure varies seasonally, with higher values in the winter and lower values in the summer, and this is independent of treatment with haemodialysis (HD) [10–12], peritoneal dialysis (PD) [13] or renal transplantation [14]. In addition to blood pressure, seasonal variation may also affect blood biochemical composition in HD patients. Even though the magnitudes were modest, serum sodium, potassium, bicarbonate, BUN, albumin and ultrafiltration volume were reported to be higher in the winter and inversely correlated with outdoor temperatures in HD patients [11]. Although the authors suggested that seasonal protein intake may explain variations in BUN, they did not comment on the changes in electrolytes. In an additional study conducted in the Mediterranean region, higher total cholesterol, LDL cholesterol, albumin and glucose level were observed in warmer months among HD patients, and the authors speculated that these increases resulted from neuro-hormonal influences [15]. However, the primary mechanism responsible for these phenomena has not been well established. In order to identify the influence of climate on PD patients, we measured and analysed serum biochemical parameters during changes in climate variables.

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## Materials and methods

### Subjects

Forty-four anuric PD patients (M/F = 15/29) from Taipei Veteran General Hospital were enrolled and studied between October 2004 and October 2006. Their demographic data are listed in Table 1. The mean age was 52.4 years and the mean dialysis duration at first recording was 62.8 months. All patients received lactate-based PD fluid and the PD prescription varied according to individual need. The sodium, lactate and chloride levels of the PD fluid were 132, 40 and 96 mmol/l, respectively. The target dry weight for each patient was determined by his or her primary nephrologist. Body weight and serum biochemical data were recorded on monthly fixed days. Peritoneal membrane function was evaluated with a standard peritoneal equilibration test at six-month intervals. Both nKT/V and nWCC were calculated using 24-hr effluent at 4-month intervals. For analysis, data of peritoneal function and dialysis adequacy were divided into cold months and hot months based on calendar months. The PD dialysate consumption was obtained from delivery records from dialysate suppliers. In Taiwan, every PD patient keeps his or her record of daily ultrafiltration volume. The monthly mean of daily-recorded peritoneal ultrafiltration volume was used in this study.

### Assays

Blood samples were centrifuged and sera were measured immediately with a Hitachi 7600 chemical auto-analyzer (Hitachi, Co., Ltd, Tokyo, Japan). Albumin level was obtained by the BCG method. Serum sodium, potassium and chloride concentrations were analysed by ion selective electrodes. Bicarbonate concentration was measured by the PEPC method. BUN was measured by standard urease assays and creatinine level was measured by Jaffe reaction. Body weight was measured using an electrical scale with minimal units of 0.1 kg. The subjects were weighed with light clothes in a temperature-controlled room.

### Climatic data

As a subtropical island (22–25.5°N) within the Western Pacific Island chain, Taiwan experiences an annual variation in climate. This variation is basically established by the alternation of two monsoon components: the summer southwest monsoon and the winter northeast monsoon.

**Table 1.** Characteristics of PD patients at study onset

Characteristic	Value
Gender-M/F	15/29
Mean age (year)	52.4(36–67)
Treatment model (CAPD/APD)	38/6
Length of PD (month)	62.8(32–118)
nKT/V	2.17 ± 0.36
nWCC (l/week/1.73 m <sup>2</sup> )	55.83 ± 9.84
D/P creatinine ratio	0.67 ± 0.12
Dwell volume (l/day)	9.38 ± 1.91

Data are expressed in Mean ± SD.

Taipei (25°N), which is located in the north of Taiwan with a typical subtropical monsoon climate, has an abundant temperature variation and high relative humidity. Climate data were obtained from the Taiwan Central Weather Bureau (<http://www.cwb.gov.tw>). Monthly precipitation, monthly means of daily averages of temperature, and relative humidity measurements were used in the study.

### Statistical analysis

All data grouped according to calendar months were expressed as means ± SD. Data that were not normally distributed were analysed using non-parametric methods. D/D0, D/P ratio, nKT/V and nWCC were analysed with paired *t*-tests. Multivariate analysis was used to identify the effect of climate parameters on clinical and laboratory data. Statistical analysis was performed using SPSS 14.0 for windows web version provided by Taipei Veteran General Hospital. All probabilities were two-tailed. A *P*-value less than 0.05 was considered as statistically significant.

## Results

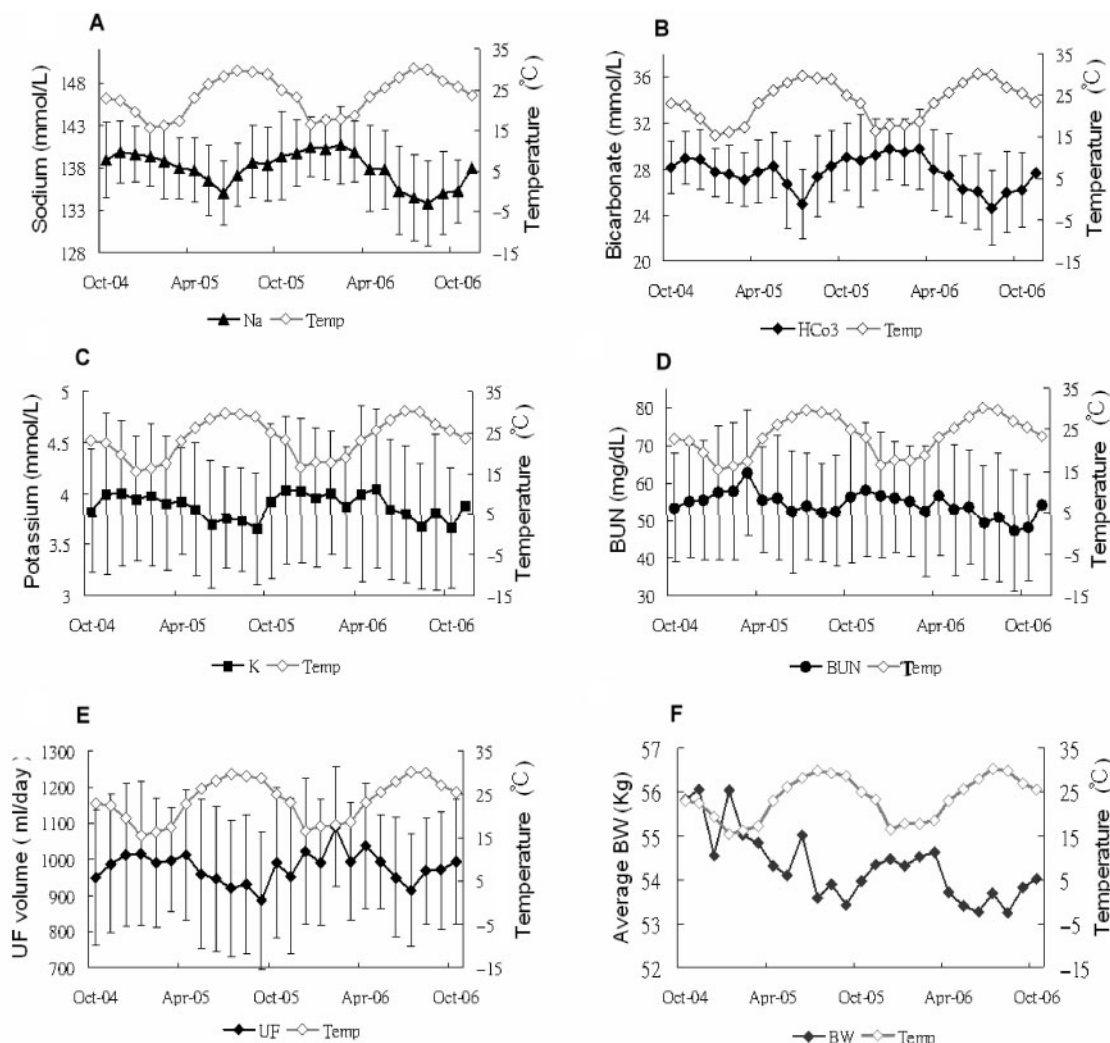
### Climatic data

During the 2-year study period, monthly mean outdoor temperatures ranged from 16°C in winter to 30°C in summer. Relative humidity ranged from 70 to 85%. Monthly precipitation ranged from 20 to 666 mm, with the most humid days occurring during the typhoon season and rainy months.

### Variations in biochemical data and ultrafiltration volumes

There was a cyclic variation in serum sodium, potassium, bicarbonate, BUN concentration and ultrafiltration volume during the 2-year study period (Figure 1). The mean (±SD) peak values of sodium (140.70 ± 4.5 mmol/l), potassium (4.05 ± 0.78 mmol/l), bicarbonate (29.72 ± 2.64 mmol/l), BUN (62.65 ± 16.75 mg/dl), albumin (4.05 ± 0.46 g/dl), peritoneal ultrafiltration volume (1089 ± 165 ml/day) and body weight (56.05 ± 10.26 kg) all occurred in the winter. The nadir values of sodium (133.74 ± 4.9 mmol/l), potassium (3.65 ± 0.55 mmol/l), bicarbonate (24.61 ± 3.20 mmol/l), BUN (47.3 ± 14.19 mg/dl), albumin (3.76 ± 0.38 g/dl), peritoneal ultrafiltration volume (886 ± 190 ml/day) and body weight (53.25 ± 10.76 kg) occurred in the summer.

Of the three climate variables that were studied, only monthly mean outdoor temperature was significantly correlated with the serum biochemical parameters (*P* < 0.05) in multivariate analysis. It was inversely correlated with serum sodium (*r* = −0.712, *P* < 0.001), potassium (*r* = −0.697, *P* < 0.001), bicarbonate (*r* = −0.642, *P* < 0.001), BUN (*r* = −0.654, *P* < 0.001), albumin (*r* = −0.496, *P* = 0.012), peritoneal ultrafiltration volume (*r* = −0.723, *P* < 0.001) and body weight (*r* = −0.623, *P* < 0.001). Chloride (*P* = 0.062) and creatinine (*P* = 0.65) were not correlated with temperature or the other climate variables. In the linear



**Fig. 1.** Longitudinal data of serum sodium (A), bicarbonate (B), potassium (C), BUN (D), UF volume (E) and body weight (F). Biochemical data and UF volume are expressed as means  $\pm$  SD. Monthly mean outdoor temperature is expressed in open squares. The biochemical parameters have a yearly cyclic pattern, with lower values in the summer and higher values in the winter.

regression model, the serum sodium concentration prediction equation was  $\text{Na (mmol/l)} = -0.31 \times \text{temperature (}^{\circ}\text{C)} + 145.18$ . These findings are summarized in Table 2 and Figure 2.

#### *Peritoneal function and dialysis adequacy*

We defined hot months as April to September and cold months October to March. There were no differences in D/D0 ( $0.391 \pm 0.057$  vs  $0.386 \pm 0.074$ ,  $P = 0.242$ ), D/P ratio ( $0.654 \pm 0.089$  vs  $0.654 \pm 0.102$ ,  $P = 0.686$ ), nWCC ( $60.85 \pm 11.43$  vs  $59.59 \pm 10.71$ ,  $P = 0.379$ ) or nKT/V ( $2.17 \pm 0.29$  vs  $2.20 \pm 0.31$  l/week/1.73m<sup>2</sup>,  $P = 0.851$ ) between hot and cold months.

## **Discussion**

In contrast to healthy individuals, ESRD patients are unable to maintain homeostasis. There have been

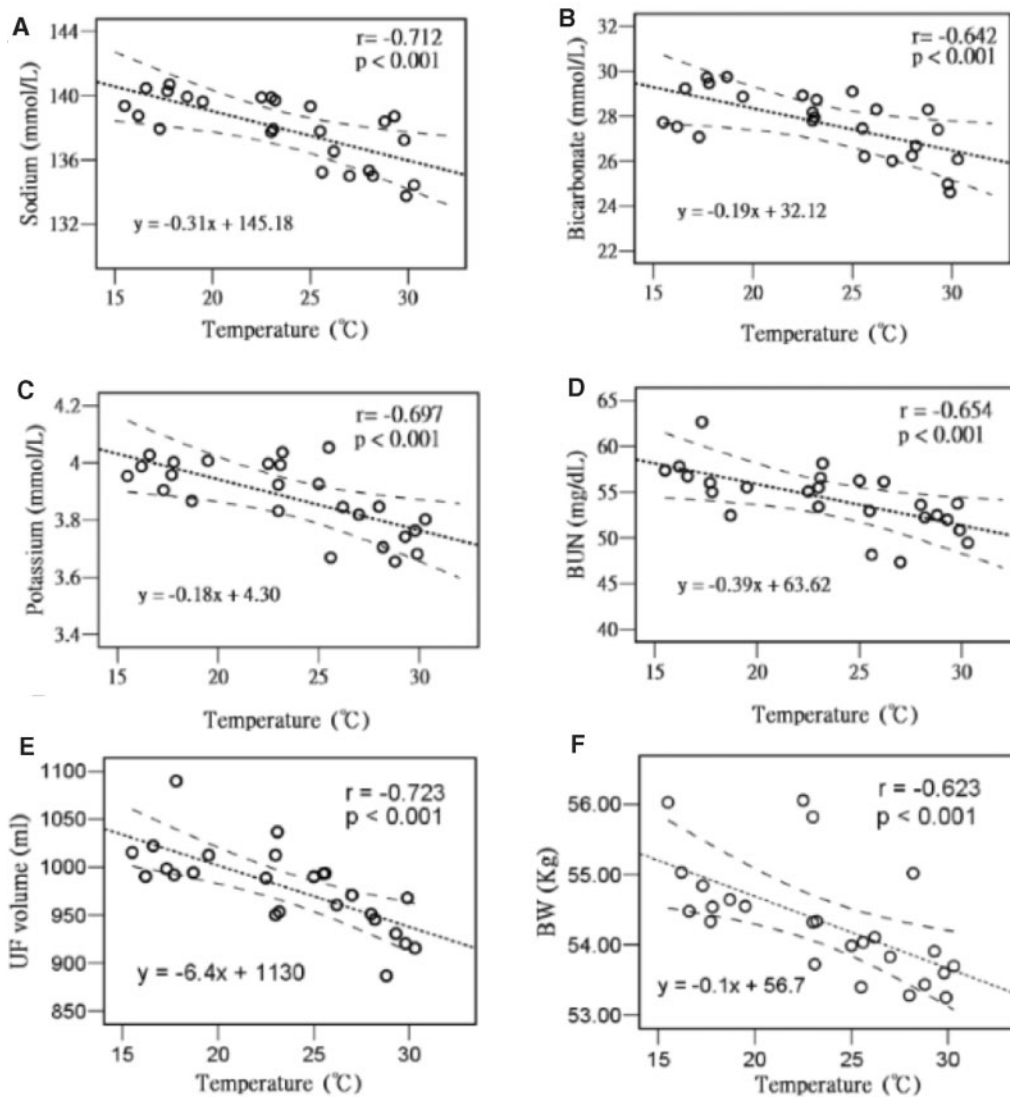
several previous studies that examined the effects of climate on uremia patients [11,12,15–21]. Most of these focused on seasonal blood pressure variations. Outdoor temperature, relative humidity, rainfall and light span were all reported to affect blood pressure in HD patients [16]. However, only temperature has been correlated with serum biochemical parameters [11]. In the current study, only temperature and not the other climate variables affected biochemical parameters in multivariate analysis. Neither annual differences in humidity nor rainfall had an effect on biochemical variables.

Theoretically, the variation in body weight can be attributed to the change in lean body mass or fluid weight. Furthermore, we speculate that the seasonal variation in biochemical parameters was due simply to the dilution effect. However, the simultaneous changes in sodium and body weight, both in the same direction, contradict this hypothesis. An alternate explanation is that higher protein and energy intakes in winter result

**Table 2.** Variations in clinical/biochemical data and correlations with monthly mean temperature

Variable	Mean	Peak	Nadir	Difference	<i>r</i>	<i>p</i>
Sodium (mmol/dl)	137.96 ± 4.20	140.70	133.74	6.96	-0.712	<0.001
Potassium (mmol/dl)	3.88 ± 0.68	4.05	3.65	0.40	-0.697	<0.001
Chloride (mmol/dl)	97.54 ± 3.70	100.57	93.14	7.43	-0.378	0.062
Bicarbonate (mmol/dl)	27.69 ± 3.02	29.72	24.61	5.11	-0.642	<0.001
Albumin (g/dl)	3.90 ± 0.42	4.05	3.76	0.29	-0.496	0.012
BUN (mg/dl)	54.28 ± 17.02	62.65	47.30	15.35	-0.654	<0.001
Creatinine (mg/dl)	10.73 ± 2.50	11.45	10.26	1.19	0.094	0.65
Body weight (kg)	54.29 ± 10.65	56.05	53.25	2.80	-0.623	<0.001
UF volume (ml/day)	978 ± 289	1089	886	203	-0.723	<0.001

Data are expressed in Mean ± SD.

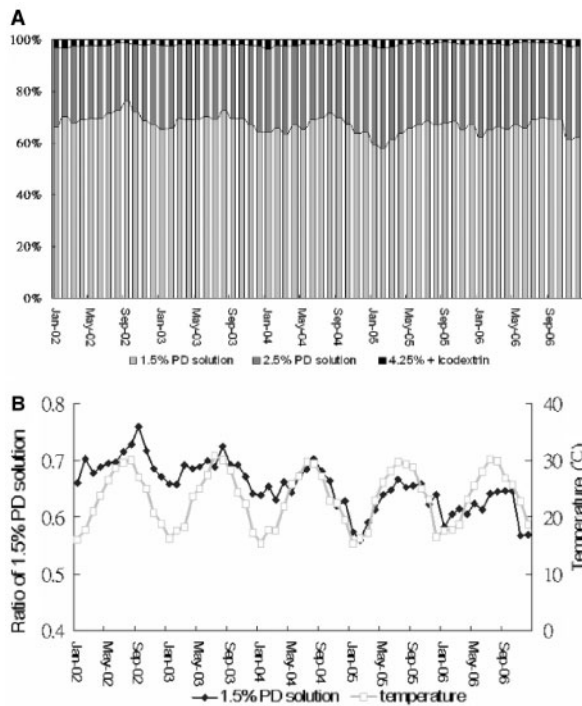


**Fig. 2.** Each dot represents the monthly mean value of 44 patients. The graphs show inverse correlations between temperature and serum concentrations of sodium (A), bicarbonate (B), potassium (C), BUN (D), UF volume (E) and body weight (F), respectively.

in greater weight and sodium concentration. This would explain the variation in BUN but not the changes in electrolytes. The most reasonable hypothesis is that the loss of homeostatic capability, which

functions in normal kidneys, cannot be totally replaced by current renal replacement therapies. For example, people in summer have greater perspiration than water intake, and subjects with normal kidneys are able to





**Fig. 3.** The uptake of different glucose concentrations in PD fluid has a seasonal cyclic pattern (A). The ratio of 1.5% PD dialysate consumption is higher in the summer, indicating that PD patients require higher PD dialysate glucose in the winter (B).

maintain fluid and electrolyte homeostasis whereas ESRD patients are not. PD patients tend to have less peritoneal ultrafiltration volume in summer (Figure 1), which is similar to the findings observed in HD patients [11,12,16,20]. Our PD dialysate consumption records also confirmed greater requirements for high glucose PD solutions in winter (Figure 3). Because sodium removal during PD is strongly related to the ultrafiltration volume [22–24], PD patients should have less peritoneal sodium extraction in hot months. However, we observed that the serum sodium nadir occurred in summer. Because patients lost more sodium from sweating and received identical electrolyte concentration in PD fluid, this may result in greater net sodium loss and explain the decrease in summer. In the current study, differences in sweat volume from summer to winter were around 200 ml/day (the mean difference in daily peritoneal ultrafiltration volume from summer to winter). By factoring in sweat sodium concentration (43 mmol/l) in renal failure patients [25], we calculate that 258 mmol more sodium is lost monthly in the summer  $[0.2(l) \times 43(\text{mmol}/l) \times 30(\text{day})]$ , which would create an 8 mmol/l decrease in serum sodium concentration in these patients.  $[258(\text{mmol}) / (54(\text{kg}) \times 0.6)]$ . This prediction is close to our observation of a 7 mmol/l decrease in average sodium concentration. In contrast to the small difference in sweat sodium concentration between uremic and healthy subjects [25], potassium [25] and urea [26] concentrations in sweat fluid are much higher in uremic patients, which accounts for

the higher magnitudes in seasonal variations in our study (5, 10 and 28% for sodium, potassium and urea, respectively). Although albumin and BUN levels may be also affected by seasonal protein intakes and catabolism differences, cyclic serum electrolyte variations still support the hypotheses that the skin acts as an excretory organ in uremia [27] and that perspiration contributes, at least in part, to the seasonal electrolyte variations. In contrast to HD, PD is characterized by continuous treatment with less abrupt serum composition changes and less haemodynamic changes. Because of these features associated with PD, we are confident about the present correlations and feel that PD use may explain differences between the present and previous reports using HD. Nevertheless, even though our patients did not have three times a week correction by diffusion during HD, the magnitude of these serum biochemical seasonal variations in our study are much greater than in previous reports using HD (0.6, 1.5 and 4.0% for sodium, potassium and BUN, respectively) [11]. These variations are about seven times greater in PD than in HD for all studied serum parameters. In the linear regression model, serum sodium concentration fell by  $\sim 0.31$  mmol/l for each centigrade increase in monthly mean temperature. This effect may be trivial in countries having relatively constant temperatures, but should not be ignored in areas with abundant temperature variations.

Ancient medicine was aware of environmental temperature effects on blood purification via the skin. In early Rome and later in the Middle Ages, hot baths and sweating therapies had been used for treating uremia (Greek for urine poisoning, or literally, ‘urine in the blood’) [27]. The present study, which included in 44 patients over a period of 2 years, demonstrated the influence of climate on biochemical data in ESRD patients treated with PD. This is the first detailed report showing seasonal variation effects on biochemical parameters, body weight and peritoneal ultrafiltration volume in PD patients. There were several limitations in the current study. In this retrospective observational study, we did not have bioimpedance data to demonstrate body water change; however, a previous study by Cheng *et al.* [13] failed to show seasonal variations in extracellular water in PD patients. The calculation of sweat volume is another limitation. Actual sweat volume and electrolyte concentration measurements were lacking. Sweat volume was calculated based on the concept of dynamic balance. Despite these limitations, we believe that our study has some useful features. As a novel finding, we found that PD patients tend to have a relative hyponatremia in summer. In terms of fluid and blood pressure control, low sodium-containing PD solutions have been widely discussed [28,29], and our findings have the potential to affect clinical decisions with regard to peritoneal dialysate composition.

In conclusion, PD patients exhibit seasonal variations in serum sodium levels and other biochemical parameters. This knowledge may have future effects on

clinical decisions with regard to peritoneal dialysate composition and medication dosage. In addition, ignorance of this annular cycle in PD patients could potentially lead to biases in the interpretation of clinical studies and individual laboratory data. Although the causes of these variations are not yet clear, elimination of toxins and electrolytes through perspiration is an attractive explanation. The ancient idea that substitution of renal function by the detoxification ability of skin may still play a role in PD in current practice.

*Conflict of interest statement.* None declared.

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