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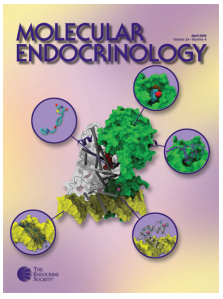

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Urban Tropospheric Ozone Increases the Prevalence of Vitamin D Deficiency among Belgian Postmenopausal Women with Outdoor Activities during Summer

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Context: By absorbing sunlight UVB and thereby reducing cutaneous vitamin D photosynthesis, ozone, a common urban pollutant, could cause hypovitaminosis D.

Objectives: The objective of the study was to establish the characteristics and percentage of subjects with serum 25-hydroxyvitamin D [25(OH)D] less than 75 nmol/liter among postmenopausal women engaging in outdoor activities in either Brussels or the countryside.

Design/Setting: This was a cross-sectional study conducted in a university research hospital.

Patients/Methods: Among 249 women consulting for either shoulder tendonitis or lumbar spine osteoarthritis, 121 free of conditions and drugs affecting bone and calcium metabolism completed two food-frequency questionnaires within 15 d and we selected the 85 subjects with retest scores within the ± 15% of test scores. Other parameters included sun exposure index (SEI), PTH levels, and femoral neck T-score.

Results: Urban residents (n = 38) and rural residents (n = 47) did not differ in mean ages, body mass indices, and vitamin D intakes. When compared with rural inhabitants, urban inhabitants were exposed to ozone levels 3 times higher, and despite a higher mean SEI (113 *vs.* 87; $P < 0.001$), they had a higher prevalence of 25(OH)D less than 75 nmol/liter (84 *vs.* 38%). After adjusting for SEI, 25(OH)D was 2-fold higher in rural residents, and after adjusting for 25(OH)D, SEI was 3-fold higher in urban residents. Femoral neck T-scores correlated positively with 25(OH)D and negatively with PTH levels.

Conclusions: Air pollution may be a neglected risk factor for hypovitaminosis D, which is known to compromise several health outcomes. As long as 25(OH)D is greater than 75 nmol/liter, calcium intakes greater than 17.5 mmol/d are unnecessary to prevent elevations in PTH levels. (***J Clin Endocrinol Metab*** **93: 3893–3899, 2008)**

Whereas serum concentrations of 25-hydroxyvitamin D [25(OH)D] are the best clinical indices of vitamin D status (1), 1,25-dihydroxyvitamin D, the biologically active form of the hormone, optimizes intestinal calcium absorption and regulates bone turnover (2, 3). Low 25(OH)D levels lead to alterations in calcium homeostasis, secondary hyperparathyroidism, bone loss, osteoporosis, and fragility fractures (4). More severe degrees of vitamin D deficiency impair bone mineralization and lead to painful osteomalacia (2, 4).

The optimal serum levels of 25(OH)D remain the subject of much debate. Because there is an inverse relationship between serum 25(OH)D and serum PTH, the levels of 25(OH)D necessary to prevent or minimize secondary hyperparathyroidism have been interpreted as a marker of vitamin D sufficiency (5–9). However, this approach, based on PTH levels, has resulted in a wide range of 25(OH)D estimates ranging from 45 to 110 nmol/liter (18 to 44 ng/ml). Furthermore, up to one third of patients with hypovitaminosis D might be magnesium

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Abbreviations: ANCOVA, Analysis of covariance; BMI, body mass index; CI, confidence interval; CV, coefficient of variation; FFQ, food frequency questionnaire; 25(OH)D, 25-hydroxyvitamin D; SEI, sun exposure index; UVB, UV B.

deficient and hence have functional hypoparathyroidism (10). On the other hand, vitamin D has additional functions not related to calcium and bone homeostasis (11), and a recent meta-analysis (12) concluded that serum 25(OH)D of 75 nmol/liter (30 ng/ml) was the minimum needed to optimize multiple health outcomes including musculoskeletal function of the lower extremities, dental health, and prevention of colorectal cancer.

Hypovitaminosis D remains an important health problem for adults over 50 yr of age (9, 13). Because few human foods naturally contain or are fortified with vitamin D (2), dietary intake is unlikely to meet the daily body's needs that might be as high as 3000–5000 IU (14). Therefore, casual exposure of the skin to sunlight might be the major source of the vitamin for most people, but cutaneous vitamin D synthesis decreases with aging. Moreover, the penetration of UV B (UVB) photons into the skin is impaired by various factors such as latitude, season, skin pigmentation, and protection of sun-exposed skin areas by sunscreens and clothing (15, 16). By efficiently absorbing solar UVB photons reaching ground level, tropospheric ozone also could reduce cutaneous vitamin D synthesis, but the impact of this common urban air pollutant on vitamin D status remains poorly documented (17). Therefore, during the summer, we determined the vitamin D status of healthy, postmenopausal Caucasian women engaging in outdoor activities in either rural Belgium or in Brussels (latitude, 50° N), two areas with quite different levels of ozone air pollution. Serum 25(OH)D levels were related to serum PTH levels and potential risk factors for hypovitaminosis D such as sun exposure, body mass index, and dietary vitamin D intake.

Subjects and Methods

Study subjects

During June and July 2006, we recruited a cohort of Caucasian women from subjects attending the rheumatology outpatient clinic for either osteoarthritis of the lumbar spine or tendonitis of the shoulder. Eligible women had to be postmenopausal for at least 3 yr and not taking medications known to affect calcium or vitamin D metabolism such as antiresorptive drugs, calcium and vitamin D supplements, anticonvulsants, glucocorticoids, and hormone replacement therapy. Other inclusion criteria included: 1) a creatinine clearance above 50 ml/min, renal formation of 1,25-dihydroxyvitamin D being impaired below this threshold (18); 2) outdoor activities without use of sunscreens; 3) no clinically evident hepatic, renal, cardiovascular, pulmonary, endocrine, and/or hematological diseases; and 4) no travel to sunny southern locations during the previous 6 months.

Study conduct

Eligible women gave informed consent, and fasting blood was sampled. On two occasions with a median of 15 d between interviews, subjects completed identical semiquantitative questionnaires evaluating their dietary calcium and vitamin D intakes (19–21) as well as their sun-associated behavior (9).

Semiquantitative food frequency questionnaires (FFQs) evaluate the entire diet, including supplements and have been validated by using repeated 24-h recalls and biomarkers such as 25(OH)D levels (19, 20). Calcium intakes assessed by using FFQs have been associated with both PTH levels and bone mineral density (19, 20). However, whereas dietary intakes assessed by both FFQs and repeated 24-h recalls gave similar results in men, dietary values from FFQs might amount to less than 85% of values from two 24-h recalls in women, especially if they think they are overweight (21). Therefore, in an attempt to uncover most of the unreliable female reporters, we used the following strategy. For each individual item on the questionnaires, the retest score was divided by the corresponding test score to yield relative percentage value, and subjects with retest values outside the 85–115% range of test values were discarded. In subjects with retest values within the 85–115% range, the mean values of test and retest scores were entered in a database and compared with food composition tables to yield calcium and vitamin D intakes.

Questionnaires also evaluated the number of body parts exposed to sunlight as well as the number of hours per week spent outside between 1000 and 1600 h without sun protection during the previous 6 wk. A sun exposure index (SEI) then was computed (9) by multiplying the average number of hours spent outside by the percentage of the body surface exposed to sunlight (9% for the face, 9% for forearms, 2% for the hands, and 18% for the lower extremities below the knee). In a recent large cross-sectional survey of sun-associated behavior (22), the test-retest reliability of questionnaires was high ($\kappa > 0.7$).

Because we were unable to measure the tropospheric ozone content and the amount of solar UVB photons reaching ground level in the residence area of each subject during the hours spent outside, we referred to the mean of values recorded by official agencies of the Federal State of Belgium (http://www.ibgebim.be; www.irceline.be; //www.issep.be; and //www.wallonie.be/DGRNE) in different areas of Brussels and the countryside of south Belgium during spring and summer.

Laboratory studies

Serum 25(OH)D levels were measured by the chemiluminescence-based LIAISON assay (Dia-Sorin, Stillwater, MN) with an intra- and an interassay coefficient of variation (CV) less than 10%. The Nichols Advantage chemiluminescence intact immunoassay (Nichols Institute Diagnostics, San Clemente, CA) measured serum biointact PTH concentrations with an intra- and interassay CV less than 9%; the normal range is 0.74–4.2 pmol/liter in adults.

Calcium, phosphorus, albumin, creatinine, and alkaline phosphatase levels were measured by automated standard laboratory methods. Creatinine clearance was measured on 24-h urine. Serum total calcium was corrected for albumin according to the following formula: corrected calcium = total calcium (milligrams per deciliter) + [0.8 × (4-albumin [grams per deciliter])].

Bone mineral density was measured by dual-energy x-ray absorptiometry (QDR-2000 instrument from Hologic, Waltham, MA) at femoral neck with a CV less than 1.6% (23). The T score or the number of SDs of the subject's value from the mean of a young population was computed, osteoporosis being defined by a T score −2.5 SD or less.

Outcome measures

Many authors agree that 25(OH)D levels less than 25 nmol/liter define overt vitamin D deficiency, but there is no consensus for optimal 25(OH)D levels (2). Therefore, we used 25(OH)D levels less than 75 nmol/liter to define vitamin D deficiency. Biochemical evidence of secondary hyperparathyroidism was defined by normal serum calcium with a PTH value above the upper limit of the manufacturer's normal reference (4.2 pmol/liter).

Risk factors evaluated for association with 25(OH)D and PTH levels included subject's area of residence (urban or rural), age, body mass index (BMI; in kilograms per square meter), and other variables collected from either questionnaires (SEI, dietary calcium and vitamin D intakes) or official state agencies (tropospheric ozone content).

Statistical analysis

Analyses were performed using SPSS (version 11.01; SPSS Inc., Chicago, IL). Variables were checked for normality. Univariate analyses of variance were used to study the associations between serum 25(OH)D or PTH levels (dependent variables) and potential risk factors for vitamin D and/or PTH deficiency (predictors or constant independent variables). To facilitate direct comparisons of the strengths of the associations, the results of the regression models are reported as standardized β-values. A standardized β-value of 0.2 indicates that, if the independent variable increases by 1 SD, the dependent variable increases by 0.2 SD.

Subjects were divided into groups according to their area of residence, calcium intake (<17.5 mmol/d and >17.5 mmol/d), and 25(OH)D levels (≤37.5, 40–75, and >75 nmol/liter). Analysis of covariance (ANCOVA) was used to study the relationship between serum PTH levels and both calcium intakes and vitamin D levels. Calcium intake groups and 25(OH)D groups were fixed factors, and variables known to be associated with PTH levels were entered as covariates, which included BMI. $P < 0.05$ was considered statistically significant. Unless otherwise noted, data are presented as the mean ± SD.

Results

Subject sample and characteristics

One hundred twenty-eight of the 249 women screened during June to July 2006 were excluded because of estrogen replacement therapy (n = 44), daily supplementation with calcium and vitamin D (n = 60), bisphosphonate therapy (n = 10), and/or travel to sunny countries during the previous 6 months (Florida/Caribbean: n = 5; Mediterranean countries: n = 9; Indochina: n = 2; South America: n = 2). The remaining 121 volunteered to participate in this study, provided blood samples and completed the questionnaires during the two study visits. Unfortunately, because their retest scores were outside the 85–115% value of corresponding test score for both SEI and food questionnaires, 36 subjects had to be discarded, thus leaving 85 subjects whose major characteristics are given in Table 1.

Only one woman had a daily calcium intake above the 30 mmol recommended in the United States for people over 50 yr of age, and 55 subjects had a daily calcium intake above the 17.5 mmol recommended in Europe for subjects of all ages (24). In all subjects, the dietary vitamin D intake was below the level of 400 IU/d recommended in the United States for people aged 51–70 yr and in Europe for people over 65 yr of age (25).

Forty-seven women (55%) were living in the countryside (rural group) and 38 women (45%) lived in Brussels (urban group), a city with heavy motor vehicle traffic and near an international airport. When compared with rural residents, urban residents had a higher mean SEI ($P < 0.001$), lower mean 25(OH)D level ($P < 0.001$), and higher mean PTH level ($P < 0.001$). On the other hand, the two groups did not differ in their mean age ($P = 0.498$), BMI ($P = 0.662$), calcium intake ($P = 0.067$), and vitamin D intake ($P = 0.307$).

From April to July 2006, the mean ± SD of ozone levels measured in Brussels between 0900 and 1800 h was 80.4 ± 18.2 $\mu g/m^3$ [lower and upper 95% confidence interval (CI) of mean 69 and 91; range 42–99], a value 3-fold higher than that of 27 ± 10 $\mu g/m^3$ (lower and upper 95% CI of mean 23 and 33; range 11–43) measured in the countryside during the same months and hours. The difference in the level of air pollution between Brussels and the countryside was similar from April to June 2004 (68.2 ± 12.6 $\mu g/m^3$; range 42–80 *vs.* 33.1 ± 7.4 $\mu g/m^3$; range 24–47) and from April to June 2005 (71.1 ± 11.4 $\mu g/m^3$; range 50–84 *vs.* 33.2 ± 5.1 $\mu g/m^3$; range 25–40).

Distribution of serum 25(OH)D and PTH levels

The prevalence of 25(OH)D less than 75 nmol/liter (30 ng/ml) was much more common in urban than rural dwellers (32 of 38 *vs.* 18 of 47), and serum 25(OH)D was negatively associated with serum PTH (Fig. 1, *upper panel*; r = −0.746; $P < 0001$).

Secondary hyperparathyroidism was observed in women with 25(OH)D<60 nmol/liter (25 of 40) but not in subjects with 25(OH)D greater than 60 nmol/liter, and for any given 25(OH)D concentration, the variation in PTH levels was much greater in women with 25(OH)D less than 60 nmol/liter than in those with 25(OH)D greater than 60 nmol/liter when the 85 included subjects were divided into two groups according to levels of calcium intakes [<17.5 mmol/d (Fig. 1, *open circles*, and greater than 17.5 mmol/d (Fig. 1, *closed circles*)]. ANCOVA disclosed that in women with 25(OH)D less than 60 nmol/liter, the adjusted mean PTH value was higher in the group with low calcium intake (5.1 *vs.* 3.3 pmol/liter; $P < 0.0001$). In contrast, in subjects with 25(OH)D greater than 60 nmol/liter, there was no difference in

TABLE 1. Characteristics of postmenopausal women engaging in outdoor activities during summer and living in either Brussels (urban group) or the Belgian countryside (rural group)

	Age (yr)	25(OH)D (nmol/liter)	PTH (pmol/liter)	Calcium intake (mmol/d)	Vitamin D intake (IU/d)	BMI (kg/m^2)	SEI
All women (n = 85)	65 ± 8 (51–81)	64 ± 27 (13–115)	3.6 ± 1.3 (1.5–8.7)	17.3 ± 4.1 (6–31)	195 ± 43 (100–280)	24 ± 3 (17–28)	99 ± 54 (14–280)
Urban group (n = 38)	65 ± 9 (51–81)	47 ± 22 (13–95)	4.1 ± 1.4 (2.0–8.7)	16.4 ± 5.3 (6–31)	200 ± 48 (100–280)	24 ± 3 (18–28)	113 ± 65 (25–280)
Rural group (n = 47)	66 ± 7 (53–80)	79 ± 22 (33–115)[a]	3.1 ± 1.1 (1.5–5.8)[a]	18 ± 2.5 (11–23)	191 ± 38 (120–260)	24 ± 3 (17–28)	87 ± 39 (14–190)[a]

Among women consulting the rheumatology outpatient clinic for shoulder tendonitis or lumbar spine osteoarthritis in June or July, the fasting serum levels of 25(OH)D and PTH were measured in 85 subjects who were free of conditions and/or drugs affecting bone and calcium metabolism. Their BMI, SEI, and daily dietary intakes of calcium and vitamin D also were recorded. Values are the mean ± 1 SD (range); 1 IU corresponding to 0.025 μg of 25(OH)D.

[a] $P < 0.05$ for the difference between the urban and rural group by unpaired *t* test. Divide by 2.5 to convert 25(OH)D from nanomoles per liter to nanograms per milliliter and divide by 0.105 to convert PTH from picomoles per liter to picograms per milliliter or nanograms/liter.

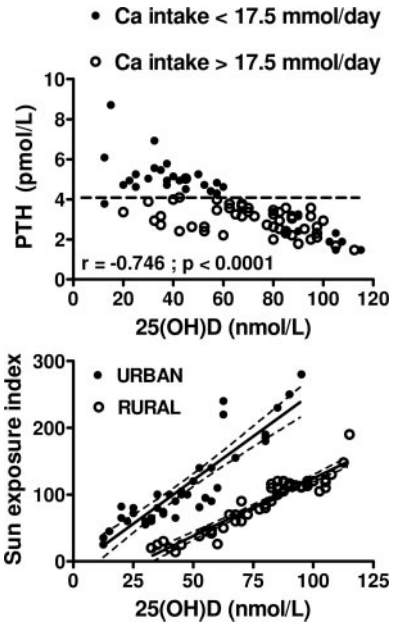

FIG. 1. Relationships among vitamin D status, serum levels of PTH, and sun exposure index. *Upper panel*, A statistically significant negative association (Spearman r = −0.746; $P < 0.001$) was disclosed between serum levels of 25(OH)D and serum levels of PTH. When women were divided into two groups according to their calcium intake (>17.5 mmol/d, open circles, and <17.5 mmol/d, *closed circles*), the statistically significant association between PTH and 25(OH)D persisted in both the high (r = −0.494; $P = 0.0003$) and low (r = −0.854; $P < 0.0001$) calcium intake group. *Lower panel*, In both urban (*closed circles*) and rural residents (*open circles*), a statistically significant linear correlation ($P < 0.001$) was observed between serum levels of 25(OH)D and the sun exposure index. The *dotted lines* show the 95% confidence limits. For urban residents, the correlation coefficient was 0.89 and the slope was 2.6 ± 0.2 (95% CI 2.2–3.1), whereas for rural residents, the coefficient correlation was 0.90 and the slope was 1.7 ± 0.1 (95% CI 1.5–1.9).

adjusted mean PTH level between the low and high calcium intake groups (2.78 *vs.* 2.76, respectively; $P = 0.901$).

Associations with serum 25(OH)D concentration

Univariate analyses of variance (Table 2) disclosed that 25(OH)D was inversely associated with BMI and positively related to both SEI and area of residence. The slope of the line depicting the 25(OH)D-SEI relationship (Fig. 1, *lower panel*) was 2.6 ± 0.2 (95% CI 2.2–3.1) in urban residents and 1.7 ± 0.1 (95% CI: 1.5–1.9) in rural residents. For the same 25(OH)D level, the SEI was 2–3 times higher in the urban group than the rural group. However, this difference was not related to the BMI because this negative determinant of 25(OH)D levels was similar in the two groups (Table 1).

ANCOVA confirmed that 25(OH)D was significantly and positively associated with both SEI and site of residence. Importantly, ANCOVA also showed that after adjusting for SEI, the mean 25(OH)D concentration was about 2 times higher in rural residents than urban residents (Fig. 2, *upper panel*) and that, after adjusting for 25(OH)D, the SEI was about 3 times higher in urban residents than rural residents (*lower panel*).

TABLE 2. Associations (standardized β-values [sβ]) of BMI, SEI, residence (Brussels city or countryside), calcium (Ca) dietary intake, and vitamin D dietary intake (continuous, independent variables) in relation to serum 25(OH)D (continuous, dependent variable) and serum PTH (continuous, dependent variable)

	sβ	*P*
25(OH)D		
BMI	−0.383	0.001
SEI	0.395	0.001
Residence	0.683	0.001
Ca intake	0.041	0.206
Vitamin D intake	−0.056	0.063
PTH		
BMI	0.539	0.001
SEI	0.029	0.813
Residence	−0.252	0.001
Ca intake	−0.474	0.001
Vitamin-D intake	−0.007	0.911

Associations with serum PTH concentration

As shown in Table 2, PTH was positively associated with BMI and negatively associated with both dietary calcium intake and the area of residence. There was no statistically significant association between PTH and creatinine clearance ($P = 0.36$).

ANCOVA confirmed that PTH was statistically associated with 25(OH)D ($P = 0.023$), calcium intake ($P = 0.001$) and the interaction between the two ($P = 0.001$). Figure 3 shows the adjusted means for PTH according to serum 25(OH)D levels in the two calcium intake groups. In subjects with 25(OH)D less than 40 nmol/liter and subjects with 25(OH)D between 40 and 75 nmol/liter, the group with calcium intakes less than 17.5 mmol/d had higher mean PTH levels than the group with calcium intakes greater than 17.5 mmol/d. On the other hand, in subjects with 25(OH)D above 75 nmol/liter, the level of calcium intake had no effect on PTH concentrations.

When the urban and rural groups were adjusted for 25(OH)D, the two groups had a similar mean PTH ($P = 0.531$), therefore suggesting that the negative association between PTH and area of residence reflects, at least in part, the difference in mean 25(OH)D between the two groups (Table 1) as well as the negative relationship between 25(OH)D and PTH (Fig. 1).

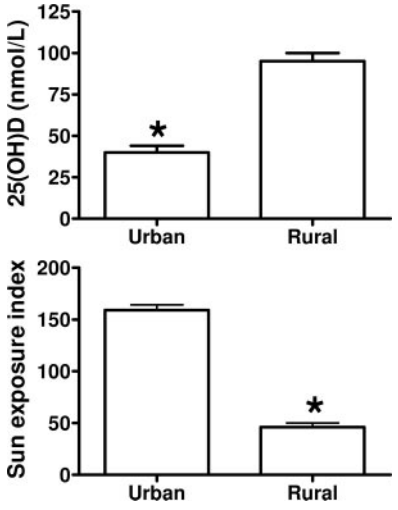

FIG. 2. Mean serum levels of 25(OH)D obtained after adjusting for sun exposure index (*upper panel*) and mean sun exposure index obtained after adjusting for serum levels of 25-hydroxyvitamin D (*lower panel*) in urban and rural residents. Data are presented as mean ± SE of the mean. *, $P < 0.001$ by the Tukey test.

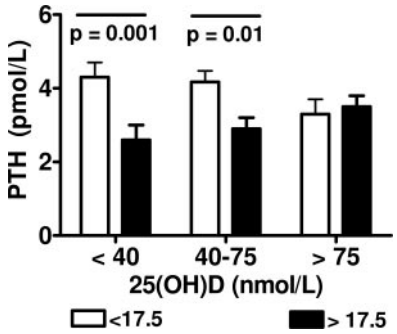

FIG. 3. Adjusted mean serum concentrations of PTH according to serum levels of 25(OH)D and levels of daily calcium intakes (mmol). Data are presented as mean ± SE of the mean. *P* values are by the Tukey test.

Femoral neck T score

Femoral neck bone mineral density values were obtained in 47 women. The T score was positively associated with 25(OH)D levels ($r = 0.45$; $P = 0.002$). The negative association between the T score and PTH levels was at the limit of statistical significance ($r = -0.26$; $P = 0.05$).

Discussion

Sunlight is an important source of vitamin D (2, 11), but from November to March at latitudes above 35° N, very little, if any, vitamin D is produced in human skin during exposure to sunlight (15). Therefore, during June and July in Belgium (latitude, 50° N), we were surprised to find that 50 of 85 postmenopausal women (59%) had serum 25(OH)D levels less than 75 nmol/liter. The prevalence of vitamin D deficiency in this population should be even higher during winter because 25(OH)D has a half-life of 2–3 wk (26). Although comparisons between reports are difficult because of differences in 25(OH)D cutoffs and the 25(OH)D assays used (27), epidemiological studies conducted in postmenopausal populations at the end of winter have reported that 52% of North American women treated for osteoporosis had 25(OH)D less than 75 nmol/liter (9) and that 39% of ambulatory Spanish women had 25(OH)D less than 37.5 nmol/liter (28).

The prevalence of 25(OH)D less than 75 nmol/liter was much higher in urban residents (32 of 38 or 84%) than in rural residents (18 of 47 or 38%). The factors responsible for this marked difference in the prevalence of vitamin D deficiency between urban dwellers and rural dwellers were not obvious. According to inclusion criteria, urban and rural residents all had daily outdoors activities and were free of diseases and/or drugs influencing vitamin D metabolism and serum 25(OH)D levels (2). Furthermore, in this and previous studies (29, 30), BMI was negatively associated with 25(OH)D levels, but our urban residents and rural residents did not differ in either their mean BMI or vitamin D intakes.

The observation that 25(OH)D levels were positively associated with SEI in urban and rural dwellers supports the contention that skin exposed to sunlight is an important source of vitamin D for many people (2). The mean SEI was moderately (1.3 times) but significantly higher in urban residents, a finding likely to result, at least in part, from differences in lifestyles between urban and rural women in Belgium. When the weather permits, urban residents spend more time outdoors during daylight hours. In contrast, rural women may tend to avoid outdoor activities during peak sunny hours and often must drive to a shopping mall for purchases in which they are protected from sunlight.

Furthermore and importantly, our data provide strong, albeit indirect, evidence that the cutaneous synthesis of vitamin D was less efficient in urban than rural residents. To obtain the same 25(OH)D level, urban inhabitants required a SEI about 3-fold higher than that required by rural inhabitants, and, in turn, for any given SEI, the mean 25(OH)D level of urban dwellers was about 2 times lower than that of rural dwellers.

The reasons urban and rural residents differed in the efficiency of cutaneous synthesis of vitamin D were not obvious (2, 11). Although sunscreen use, aging, and skin pigmentation all decrease skin vitamin D synthesis, the two groups did not use topical sunscreens, and both had similar mean ages and skin tones. Furthermore, because the study was conducted during the same months and at the same latitude, the zenith angle by which sunlight penetrates the earth's atmosphere was similar for the two groups, a point worth stressing because this angle dramatically influences the amount of UVB photons reaching the earth's surface and ultimately penetrating the skin (2, 15).

On the other hand, because stratospheric ozone efficiently absorbs solar UVB photons (15, 31), any increase in the ozone content of the troposphere is likely to reduce the amount of photons penetrating the skin and hence to diminish the cutaneous production of vitamin D (2). Therefore, the observation that levels of tropospheric ozone were 3 times higher in Brussels than the countryside helps put into perspective an important finding: to obtain the same 25(OH)D level, urban residents required an SEI that was 2–3 times higher than that of rural residents. Of course, definitive proof of the effect of tropospheric ozone on 25(OH)D levels would have required moving the urban residents to the countryside and vice versa, but this approach was impossible for practical reasons. Nevertheless, although there is concern that the decrease in stratospheric ozone contributes to the increasing incidence of skin damage and cancers (31), our observations strongly suggest that, as do dark skin pigmentation and protection of sun-exposed skin areas by sunscreens and clothes, tropospheric ozone adversely affects vitamin D status by interfering with skin penetration of UVB.

Levels of 25(OH)D required to prevent secondary hyperparathyroidism have been reported to be as low as 45–50 nmol/liter (7, 20), greater than 100 nmol/liter (8), or around 60–75 nmol/liter as observed herein and by others (5, 9). This discrepancy in thresholds for 25(OH)D levels might be related to different factors such as the 25(OH)D assay used (27), the age-related reduction in renal function (32), and/or different dietary calcium intakes in study populations (20). In our study, levels of dietary calcium had no effect on PTH levels in subjects with 25(OH)D greater than 75 nmol/liter, whereas among subjects with 25(OH)D less than 75 nmol/liter, those with a calcium intake less than 17.5 mmol/d had a higher mean

PTH level than those with a calcium intake greater than 17.5 mmol/d. Thus, as suggested previously (20), high dietary calcium intakes may be unnecessary for preventing secondary hyperparathyroidism in subjects with 25(OH)D levels above 75 nmol/liter.

It is noteworthy that the femoral neck T score, a strong predictor of fracture risk (33), was positively associated with 25(OH)D and negatively associated with PTH. Secondary hyperparathyroidism associated with hypovitaminosis D induces and/or exacerbates bone loss (2, 4), and many elderly patients (75–95%) hospitalized for hip fractures have 25(OH)D levels less than 50 nmol/liter (34).

Our study has several limitations. First, the reported ozone levels are not those experienced by each subject but those experienced by each group as a whole. Second, to reduce the potential unreliability of sun exposure and dietary reports, women were interviewed twice using the same validated questionnaires, and subjects with retest values outside the 85–115% range of test values were discarded. However, even by doing this, we are not sure to have eliminated all unreliable reporters. Third, because we only studied ambulatory, community-dwelling Caucasian women, the prevalence of vitamin D deficiency might be even higher in urban non-Caucasians with daily outdoor activities.

In conclusion, the high tropospheric ozone content of urban areas is a neglected risk factor for vitamin D deficiency. Considering the important role of vitamin D in bone health and calcium metabolism as well as the possible role of the vitamin in several other health outcomes, including the development of cancer, muscle weakness, insulin resistance, diabetes, cardiovascular disease, and several autoimmune diseases (11, 12), it may be relevant to take air pollution into account when assessing vitamin D requirements and identifying key risk factors associated with suboptimal 25(OH)D levels.

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The authors have nothing to disclose.

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