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Metabolism Clinical and Experimental 57 (2008) 741 – 748
Metabolism
Clinical and Experimental
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# 25-Hydroxyvitamin D, cholesterol, and ultraviolet irradiation

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Received 22 June 2007; accepted 10 January 2008

**Abstract**

Vitamin D deficiency may have implications for cardiovascular health. The purpose of this study was to determine the relationship of 25-hydroxyvitamin D (25[OH]D) to cholesterol and lipoprotein particles and to determine whether increasing 25(OH)D through ultraviolet (UV) irradiation impacted on these parameters in healthy young men and women. This was a randomized trial of 51 adults exposed to suberythemal doses of whole-body irradiation using UV lamps that emitted UV-A and UV-B radiation, compared with a control group, twice weekly for 12 weeks. 25-Hydroxyvitamin D, cholesterol, and lipoprotein subfractions were measured at baseline and after 12 weeks. There was a significant ($P < .03$) positive association between 25(OH)D and apolipoprotein A-I (Apo A-I) and lipoprotein A-I (Lp A-I). The ratio of low-density lipoprotein to high-density lipoprotein was significantly ($P \leq .044$) negatively correlated with 25(OH)D levels. The levels of 25(OH)D increased significantly in the treated compared with control group ($P < .05$). Overall, there were no significant differences between the treated and control groups in any lipoproteins or apolipoproteins after administration of UV irradiation. Subgroup analysis for Apo A-II confined to those with 25(OH)D insufficiency (25[OH]D <75 nmol/L [30 ng/mL]) revealed decreases in Apo A-II in the treated group and increases in the control group that were statistically significantly different between the groups ($P = .026$). We found a significant positive correlation between 25(OH)D and Apo A-I and Lp A-I and a significant negative correlation between 25(OH)D and the ratio of low-density lipoprotein to high-density lipoprotein. In those with vitamin D insufficiency, we found small decreases in Apo A-II in the treated relative to the control group. Overall, though, twice weekly exposure to UV radiation resulting in an increase in serum 25(OH)D had no significant impact on lipoprotein composition.
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## 1. Introduction

Vitamin D is an essential hormone produced primarily from exposure to ultraviolet (UV) B radiation from sunlight [1], with small amounts also obtained through diet [2]. Worldwide, vitamin D deficiency is becoming a problem of epidemic proportions [3,4]. This has serious public health ramifications because vitamin D plays a role in both skeletal and nonskeletal disorders [5-9]. A 25-hydroxyvitamin D (25[OH]D) level of less than 75 nmol/L (<30 ng/mL) is considered to be suboptimal vitamin D status; this level is the minimal level of 25(OH)D necessary to suppress parathyroid hormone secretion [10-13]. A 25(OH)D level of between 52 nmol/L (21 ng/mL) and 74 nmol/L (29 ng/mL) is considered to be vitamin D insufficiency [12]. Darker-skinned individuals are at particular risk for vitamin D deficiency because melanin is a natural sunscreen [9]. The

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0026-0495/$ – see front matter © 2008 Published by Elsevier Inc.
doi:10.1016/j.metabol.2008.01.011

duration or dose of exposure to UV-B to achieve equivalent 25(OH)D levels may differ by degree of pigmentation or skin type [14]. Cross-sectionally, users of tanning beds have been noted to have higher 25(OH)D levels than nonusers [15].

Dyslipidemia is a potent risk factor for cardiovascular disease (CVD) [16]. There are seasonal variations in lipid levels, with total cholesterol, triglyceride, low-density lipoprotein (LDL), and lipoprotein A highest in the winter, a time at which UV-B–induced synthesis of vitamin D would be expected to be at its minimum [17]. The purpose of this study was to determine the relationship of 25(OH)D to cholesterol and lipoprotein particles and to determine the effects of UV-B and UV-A irradiation on changes in 25(OH)D, cholesterol, and lipoprotein particles.

## 2. Methods

The study was approved by the University of Tennessee Health Science Center Institutional Review Board, and all participants gave written informed consent in accordance with Helsinki guidelines. Between February and March 2005, 51 healthy participants, with no history of CVD, including 21 men and 30 women, were enrolled in this study in Memphis, TN (latitude 35°N to 36°41′N).

Participants were stratified into 3 groups according to skin types, with higher numbers indicating darker skin [18,19]: group A = skin type II, group B = skin types III and IV, and group C = skin type V; whites, Asians, and African Americans were all included in this study in their respective skin type groups. A total-body skin examination was performed at the beginning of the study to determine skin type and to exclude any potential participants with cancerous or precancerous lesions; this was repeated at study end.

Exclusion criteria included a history of skin cancer, dysplastic nevi, or moles; use of lipid-lowering medications or medications with photosensitizing adverse effects (including tetracycline, retinoic acid, angiotensin-converting enzyme inhibitors, or thiazide diuretics); use within 1 month of study of a tanning bed or use during duration of study; or use of calcium or vitamin D supplementation (including multivitamins) within 1 month of the study and for the duration of study. No participants were employed in occupations associated with sunlight exposure. Participants were instructed to continue their usual dietary and exercise habits, without change, for the duration of the study.

All blood work for this study was drawn in the morning, after an overnight fast.

### 2.1. Sources of UV radiation

Two identical Sunvision model tanning beds (ETS, Indianapolis, IN) were used in this study. The treated group received primarily broad-spectrum UV radiation from a tanning bed that also emitted visible and near-infrared radiation. The UV irradiance of this bed was 2.0 W/m$^2$ UV-B (280-315 nm) and 135.2 W/m$^2$ UV-A (315-400 nm). In the control group, the tanning bed was modified by the substitution of a UV-attenuating acrylic in place of the normal UV-transmitting shields. To block all UV, the UV-attenuating acrylic would not have appeared colorless, precluding blinding of the participants as to treatment arm. Consequently, the control tanning bed emitted no UV-B radiation and only approximately <4% (5.4 W/m$^2$) UV-A radiation, at wavelengths >350 nm, in addition to the same visible and infrared radiation as the treated group.

### 2.2. UV dosimetry

All participants received serial whole-body (except for areas covered by underwear) exposure to broad-spectrum UV radiation (treated group) or UV-attenuated (<4% UV-A at wavelengths >350 nm with no UV-B, control group) radiation in a tanning bed 2 times per week for 12 weeks. The spectrum of each UV source (Fig. 1) was measured using a scanning double monochromator spectroradiometer (model OL 754l; Optronic Laboratories, Orlando, FL) scanning at 1-nm increments from 250 to 800 nm. The instrument was configured with 0.125/0.5/0.125-mm slits interfaced to a 4-in–diameter integrating sphere with a 19-mm entrance aperture by an I meter quartz fiber-optic bundle. The spectroradiometer was calibrated by scanning a National Institutes of Standards and Technology traceable tungsten-halogen spectral irradiance standard (model 752-10E, Optronic Laboratories) with a precision current source (model 65, Optronic Laboratories) at 1-nm increments using procedures established by the manufacturer of the instrument. This system also used a small portable dual-source calibration module (model 752-150, Optronic Laboratories) to check both the photometric gain, using a

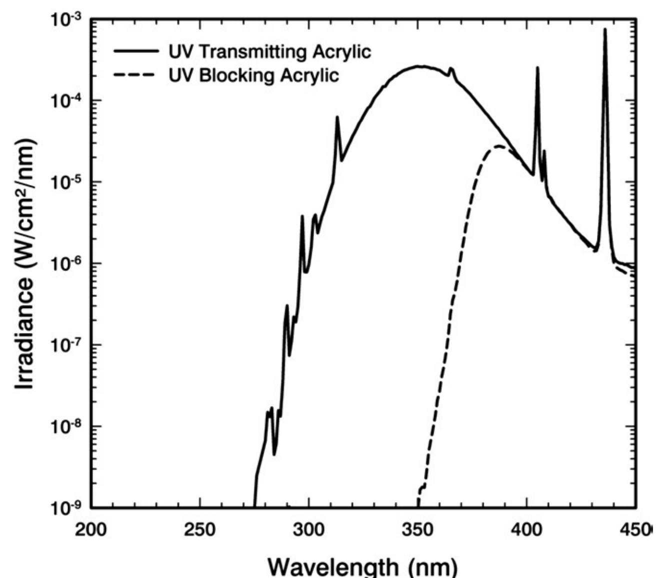


Fig. 1. The spectral irradiance of the unmodified units with UV-transmitting acrylics compared with that of the units modified with UV-blocking acrylics shows that the placebo group was not exposed to detectable levels of UV-B or UV-A.

small tungsten-halogen source, and the wavelength accuracy, using Hg lines from a small fluorescent source. Before each calibration or measurement, the wavelength calibration and gain are established or verified. Because we did not clinically determine minimal erythemal doses (MEDs) for our participants, we describe the erythemally effective UV doses given in units of International Standards Organization standard erythema dose (SED) [20]. According to the International Standards Organization 17166:1999(E), "1 SED is equivalent to an erythemal effective radiant exposure of 100 J/m$^2$." The MEDs in participants with skin types II to V would be expected to lie between erythemal effective radiant exposures of 150 to 600 J/m$^2$, equivalent to 1.5 to 6 SEDs.

Participants in the treated group received suberythemal UV exposures adjusted for relative UV photosensitivity by skin type. Group A (skin type II) received 4 minutes of exposure or 0.84 SED, group B (skin types III and IV) received 6 minutes of exposure or 1.26 SEDs, and group C (skin type V) received 8 minutes of exposure or 1.69 SEDs 2 times per week. Relative to MEDs, skin type II participants would be expected to have a MED approximately equal to 2 to 3 SEDs; skin types III and IV would be expected to have a MED approximately equal to 3 to 6 SEDs; and skin type V would be expected to have MEDs equal to 5 to 8 SEDs. The control groups received the same exposure times based on skin type. Participants and investigators were blinded as to treatment assignment.

### 2.3. 25-Hydroxyvitamin D

Serum 25(OH)D was measured by competitive protein binding assay after extraction with 100% ethanol as previously described [21]. The intra- and interassay coefficients of variation are 5% to 10% and 10% to 15%, respectively. The assay has a sensitivity of 5 ng/mL. The normative reference range is 50 to 250 nmol/L (20-100 ng/mL) [21].

### 2.4. Analysis of lipids

#### 2.4.1. Lipoprotein separation by ultracentrifugation

Lipoproteins were isolated and analyzed as previously described [22,23] using a gradient ultracentrifugation–high-performance liquid chromatography (HPLC) technique.

#### 2.4.2. Apolipoprotein analysis by HPLC

One milliliter of very low-density lipoprotein (VLDL) and 2 mL of intermediate-density lipoprotein (IDL) were delipidated with 2 mL of hexane–isopropyl alcohol (3:2) after adding human insulin as an internal standard. Aliquots from each of the 3 high-density lipoprotein (HDL) subfractions were pooled in proportion to their original volumes, and then 0.5 mL was delipidated by the same technique as VLDL and IDL. After the hexane was removed, an aliquot from the aqueous layer was injected onto an HPLC column and analyzed as previously described [23]. The coefficient of variation for the apolipoprotein concentrations were as follows: Apo A-I, 0.4; Apo A-II, 3.9; Apo C-III, 3.6; Apo C-II, 2.3; and Apo C-I, 5.4. Lipoprotein A-I:A-II particles (HDL particles containing both Apo A-I and Apo A-II) in HDL-L and HDL-M have a molar A-II/A-I ratio of 3:4, whereas HDL-D has a ratio of 1:2. From these known ratios, the number of Lp A-I (HDL containing Apo A-I without Apo A-II) particles can be estimated from the measured Apo A-II to Apo A-I ratios.

#### 2.4.3. Enzymatic and chemical assays

Total cholesterol and triglycerides were assayed using standard enzymatic assays. The Apo B (in millimoles per liter) content of LDL was determined [24,25] by Lowry assay with bovine serum albumin used as a standard. The number of LDL particles can be calculated from the Apo B concentration because there is only one molecule of Apo B per LDL particle.

### 2.5. Statistical analysis

The experimental design was a randomized block with repeated measurements assessed over time; thus, participants were used as their own controls. Randomization was blocked by skin type and sex. Blocking was done by a study coordinator who did not participate in data analysis or care of the participants; all investigators and participants remained blinded to the randomization scheme. Within blocks, participants were randomized to receive 1 of 2 treatments (UV irradiation or placebo). Except where noted in the results, analyses and preplanned contrasts were made ignoring blocks. Demographic characteristics for the 2 groups were compared with $\chi^2$ tests or Fisher exact 2-tailed tests for categorical variables or $t$ tests for continuous variables. For outcome measurements, 2 types of analyses were performed. First, actual values were compared in the context of repeated-measures analysis of variance with the pooled within-participant error term used for contrasts made within treatment group (ie, baseline vs final assessment). Second, to determine whether changes in outcome variables were different for the 2 treatment groups, change scores were computed (ie, final assessment minus baseline assessment); and these were compared with $t$ tests or 1-way analysis of variance. A $P$ value $< .05$ was considered statistically significant.

## 3. Results

Fifty-one participants enrolled in this study. Two participants withdrew before study completion (both in the treated group): one was withdrawn because of elevated blood pressure noted at the baseline visit and one because of scheduling conflicts. Overall, there were no significant differences between the controls and the treated participants with respect to age, sex, skin type, skin group, or body mass index (Table 1).

At baseline, there were statistically significant positive associations between 25(OH)D and Apo A-I ($P$ = .028,

Table 1
Baseline characteristics of study population

| Characteristic | Control group (UV-A attenuated) n = 24 | Treated group (broadband UV, UV-B plus UV-A) n = 27; (completed all visits, n = 25) | *P* value |
|---|---|---|---|
| Age (y) | 30 ± 2 | 32 ± 2 | .538 |
| Sex | | | |
| Male | 9 (43) | 12 (57) | .615 |
| Female | 15 (50) | 15 (50) | |
| Skin type | | | |
| II | 9 (47) | 10 (53) | .485 |
| III | 9 (60) | 6 (40) | |
| IV | 2 (25) | 6 (75) | |
| V | 4 (44) | 5 (56) | |
| Skin group | | | |
| A | 9 (47) | 10 (53) | .999 |
| B | 11 (48) | 12 (52) | |
| C | 4 (44) | 5 (56) | |
| BMI (kg/m$^2$) | 27.4 ± 1.9 | 26.5 ± 1.1 | .670 |

Mean ± SEM or frequency (percentage of a category). BMI indicates body mass index.

*r* = 0.315) and Lp A-I (*P* = .016, *r* = 0.344), with a trend toward an inverse relationship between 25(OH)D and Apo B/Apo A-1 (*P* = .062, *r* = −0.268) (Table 2A). These relationships were similar or slightly stronger at the conclusion of the study (Apo A-I: *P* = .010, *r* = 0.363; Lp A-I: *P* = .014, *r* = 0.350; and Apo B/Apo A-1: *P* = .059, *r* = −0.272) (Table 2B>). The ratio of LDL cholesterol (LDL-C) to HDL cholesterol (HDL-C) was significantly negatively correlated with 25(OH)D levels at baseline; this relationship weakened but remained significant at the conclusion of the study (*P* = .010, *r* = −0.367 and *P* = .044, *r* = −0.289, respectively) (Tables 2A and 2B). There was an even stronger significant correlation between the baseline 25(OH)D levels (all *P* < .001) and total HDL (*r* = 0.528), HDL-L (*r* = 0.451), and HDL-M (*r* = 0.556) (Table 2A, Fig. 2). There was a significant trend for a positive association between total HDL and HDL-M and 25(OH)D that remained at the final visit (*P* = .090 and *P* = .095); however, there was no significant relationship between 25(OH)D and HDL-L at the final visit (*P* = .144) (Table 2B). There was no statistically significant relationship between 25(OH)D and total cholesterol, other lipoprotein particles, or triglyceride (Tables 2A and 2B).

Table 2A
Relationship of baseline 25(OH)D levels to baseline total cholesterol and lipoprotein particles (n = 49)

| Parameter | Correlation coefficient (*r*) | *P* value |
|---|---|---|
| Total cholesterol (mg/dL) | 0.058 | .692 |
| LDL (mg/dL) | −0.142 | .329 |
| HDL (mg/dL) | 0.528 | <.001 |
| HDL-L | 0.451 | .001 |
| HDL-M | 0.556 | <.001 |
| HDL-D | 0.137 | .347 |
| LDL/HDL | −0.367 | .010 |
| Triglycerides (mg/dL) | −0.118 | .421 |
| Apo A-I (mg/dL) | 0.315 | .028 |
| Apo A-II (mg/dL) | 0.154 | .291 |
| Apo B/Apo A-I (μmol/L) | −0.268 | .062 |
| Lp A-I | 0.344 | .016 |

Table 2B
Relationship of final 25(OH)D levels to final total cholesterol and lipoprotein particles (n = 49)

| Parameter | Correlation coefficient (*r*) | *P* value |
|---|---|---|
| Total cholesterol (mg/dL) | 0.007 | .963 |
| LDL (mg/dL) | −0.163 | .263 |
| HDL (mg/dL) | 0.245 | .090 |
| HDL-L | 0.212 | .144 |
| HDL-M | 0.241 | .095 |
| HDL-D | 0.152 | .297 |
| LDL/HDL | −0.289 | .044 |
| Triglycerides (mg/dL) | −0.090 | .540 |
| Apo A-I (mg/dL) | 0.363 | .010 |
| Apo A-II (mg/dL) | 0.200 | .169 |
| Apo B/Apo A-I (μmol/L) | −0.272 | .059 |
| Lp A-I | 0.350 | .014 |

Participants in the treated group significantly increased their 25(OH)D levels relative to the control group (treated: baseline 25[OH]D, 80 ± 5 nmol/L [32 ± 2 ng/mL]; final 25(OH)D, 142.5 ± 5 nmol/L [57 ± 2 ng/mL], *P* < .05; control: baseline 25[OH]D, 107.5 ± 5 nmol/L [43 ± 2 ng/mL]; final 25[OH]D, 120 ± 5 nmol/L [48 ± 2 ng/mL], *P* > .05) (*P* < .05 for differences between groups). The increases in 25(OH)D that occurred in the treated group were a function of baseline 25(OH)D levels (Fig. 3), and the changes in 25(OH)D from baseline were significant only in those with baseline 25(OH)D insufficiency (25[OH]D level of <75 nmol/L [30 ng/mL]) (Table 3). Vitamin D deficiency and insufficiency were very common in African Americans (skin types IV and V), with 75% of the participants of African American descent having a 25(OH)D level of <75 nmol/L (30 ng/mL).

Significant differences in the changes from baseline to 12 weeks occurred between the treated and the control groups in Apo A-II levels; however, this was a result of significant increases in Apo A-II occurring in the control and not the treated group (Table 4). There were no statistically significant differences in the changes from baseline to 12 weeks between the treated and control groups for total cholesterol or other lipoprotein particles or triglycerides (Table 4). The VLDL and IDL also did not significantly change with phototherapy (data not shown).

A subgroup analysis of all lipoprotein subfractions and apolipoproteins was done in those participants with a low baseline 25(OH)D (<75 nmol/L [<30 ng/mL]). There were statistically significant differences in Apo A-II between the treated and the control group (baseline levels subtracted from 12-week values); however, again these differences were largely a function of the increases in Apo A-II that occurred in the control group (Fig. 4). There were no significant differences in any other lipoprotein subfraction or apolipoprotein with the intervention (data not shown).

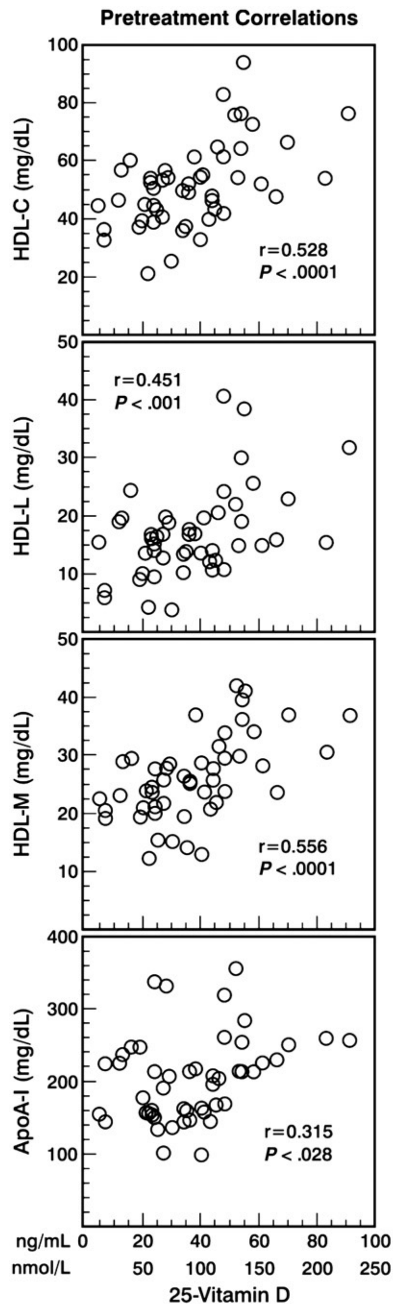


Fig. 2. Relationship between 25(OH)D and HDL-C, HDL-L, HDL-M, and Apo A-I.

One participant in the treated group (an African American woman, skin type V) reported mild erythema that occurred after the first treatment and resolved within 24 hours. There were no skin abnormalities noted by the study dermatologist at study end.

## 4. Discussion

In a racially diverse population of men and women, there were significant positive associations between 25(OH)D and HDL-C, HDL-L, HDL-M, Apo A-I, and Lp A-I, and a significant negative association between 25(OH)D and the ratio of LDL-C to HDL-C. Exposure to broadband UV, UV-B plus UV-A radiation significantly increased serum 25(OH)D levels relative to controls in those with baseline vitamin D deficiency or insufficiency. It is likely that the UV-B irradiation was responsible for the increases seen in 25(OH)D levels because only UV-B radiation is responsible for producing vitamin D in the skin.

Lipoprotein A-I is a subset of HDL particles that contains Apo A-I but not Apo A-II. The concentrations of Lp A-I are inversely related to CVD [25-27], whereas the ratio of LDL-C to HDL-C is positively correlated with CVD [28]. Therefore, given the relationships between these cholesterol subfractions and serum 25(OH)D levels demonstrated in our study, it is plausible that vitamin D status may have a significant impact on CVD. In accord with our findings, a significant positive linear association between Apo A-I and 25(OH)D in Belgian men and women [29] and in South Asians [30] has been reported. Our study extends this finding to include all racial groups and is the first report to suggest that apolipoprotein Lp A-I and the lipoprotein ratio of LDL to HDL are also correlated with 25(OH)D levels. Notably, there were consistent relationships between these lipoprotein and apolipoprotein levels and 25(OH)D in our study, with similar results obtained at the baseline and end-of-study analyses.

Theoretically, it is plausible that UV-B irradiation may have positive effects on lipids through the photoconversion of 7-dehydrocholesterol (7-DHC) to lumisterol or 7-dehydropregnenolone or its 5,7-steroidal diene hydroxyl derivatives to other vitamin $D_3$–like photoproducts [31]. Exposure to UV irradiation in our study, however, did not produce significant changes in lipoproteins or apolipoproteins. Cross-sectionally, there was no relationship between Apo A-II and 25(OH)D, so we would not predict that this

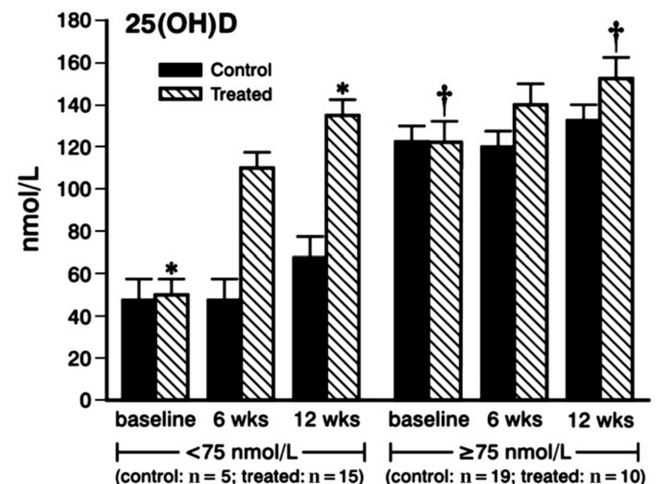


Fig. 3. Effects of exposure to broadband UV, UV-B plus UV-A (treated), and attenuated UV-A (control) irradiation on 25(OH)D levels stratified by baseline levels of 25(OH)D (mean ± SEM; n = 49; *$P < .01$, †$P < .05$).

Table 3
Effects of exposure to broadband UV (treated) and attenuated UV-A (control) irradiation on 25(OH)D levels stratified by baseline levels of 25(OH)D (mean ± SEM) (n = 49)

| Parameter | 25(OH)D (nmol/L) | | | *P* value for difference from final to initial in each group | *P* value for change between groups |
|---|---|---|---|---|---|
| | Baseline | 6 wk | 12 wk | | |
| 25(OH)D <75 nmol/L (<30 ng/mL) | | | | | |
| Control (n = 5) | 47.5 ± 10 | 47.5 ± 10 | 67.5 ± 10 | .222 | <.001 |
| Treated (n = 15) | 50 ± 7.5 | 110 ± 7.5 | 135 ± 7.5 | <.001 | |
| 25(OH)D ≥75 nmol/L (>30 ng/mL) | | | | | |
| Control (n = 19) | 122.5 ± 7.5 | 120 ± 7.5 | 132.5 ± 7.5 | .329 | .363 |
| Treated (n = 10) | 122.5 ± 10 | 140 ± 10 | 152.5 ± 10 | .051 | |

would have meaningfully changed with the intervention. The stability of Apo A-II levels in the treated relative to the control group may reflect the small sample size or an $\alpha$ error. If indeed, however, in repeated studies, UV irradiation does lower Apo A-II levels, this would be important, as Apo A-II inhibits almost every step of reverse cholesterol transport [22,32-34]. In humans, Apo A-II influences HDL functional status and is likely a contributor to atherogenesis [35]. In our study, there was no significant effect of the intervention on any other lipoprotein/apolipoprotein. This suggests that UV irradiation does not have an impact on lipoprotein/apolipoprotein levels. Alternatively, it is possible that the failure to affect other lipoprotein/apolipoproteins with our intervention may be a reflection of sample size, short duration of the intervention, and the failure to confine our study to those with hyperlipidemia and/or baseline 25(OH)D insufficiency.

Table 4
Changes in total cholesterol, cholesterol subfractions, and triglycerides in treated vs control group (mean ± SEM) (n = 49)

| Parameter | Initial | Final | *P* value for difference from final to initial in each group | *P* value for change between groups |
|---|---|---|---|---|
| Total cholesterol | | | | |
| Control | 169 ± 3 | 179 ± 3 | .022 | .152 |
| Treated | 173 ± 3 | 173 ± 3 | .922 | |
| LDL | | | | |
| Control | 90 ± 3 | 100 ± 3 | .012 | .577 |
| Treated | 97 ± 2 | 103 ± 3 | .086 | |
| HDL | | | | |
| Control | 54 ± 2 | 59 ± 2 | .072 | .148 |
| Treated | 49 ± 2 | 50 ± 2 | .716 | |
| Triglycerides | | | | |
| Control | 111 ± 10 | 90 ± 10 | .141 | .893 |
| Treated | 126 ± 9 | 102 ± 10 | .085 | |
| LDL/HDL | | | | |
| Control | 1.9 ± 1 | 1.9 ± 1 | .902 | .483 |
| Treated | 2.1 ± 1 | 2.2 ± 1 | .234 | |
| Apo A-I | | | | |
| Control | 198 ± 7 | 178 ± 7 | .031 | .281 |
| Treated | 206 ± 6 | 171 ± 7 | .0003 | |
| Apo A-II | | | | |
| Control | 47 ± 2 | 53 ± 2 | .034 | .045 |
| Treated | 54 ± 2 | 52 ± 2 | .448 | |
| Apo B/Apo A-I | | | | |
| Control | 0.32 ± 0.01 | 0.38 ± 0.01 | .003 | .420 |
| Treated | 0.32 ± 0.01 | 0.35 ± 0.01 | .053 | |
| Lp A-I | | | | |
| Control | 34 ± 1 | 23 ± 1 | <.0001 | .842 |
| Treated | 32 ± 1 | 21 ± 1 | <.0001 | |

It is also possible that the association between lipoproteins and vitamin D is actually in the reverse direction, that is, that antiatherogenic lipoproteins (HDL, HDL-L, Apo A-I, and Lp A-I) increase vitamin D and not that vitamin D increases antiatherogenic lipoproteins, especially at times when vitamin D levels are typically suppressed. Cholesterol is an important component of the barrier function of the skin; and during times of stress, the requirement for additional cholesterol increases [36]. This requirement can be met with either endogenous synthesis of cholesterol or accrual from the plasma. The final precursor of endogenous cholesterol synthesis is 7-DHC, which is also the substrate that reacts with UV-B to produce vitamin D. Vitamin D synthesis is dependent upon the concentration of 7-DHC [37,38]. There is evidence that a reduction in cellular cholesterol concentration increases 7-DHC reductase (the enzyme that converts 7-DHC to cholesterol) messenger RNA and activity [39]. It is possible that an influx of cholesterol from plasma lipoproteins could increase 7-DHC concentrations, which would, in turn, increase vitamin D synthesis. Our study

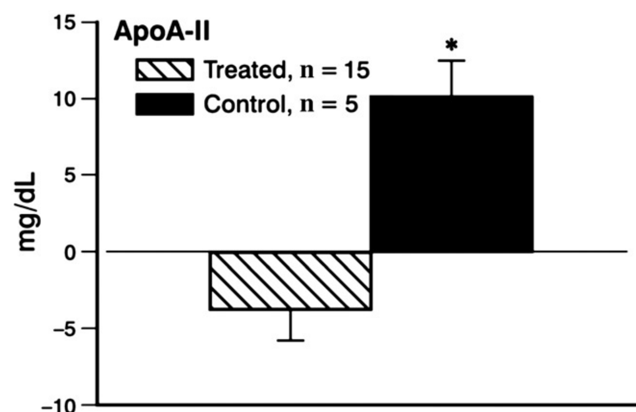


Fig. 4. Effects of exposure to broadband UV, UV-B plus UV-A (treated), and attenuated UV-A (control) irradiation on Apo A-II levels in those with baseline vitamin D deficiency (25[OH]D <75 nmol/L [<30 ng/mL]). *$P$ = .026.

began at the end of winter when the skin is most stressed. At that time, we found very strong correlations between 25(OH)D and total HDL, HDL-L, HDL-M, Apo A-I, and Lp A-I. These correlations were strongest in women (data not shown) who typically have the highest concentrations of Lp A-I and HDL-L. Later, in the spring, when the skin would be less stressed, the correlations with the HDL-C levels were less strong; but similar trends were still present in both treatment groups. However, the correlations with the HDL particle number parameters (Apo A-I and Lp A-I) were the same or stronger. Given this proposed model, we speculate that the additional UV stimulus might have reduced the influence of 7-DHC concentration on vitamin D synthesis, thereby accounting for the lack of response of the lipoproteins to the intervention. It is possible, therefore, that antiatherogenic lipoproteins (HDL, HDL-L, Apo A-I, and Lp A-I) increase vitamin D, especially at times when vitamin D levels are typically suppressed.

Vitamin D deficiency has been reported in 36% of otherwise healthy young adults and, similar to what we saw in our study, is particularly common among African Americans [40]. Exposure to the UV irradiation in the treated group was effective in significantly increasing 25(OH)D levels compared with baseline only in those with preexisting low levels of 25(OH)D. Oral vitamin D supplementation (cholecalciferol) is most effective at increasing 25(OH)D levels in those with the lowest baseline concentrations; although the reasons for this are not known, it has been suggested that it either is just regression to the mean or, conversely, might be because increased vitamin D supplementation inhibits 25-hydroxylase in the liver [41]. Although we did not explore mechanisms for this, our data extend these findings [41] to suggest that the increases in vitamin D levels with UV-B are also a function of baseline 25(OH)D levels and are most effective in those with low levels. It is possible that our intervention might have significantly affected lipoprotein/apolipoprotein levels had we selected a sufficiently large population with baseline 25(OH)D insufficiency. Future work in this area should consider targeting populations with vitamin D insufficiency.

Exposure to UV radiation is associated with a risk for skin cancer, and the incidence of skin cancer is rising [42]. We screened our participants for any cancerous or precancerous lesions, and no skin abnormalities developed during our short study. However, because of the inherent risks of UV irradiation, it will be important to determine the minimum doses of UV-B irradiation that provide adequate 25(OH)D levels in different racial groups.

There are several limitations to our study. Most of our participants with skin types II and III did not have vitamin D deficiency; one might postulate that the intervention would have been more successful had only a vitamin D–deficient population and/or one with baseline hyperlipidemia been included. Although allocation to treatment or placebo was blinded and there were greater differences in levels of 25(OH)D between the treated and control group by study end than there were at baseline, at baseline, 25(OH)D levels were already significantly higher in the treated relative to the control groups. This likely reflects the fact that we did not recruit or randomize by baseline 25(OH)D levels (and in fact, processed all 25[OH]D levels in batch at the end of the study). In addition, the correlations between cholesterol subfractions and 25(OH)D, although statistically significant, were small. There were also significant increases in 25(OH)D levels in the control group with skin type II; and because of recruitment issues, the intervention extended into June. Therefore, we may have had significant confounding from vitamin D produced by outdoor sun exposure. That sun-induced synthesis of vitamin D could have occurred during the latter months of our study has been reported [43].

In conclusion, there is a positive correlation between 25(OH)D and Apo A-I and Lp A-I and a negative correlation between 25(OH)D and the ratio of LDL to HDL. Exposure to UV-B radiation is most effective at increasing serum levels of 25(OH)D in those with baseline low levels of vitamin D. However, we found no significant effect of UV irradiation at altering lipoprotein/apolipoprotein levels in our study.

## Acknowledgment

This work was supported by a grant from the Ultraviolet Foundation and a General Clinical Research Center grant from the National Institutes of Health (M01RR 00211) awarded to the University of Tennessee Health Science Center.

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