

# Vitamin D-dependent Seasonal Variation of PTH in Growing Male Adolescents

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Twenty-eight young male adolescents (age from 13 years 6 months to 15 years 9 months) from a horseback-riding school were studied. They were studied at the end of summer (September of 1993) and, six months later, at the end of winter (March of 1994). At each timepoint their height and weight were measured and their pubertal status determined. Blood was collected and 25-hydroxyvitamin D [25(OH)D], intact parathyroid hormone (PTH1-84), and 1,25-dihydroxyvitamin D [1,25(OH)<sub>2</sub>D] were measured. After winter, weight and height had increased by a mean of  $2.9 \pm 1.3$  kg and of  $3.3 \pm 1.2$  cm, respectively. 25(OH)D concentrations which were  $29.96 \pm 7.46$   $\mu$ g/L in September had significantly ( $p = 0.0001$ ) fallen by a mean of  $23.31 \pm 6.6$   $\mu$ g/L in March ( $6.61 \pm 2.04$   $\mu$ g/L). March and September concentrations of 25(OH)D were significantly correlated ( $r = 0.536$ ,  $p = 0.0039$ ). March values were negatively correlated with the pubertal status ( $r = 0.41$ ;  $p = 0.03$ ). In the meantime, PTH had significantly ( $p = 0.0001$ ) increased by a mean of  $8.59 \pm 8.53$  ng/L ( $22.8 \pm 7.44$  ng/L in September vs.  $30.33 \pm 8.05$  ng/L in March). A statistically significant correlation between PTH and 25(OH)D concentrations ( $r = 0.493$ ;  $p = 0.0001$ ) was obtained. Serum 1,25(OH)<sub>2</sub>D concentrations measured in September ( $37.7 \pm 12.94$  ng/L) and in March ( $38.2 \pm 7.8$  ng/L) were not different. March values were positively correlated with pubertal status ( $r = 0.49$ ;  $p = 0.008$ ). Modulation of PTH secretion by vitamin D appears to be a physiological mechanism occurring during adolescence. In spite of a marked depletion of vitamin D stores after winter, PTH values remained within normal range. Nevertheless, we cannot exclude that a more prolonged vitamin D deficiency could adversely affect bone metabolism during this critical period of life characterized by an increased need of vitamin D. (*Bone* 17:513-516; 1995)

**Key Words:** Adolescents; Vitamin D; Parathyroid hormone.

## Introduction

A decade ago, a seasonal PTH variation was described in elderly people.<sup>13</sup> Its relationship with vitamin D seasonal variation was

confirmed by administrating vitamin D supplements, either as a single dose, in elderly men,<sup>9</sup> or as increased daily intakes, in postmenopausal women,<sup>10</sup> the effect of which was to suppress both 25(OH)D and PTH seasonal variations. In the same way, the effects of seasonal variations of calciotropic hormones on bone mineral density have been studied in postmenopausal<sup>7</sup> and in elderly women<sup>20</sup> and have been found to be linked to seasonal variations in vitamin D metabolism. Moreover, vitamin D supplementation was shown to reduce wintertime bone loss.<sup>7</sup> During adolescence a growth spurt occurs that implies modifications of calciotropic hormones such as elevated serum concentrations of 1,25(OH)<sub>2</sub>D.<sup>2,4,14</sup> To our knowledge, seasonal variations of vitamin D metabolites and of PTH during this critical period of life have not been studied. The aim of the present study was therefore to evaluate whether or not there is a seasonal variation in PTH and in both 25(OH)D and 1,25(OH)<sub>2</sub>D and whether there is an association between vitamin D metabolites and PTH.

## Materials and Methods

### Subjects

Twenty-eight male caucasian adolescents (age from 13 years 6 months to 15 years 9 months) from a horseback-riding school participated in the study. The study was conducted by the end of summer (September of 1993) and 6 months thereafter, by the end of winter (March of 1994). At each time point the subjects height and weight were measured and blood was collected for measurement of biochemical and hormonal variables.

The horseback-riding school is located in the north of Paris (49° northern latitude). Monthly records of hours of sunshine in the area of Paris were obtained from the Meteorological Institute (Météo-France). The experimental protocol was approved by the local hospital Ethical Committee. An informed written consent was obtained from the parents of the minors.

A group of 39 healthy young adult males (ages 23-27 years) were used as control subjects for PTH and 1,25(OH)<sub>2</sub>D. These subjects were medical students who used to participate in the experiments of the laboratory. None of them had disorders or was taking medications known to affect calcium metabolism. In twelve of them, 25(OH)D concentrations were measured in March of 1994.

### Methods

The height and weight of each subject was measured with the subject standing barefoot and lightly clothed. All the subjects

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underwent a physical examination by a pediatrician and their pubertal stage was determined using Tanner's criteria.<sup>15</sup> Their current calcium and protein diets were assessed by means of weekly dietary history. Responses were checked by the research dietitian using fake models of food portion sizes. The mean daily intake of calcium and protein were analyzed using food tables established in France.<sup>15</sup>

Serum PTH1-84 was measured by immunoradiometric assay for intact PTH (Nichols Institute, San Juan Capistrano, CA); within assay CV was less than 4% and between assay CV less than 6%. The normal range for men ( $n = 39$ ), aged 23-27 years, was 13-50 ng/L. 25(OH)D was measured by a competitive protein-binding assay after extraction and chromatographic purification (Amersham International, Amersham, UK); within assay variability: CV of this method was less than 9% for low (7.8 µg/L) and for medium (23.0 µg/L) concentrations; between assay variability: CV ranged from 7% to 10%. Serum 25(OH)D concentrations measured in March of 1994 in 12 young adult males were found to be comprised between 6.6 and 24.4 µg/L ( $12.4 \pm 5.0$  µg/L). Calf thymus receptor that was specific for both 1,25-dihydroxyergocalciferol [1,25(OH)<sub>2</sub>D<sub>2</sub>] and 1,25-dihydroxycholecalciferol [1,25(OH)<sub>2</sub>D<sub>3</sub>] was used in nonequilibrium competitive binding assay to measure 1,25(OH)<sub>2</sub>D (Incstar, Stillwater, MN). Within and between assay variations: CV were less than 10% in the normal concentration range. Normal values were determined in 39 young healthy adult males (age from 23 to 27 years). They were found to be  $29.45 \pm 3.97$  ng/L.

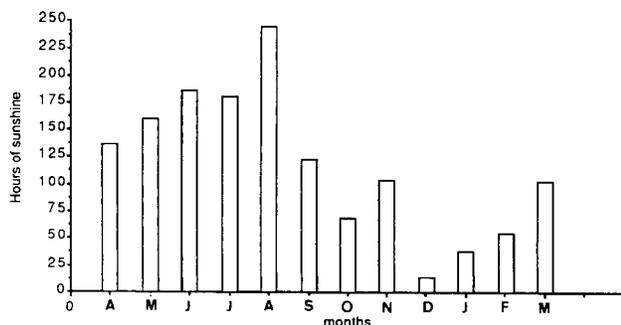
**Statistics**

Comparisons between means of paired groups of variables were performed using Student's paired *t*-test. Relationships between groups of quantitative variables were analyzed by using simple regression analysis program. The statistical program used was StatView 512+ (BrainPower Inc., Calabasas, CA).

**Results**

In **Figure 1** is presented the monthly mean of hours of sunshine. The sunny period extended from April into September with a peak in August of 1993. Descriptive data including growth parameters are presented in **Table 1**.

Individual seasonal variations in 25(OH)D and in PTH are shown in **Figure 2**. As shown in Figure 2A, a very significant ( $p = 0.0001$ ) decrease in serum 25(OH)D occurred during winter since in September of 1993, 25(OH)D was  $29.96 \pm 7.46$  µg/L and by March had fallen by a mean of  $23.31 \pm 6.6$  µg/L. By March, out of 28 subjects, 14 had 25(OH)D values less than 6



**Figure 1.** The monthly mean of hours of sunshine in Paris from April 1993 to March 1994 (Météo-France, Paris-Montsouris, France).

**Table 1.** Anthropometric and dietary variables

	September of 1993	March of 1994
<b>Anthropometric variables</b>		
Height (cm)	151.9 ± 6.6	155.2 ± 7.4
Weight (kg)	40.2 ± 4.7	43.1 ± 5.4
<b>Pubertal status</b>		
Stage 1	n = 5	n = 4
Stage 2	n = 8	n = 2
Stage 3	n = 9	n = 8
Stage 4	n = 5	n = 9
Stage 5	n = 1	n = 5
<b>Dietary variables</b>		
Ca intake (mg/day)	645 ± 455 (175-2150)	
Protein intake (g/kg b.w./day)	2.7 ± 0.8 (1.1-4.6)	

ng/mL. These levels were significantly ( $p = 0.0003$ ) lower than those found in 12 young healthy male adults at the same period (see *Methods*).

March values ( $6.61 \pm 2.04$  µg/L) were significantly correlated ( $r = 0.536$ ;  $p = 0.0039$ ) with September values ( $29.96 \pm 7.46$  µg/L). In March of 1994, 25(OH)D concentrations were negatively correlated with pubertal status ( $r = 0.41$ ;  $p = 0.03$ ).

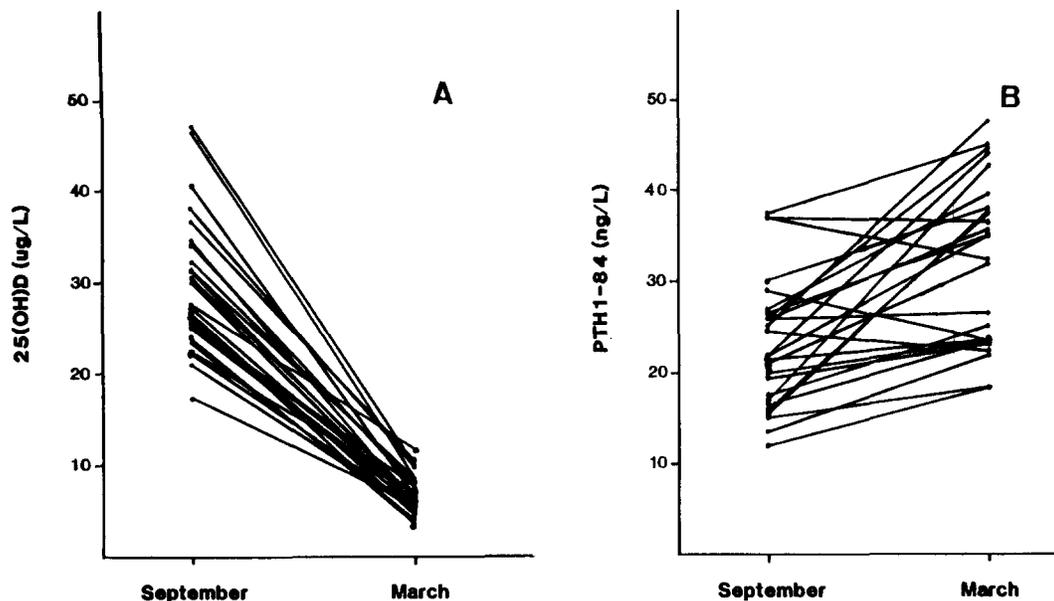
In **Figure 2B** are shown the changes in serum PTH. From September of 1993 to March of 1994, PTH concentrations were significantly ( $p = 0.0001$ ) increased by a mean of  $8.59 \pm 8.53$  ng/L ( $30.33 \pm 8.05$  ng/L in March vs.  $22.8 \pm 7.44$  ng/L in September).

A statistically significant correlation between PTH and 25(OH)D concentrations ( $r = 0.493$ ;  $p = 0.0001$ ) was obtained (see **Figure 3**). Serum 1,25(OH)<sub>2</sub>D concentrations measured in adolescents did not change from September ( $37.7 \pm 12.94$  ng/L) to March ( $38.2 \pm 7.8$  ng/L). A positive relationship between pubertal status and 1,25(OH)<sub>2</sub>D was obvious both in September ( $r = 0.36$ ;  $p = 0.06$ ) and in March but reached statistical significance in March only ( $r = 0.49$ ;  $p = 0.008$ ). There was no relationship between 25(OH)D and 1,25(OH)<sub>2</sub>D and between 1,25(OH)<sub>2</sub>D and PTH.

**Discussion**

Vitamin D and its major circulating metabolite, 25(OH)D, are under the predominant influence of UV radiation from the sun. It has been shown that, in countries located at 45° northern latitude, the capacity of sun irradiation to generate previtamin D<sub>3</sub> is restricted to late spring and to summer.<sup>20</sup> In the present study, similar effects are likely, since it was performed in an area located at 49° northern latitude where the sunshine records show that from September of 1993 to March of 1994, sun irradiation was low as compared to the summer period.

When diet is not supplemented with vitamin D, the consequence is a marked seasonal variation of 25(OH)D concentrations, characterized by a trough at the end of winter and a peak at the end of summer. Such a seasonal variation has been demonstrated in children,<sup>17</sup> in adults,<sup>12,18,23</sup> and in elderly people as long as they continue to walk outdoors.<sup>6,11</sup> As shown in the present study, male adolescents exhibit a 25(OH)D seasonal variation that is more pronounced than in other age groups of subjects. Postsummer mean level of 25(OH)D in our group of adolescents was relatively high, attesting to a prolonged expo-



**Figure 2.** Individual variations of calcitropic hormones according to season. 25(OH)D (A) and PTH1-84 (B) were measured before (September) and after (March) winter.

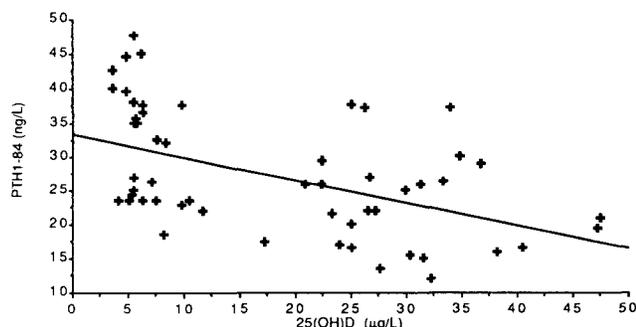
sure to sun irradiation (in France, vitamin D supply by food is minimal), whereas postwinter concentrations were very low [when compared to 25(OH)D concentrations measured at the same time in young male adults: see *Methods*]. Low concentrations of 25(OH)D were first observed in Finnish adolescents<sup>1</sup> and in Asian immigrant adolescents.<sup>5</sup> However, in these previous studies, postsummer concentrations of 25(OH)D had not been measured in the same subjects. An increase in 25(OH)D consumption due to an increase of 1,25(OH)<sub>2</sub>D synthesis seems likely during puberty since, as shown in the present study and in other ones,<sup>2,4</sup> 1,25(OH)<sub>2</sub>D mean serum concentrations are elevated in adolescents. This hypothesis is strengthened by both the negative relationship between 25(OH)D and the pubertal status and the positive relationship between 1,25(OH)<sub>2</sub>D and the pubertal status. However, increased production of 1,25(OH)<sub>2</sub>D is slight and could account for only a part of the observed disappearance of 25(OH)D. Moreover, these 25(OH)D low concentrations could be due not only to a decrease of 25(OH)D production in wintertime but also to a diminished vitamin D storage capacity in these short and thin adolescents (they were selected according to these requirements at their enlistment into the horseback-riding school), since it has been shown that vita-

min D is predominantly stored in adipose tissue<sup>21</sup> and that seasonal variation of 25(OH)D is greater in lean than in fat subjects.<sup>16</sup>

The seasonal variations of PTH and of 25(OH)D were opposite and a negative relationship between 25(OH)D and PTH concentrations was found. Such a negative relationship was first demonstrated in elderly people whose mean 25(OH)D concentrations are frequently lowered.<sup>3</sup> It has also been observed in a group of 71 subjects whose ages ranged from 20 to 88 years and whose 25(OH)D levels ranged from 0.5 to 41.8 μg/L.<sup>8</sup> Although PTH secretion is known to be regulated by 1,25(OH)<sub>2</sub>D,<sup>22</sup> 1,25(OH)<sub>2</sub>D concentrations, which were significantly more elevated in adolescents than in young adults, did not appear to modify the relationship between 25(OH)D and PTH. In contrast to 25(OH)D, serum 1,25(OH)<sub>2</sub>D concentrations did not show seasonal variations. Some authors<sup>17</sup> did not find seasonal changes in children, while others<sup>24</sup> described higher levels in summer than in winter in young adults. In the present study, an increase in 1,25(OH)<sub>2</sub>D in March could have been expected, since a positive correlation between the pubertal status and 1,25(OH)<sub>2</sub>D has been found and the pubertal status has improved from September to March. We can hypothesize that this effect is blunted by low levels of 1,25(OH)<sub>2</sub>D precursor.

Secondary hyperparathyroidism in vitamin D-depleted elderly people and its secondary effects including loss of bone mineral density and increased risk of bone fractures are well documented.<sup>3</sup> By contrast, there are few data about PTH concentrations in young subjects except those of Oliveri et al.<sup>17</sup> These authors have described radiological bone signs of hypersecretion of PTH in children living in south Argentina (latitude 55° south).

Although in the present study PTH concentration remained within the limits of normal range, we cannot exclude that negative effects on skeletal bone mass could occur in growing adolescents if low levels of vitamin D would persist.



**Figure 3.** Relation between PTH1-84 and 25(OH)D concentrations in young male adolescents measured before and after winter.

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