

Differential Effect of Race on the Axial and Appendicular Skeletons of Children*

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ABSTRACT

The prevalence of osteoporosis and the incidence of fractures are substantially lower in black than in white subjects, a finding generally attributed to racial differences in adult bone mass. Whether these racial differences are present in childhood is the subject of considerable interest, as the amount of bone gained during growth is a major determinant of future susceptibility to fractures. We measured the density and size of the vertebrae and femurs of 80 black and 80 white healthy children, 8–18 yr of age, matched for age, gender, height, weight, and stage of sexual development, using computed tomography. Race had a significant and differential effect on the bones in the

axial and appendicular skeletons. In the axial skeleton, black children had greater cancellous bone density, but similar cross-sectional area of the vertebral bodies. In contrast, in the appendicular skeleton, black children had greater femoral cross-sectional area, but similar cortical bone area and cortical bone density. Compared to white children, vertebral bone density and femoral cross-sectional area at sexual maturity were, on the average, 10.75% and 5.7% higher, respectively, in black children. Such significant variations may contribute to the racial differences in the prevalence of osteoporosis between black and white adults. (*J Clin Endocrinol Metab* 83: 1420–1427, 1998)

THE PREVALENCE of osteoporosis and the incidence of fractures are substantially lower in black than in white subjects, a finding generally attributed to racial differences in adult bone mass (1, 2). Whether these racial differences are present in childhood is the subject of considerable interest, as it is becoming increasingly apparent that the amount of bone that is gained during growth is a major determinant of future susceptibility to fractures (3, 4). Several reports, including those of cadavers (5, 6) and those using radiogrammetry (7), have suggested a greater skeletal size in black children, and most studies with single photon absorptiometry have indicated radial bone mass to be greater in black subjects (8, 9). More recent investigations using dual x-ray or photon absorptiometry techniques have yielded conflicting results. Some studies found the bone mass of black children to be greater than that of white children (10, 11), whereas others detected no racial differences in bone mass in either the axial or appendicular skeleton (12, 13).

Various factors may account for the discrepancy between the results of previous studies, including technical limitations of measurement modalities and failure to appropriately match subjects. In children, bone measurements by absorptiometry methods are greatly influenced by the size of the growing skeleton, as they are unable to assess the size and the density of bone separately (14, 15). Moreover, previous

comparisons of bone mass between black and white children did not take into account racial differences in upper and lower body segment lengths. Black children have longer legs and shorter trunks than white children, and failure to adjust for these differences may have led to inaccurate results (16, 17). Lastly, as puberty is a major determinant of bone gain during growth, the lack of precise matching of sexual maturation could explain significant differences between previous results.

Quantitative computed tomography (CT) allows for accurate measurements of the size and the density of bone in the axial and appendicular skeletons (14). In this study, we used quantitative CT to investigate whether there are differences in the size or the density of cancellous bone in the vertebrae and/or in the size or the density of cortical bone in the femur between black and white children at different stages of sexual development.

Subjects and Methods

Study subjects

The study subjects were healthy black and white children who were recruited from schools of Los Angeles County. The investigational protocol was approved by the institutional review board for clinical investigations at this facility, and informed consent was obtained from all subjects and/or their parents. The subjects ranged in age from 8–18 yr.

The children and/or their parents were asked about their racial and ethnic backgrounds. Candidates were excluded if either of their parents or either set of grandparents was not of the same race. Candidates for the study were also excluded if they had been given a diagnosis of chronic illness; if they had been ill for longer than 2 weeks during the previous 6 months; if they had taken any medications, vitamin preparations, or calcium supplements regularly within the previous 6 months; or if they had been hospitalized at any time since birth. All subjects were appropriately physically active for their age.

Candidates underwent a physical examination by a pediatric endocrinologist to determine the stage of sexual development. The grading

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system of Tanner was used, which includes assessments of the pattern of development of pubic hair in all children, of breast development in girls, and of penile and testicular size in boys (16). If discrepancies existed among criteria, greater emphasis was placed on the degree of breast development and on testicular and penile size for determinations of Tanner stage.

Measurements of height, weight, and sitting height were obtained. Children in whom either height or weight was not within the 5th and 95th percentiles for the mean age-adjusted normal values for white children were excluded from further evaluation (18). Thereafter, body surface area and body mass index were calculated as previously described (19). Skeletal maturation was assessed on the basis of roentgenograms of the left hand and wrist according to the method of Greulich and Pyle (20). On the same day, measurements of bone size and bone density were obtained by CT.

Black and white children were matched by chronological age, gender, Tanner stage, height, and weight to control for these important determinants of bone mass. Because of the smaller number of black subjects available, white subjects were evaluated and enrolled in the study before their black counterparts. Thereafter, black subjects were identified, evaluated, and matched with white subjects who had been studied within the previous 3 months. For this analysis, the ages of each pair of subjects differed by less than 6 months, and neither height nor weight differed by more than 5%. Using this approach, we studied 80 unique matched pairs of children: 40 pairs of girls and 40 pairs of boys.

Determination of sample size was based on data from our previous studies demonstrating a mean difference in the vertebral bone density of 37 mg/cm³ with a sd of 20 mg/cm³ between black and white girls at the end of puberty (21). Using a paired *t* test and a 0.05 level of significance, a power of 0.99 was achieved for a sample size of eight subjects in each racial group.

Techniques and definitions of CT measurements

All CT measurements were made with the same scanner (CT-T 9800, General Electric Co., Milwaukee, WI) and mineral reference phantom (CT-T bone densitometry package, General Electric). For determinations in the axial skeleton, the apparent density of cancellous bone and the cross-sectional area were measured at the lumbar vertebrae, and in the appendicular skeleton, the cross-sectional area, the cortical bone area, and the material density of cortical bone were measured at the midshaft of the femur, as previously described (22, 23).

For this study, the density of cancellous bone was defined as the mean value of the CT unit of measurement (milligrams per cm³) at the midportion of the first three lumbar vertebral bodies. Because of the relatively small size of the trabeculae compared with the pixel, CT values for apparent cancellous bone density reflect not only the amount of mineralized bone and osteoid, but also the amount of marrow per pixel (14). These measurements are analogous to *in vitro* determinations of the volumetric density of trabecular bone, which are obtained by washing the marrow from the pores of a specimen of cancellous bone, weighing it, and dividing the weight by the volume of the specimen, including the pores (24).

The density of cortical bone was defined as the amount of bone per pixel (milligrams per cm³) at the midshaft of the femur. Because of the thickness and the relative lack of porosity of cortical bone in the femur, CT values reflect the material or true density of the bone (the amount of collagen and mineral in a given volume of bone) (22). These measurements are analogous to *in vitro* determinations of the intrinsic mineral density of bone, which are commonly expressed as the ash weight per unit volume of bone (25).

In addition, to assess for possible differences in the lengths of the axial and appendicular skeletons, measurements of the heights of the vertebrae and the length of the femur were obtained. Vertebral height was calculated as the mean of the heights of the anterior, middle, and posterior portions of the first three lumbar vertebrae (centimeters), and the length of the femur was calculated as the distance between the acetabular roof and the distal lateral femoral condyle (centimeters).

The coefficients of variation for repeated CT measurements of vertebral cross-sectional area, cancellous bone density, femoral cross-sectional area, cortical bone area, cortical bone density, vertebral heights, and femoral lengths were between 0.6–2.5% (22, 23). The time required for the procedure was approximately 10 min, and the radiation exposure

was approximately 100–200 mrem (1.5 mSv) localized to the midportions of the first three lumbar vertebrae and the femurs; the effective radiation dose was approximately 8 mrem (26, 27).

Biochemical assessment

After an overnight fast, blood was taken for determinations of calciotropic hormones, markers of bone turnover, and levels of GH and sex steroids. Levels of intact PTH, 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D (calcitriol), alkaline phosphatase, bone-specific alkaline phosphatase, calcitonin, insulin-like growth factor I, GH, and osteocalcin in the serum and the urinary excretion of pyridinoline and deoxypyridinoline were measured by Corning Nichols Institute (San Juan Capistrano, CA). Total testosterone, bioavailable testosterone, estradiol, dehydroepiandrosterone sulfate, sex hormone-binding globulin, and androstenedione were determined in the laboratory of Dr. S. Korenman, Division of Endocrinology, University of California-Los Angeles.

Nutritional analysis

Nutritional information was obtained from all subjects using written 3-day records of dietary intake. After receiving instructions from a dietetic technician, subjects recorded their food intake over a 3-day period. The mean of the three daily determinations was calculated for each nutritional component in all subjects, and the information was entered into a computerized database.

Statistical analysis

All results are expressed as the mean \pm sd. The data were analyzed using Student's *t* test for paired samples, ANOVA, and linear regression analysis (28, 29). A significance level of $P < 0.05$ was used for all comparisons. All tests were two-sided, and $P < 0.05$ indicated statistical significance for a power of 80%.

Results

Anthropometric, dietary, and biochemical characteristics of the study population

The anthropometric characteristics of the 160 children studied are shown in Table 1. By design, average values for age, height, weight, body surface area, and body mass index were similar for black and white children. Skeletal age also did not differ between black and white children at any stage of sexual development (Table 1). However, there were significant racial differences in the lengths of the trunks and the legs. Sitting heights were greater in white than in black children at all Tanner stages. These differences were statistically significant when all subjects of the same gender were considered together, ($P < 0.01$ and $P < 0.001$ for girls and boys, respectively) and at Tanner stage I in girls ($P = 0.01$) and Tanner stage V in boys ($P = 0.03$). Concordantly, the leg length/sitting height ratio was significantly greater in black boys and girls (Table 1).

There were no significant differences in the nutritional intake of black and white children (Table 2). Weak positive correlations (r) were found between caloric intake and all anthropometric variables, including CT measurements of vertebral and femoral size ($r = 0.11$ – 0.34) in both girls and boys. There were, however, no correlations between any of the nutritional variables and the density of cancellous or cortical bone in girls, in boys, or when all children were considered together.

There were no significant differences in calcium, phosphorus, calciotropic hormones, bone turnover markers, or GH or growth factor measurements between black and white

TABLE 1a. Ages and anthropometric measurements for 40 black and 40 white girls matched for Tanner stage, age, height, and weight

Tanner stage	Race	n	Age (yr)	Skeletal age (yr)	Ht (cm)	Sitting ht (cm)	Wt (kg)	Leg length ratio	Surface area (m ²)	Body mass (kg/cm ²)
I	Black	8	9.1 ± 0.8	8.9 ± 1.0	136.0 ± 4.6	69.7 ± 3.6 ^a	35.6 ± 5.1	0.95 ± 0.05 ^b	1.19 ± 0.11	19.2 ± 2.0
	White	8	9.7 ± 0.6	9.4 ± 0.7	139.7 ± 7.6	73.6 ± 4.3	35.5 ± 4.1	0.90 ± 0.05	1.18 ± 0.09	18.2 ± 1.3
II	Black	8	11.9 ± 1.3	12.0 ± 1.5	152.9 ± 7.3	76.6 ± 1.7	46.1 ± 5.5	1.00 ± 0.08	1.41 ± 0.10	19.6 ± 1.2
	White	8	11.9 ± 1.2	11.6 ± 1.0	151.8 ± 8.2	78.9 ± 5.2	45.1 ± 4.5	0.93 ± 0.07	1.41 ± 0.12	20.0 ± 1.6
III	Black	8	13.0 ± 0.9	13.5 ± 1.0	157.5 ± 6.8	79.9 ± 4.4	51.2 ± 11.0	0.97 ± 0.05	1.49 ± 0.18	20.6 ± 3.6
	White	8	12.8 ± 0.8	12.9 ± 0.7	157.6 ± 4.5	80.9 ± 2.3	52.1 ± 11.2	0.95 ± 0.03	1.50 ± 0.18	20.9 ± 4.0
IV	Black	8	13.2 ± 1.3	14.2 ± 1.3	160.1 ± 4.6	81.8 ± 2.3	54.4 ± 9.2	0.95 ± 0.06	1.55 ± 0.15	21.2 ± 3.7
	White	8	14.1 ± 1.2	14.0 ± 0.9	158.4 ± 6.0	81.3 ± 2.6	55.4 ± 9.3	0.94 ± 0.02	1.57 ± 0.15	22.0 ± 3.0
V	Black	8	15.7 ± 2.7	15.8 ± 2.2	163.9 ± 4.2	83.6 ± 2.8	59.4 ± 8.1	0.96 ± 0.07	1.63 ± 0.13	22.0 ± 2.7
	White	8	14.3 ± 1.6	15.6 ± 1.3	162.5 ± 3.4	85.4 ± 2.7	59.2 ± 5.8	0.90 ± 0.04	1.63 ± 0.09	22.4 ± 2.0
All	Black	40	12.5 ± 2.6	13.1 ± 2.6	153.4 ± 11.0	78.2 ± 5.6 ^c	48.4 ± 10.6	0.96 ± 0.06 ^d	1.44 ± 0.19	20.3 ± 2.7
	White	40	12.5 ± 2.0	12.8 ± 2.3	153.3 ± 9.6	79.9 ± 5.1	48.5 ± 10.3	0.92 ± 0.05	1.44 ± 0.19	20.5 ± 2.7

^a P = 0.01, black vs. white girls.^b P = 0.03, black vs. white girls.^c P < 0.0001, black vs. white girls.^d P < 0.0005, black vs. white girls.**TABLE 1b.** Ages and anthropometric measurements for 40 black and 40 white boys matched for Tanner stage, age, height, and weight

Tanner stage	Race	n	Age (yr)	Skeletal age (yr)	Ht (cm)	Sitting ht (cm)	Wt (kg)	Leg length ratio	Surface area (m ²)	Body mass (kg/cm ²)
I	Black	8	10.1 ± 1.8	9.7 ± 1.3	142.7 ± 5.2	70.9 ± 5.0	35.1 ± 5.3	1.02 ± 0.10 ^a	1.17 ± 0.12	17.3 ± 2.3
	White	8	10.3 ± 1.7	9.7 ± 1.2	137.6 ± 6.9	72.3 ± 4.1	35.0 ± 6.5	0.91 ± 0.07	1.17 ± 0.14	18.3 ± 2.4
II	Black	8	12.2 ± 1.3	11.8 ± 1.2	151.0 ± 8.9	74.5 ± 4.1	41.0 ± 5.6	1.03 ± 0.06	1.30 ± 0.12	17.9 ± 1.5
	White	8	12.2 ± 0.7	12.3 ± 1.2	149.3 ± 10.6	75.8 ± 4.4	42.9 ± 10.4	0.97 ± 0.06	1.30 ± 0.12	18.5 ± 1.7
III	Black	8	13.4 ± 1.0	13.4 ± 0.5	163.6 ± 6.1	80.2 ± 4.0	53.3 ± 6.2	1.04 ± 0.06 ^a	1.58 ± 0.16	21.4 ± 4.1
	White	8	13.4 ± 0.7	13.5 ± 0.4	161.9 ± 3.0	82.5 ± 1.6	57.9 ± 11.2	0.96 ± 0.05	1.60 ± 0.17	22.1 ± 4.0
IV	Black	8	14.2 ± 1.1	14.7 ± 1.3	166.9 ± 7.3	82.4 ± 4.2	67.0 ± 17.0	1.03 ± 0.09	1.73 ± 0.23	24.1 ± 6.4
	White	8	14.1 ± 1.3	14.9 ± 1.3	167.4 ± 7.5	85.5 ± 1.6	64.3 ± 15.9	0.96 ± 0.08	1.70 ± 0.21	22.8 ± 5.1
V	Black	8	15.8 ± 1.0	16.4 ± 1.8	176.5 ± 6.3	87.1 ± 4.2 ^b	73.8 ± 11.9	1.03 ± 0.06 ^c	1.84 ± 0.16	23.9 ± 3.2
	White	8	16.0 ± 1.3	17.1 ± 1.1	174.1 ± 5.0	91.5 ± 3.1	69.6 ± 8.9	0.90 ± 0.03	1.77 ± 0.14	22.6 ± 3.2
All	Black	40	13.1 ± 2.3	13.2 ± 2.7	160.1 ± 13.7	79.0 ± 7.1 ^c	54.0 ± 17.8	1.03 ± 0.73 ^d	1.53 ± 0.30	20.9 ± 4.7
	White	40	13.2 ± 2.2	13.5 ± 2.7	158.0 ± 14.8	81.5 ± 7.6	53.9 ± 16.8	0.94 ± 0.63	1.51 ± 0.28	20.9 ± 3.9

^a P = 0.04, black vs. white boys.^b P = 0.03, black vs. white boys.^c P < 0.001, black vs. white boys.^d P < 0.0001, black vs. white boys.**TABLE 2.** Dietary intake for 80 matched pairs of black and white children

	Girls		Boys	
	Blacks (n = 40)	Whites (n = 40)	Blacks (n = 40)	Whites (n = 40)
Calories (Kc)	1899 ± 229	1767 ± 282	2337 ± 367	2199 ± 342
Protein (g)	67 ± 13	71 ± 16	89 ± 19	89 ± 18
Carbohydrates (g)	231 ± 32	234 ± 39	304 ± 61	279 ± 45
Sugar (g)	91 ± 32	78 ± 23	101 ± 29	98 ± 32
Fat (g)	81 ± 13	72 ± 17	87 ± 17	82 ± 21
Crude fiber (g)	3.6 ± 1.9	2.9 ± 1.4	4.2 ± 1.1	4.2 ± 1.5
Vitamin D (μg)	3.5 ± 2.6	4.0 ± 2.0	5.2 ± 3.0	5.4 ± 3.0
Calcium (mg)	624 ± 322	754 ± 221	926 ± 301	953 ± 368
Phosphorus (mg)	127 ± 325	179 ± 221	1370 ± 317	1334 ± 352
Magnesium (mg)	170 ± 53	191 ± 42	240 ± 85	238 ± 57
Sodium (mg)	2728 ± 711	2459 ± 579	3377 ± 879	3009 ± 765

children (Table 3). When all children were considered together, weak correlations were found between the cross-sectional areas of the vertebrae and the cross-sectional and cortical bone areas of the femurs and values for insulin-like growth factor I ($r = 0.19-0.34$). There was no significant

relationship between any of the biochemical measurements and CT measurements of cancellous or cortical bone density.

There were also no significant differences in sex steroid values for black and white children (Table 3). Total testosterone, bioavailable testosterone, dehydroepiandrosterone

TABLE 3. Means for biochemical variables in 80 matched pairs of black and white children

	Girls		Boys	
	Blacks (n = 40)	Whites (n = 40)	Blacks (n = 40)	Whites (n = 40)
Biochemical variables				
Calcium (mg/dL)	9.9 ± 1.6	9.6 ± 0.6	9.7 ± 0.8	9.6 ± 0.5
Phosphorus (mg/dL)	4.7 ± 0.9	4.9 ± 0.7	4.2 ± 0.7	4.2 ± 0.5
Calcium-regulating hormones				
PTH (pg/mL)	40 ± 17	36 ± 17	34 ± 14	31 ± 13
25 OHD ₃ (ng/mL)	24 ± 11	27 ± 8	32 ± 11	34 ± 10
1,25-(OH) ₂ D (pg/mL)	60 ± 18	55 ± 16	59 ± 21	57 ± 19
Calcitonin (pg/mL)	6.5 ± 2.3	7.0 ± 3.3	14.3 ± 9.2	11.0 ± 7.3
Bone turnover markers				
Alkaline phosphatase (U/L)	246 ± 109	262 ± 80	289 ± 120	251 ± 116
Bone alkaline phosphatase (ng/mL)	41 ± 26	42 ± 22	46 ± 33	48 ± 24
Osteocalcin (g/mL)	14 ± 11	16 ± 8	18 ± 18	20 ± 18
Urine pyridinoline (nmol/mmol)	194 ± 91	253 ± 110	230 ± 104	231 ± 119
Urine deoxypyridinoline (nmol/mmol)	56 ± 32	68 ± 39	62 ± 30	61 ± 33
GH and growth factors				
hGH (ng/mL)	2.6 ± 5.3	2.9 ± 4.0	3.1 ± 6.4	2.3 ± 4.7
GHBP (pmol/L)	291 ± 116	357 ± 218	283 ± 250	268 ± 170
IGF-I (ng/mL)	513 ± 145	553 ± 138	438 ± 180	468 ± 172
IGFBP-3 (mg/L)	3.7 ± 0.6	3.9 ± 0.7	3.6 ± 0.9	3.9 ± 1.2
Sex steroids				
Total testosterone (ng/dL)	18 ± 18	19 ± 12	179 ± 193	242 ± 223
Bioavailable testosterone (ng/dL)	13 ± 6	16 ± 9	38 ± 52	62 ± 81
Sex hormone-binding globulin (μg/dL)	29 ± 17	28 ± 21	36 ± 23	35 ± 32
Dehydroepiandrosterone sulfate	1133 ± 823	1307 ± 702	1502 ± 1129	1397 ± 1303
Androstenedione (ng/mL)	0.9 ± 0.8	1.1 ± 0.6	0.7 ± 0.5	1.0 ± 0.8
Estradiol (pg/mL)	40.5 ± 71.1	36.9 ± 37.1	18.6 ± 20.9	15 ± 7.6

TABLE 4. CT bone measurements in the vertebrae of 80 matched pairs of black and white children

Tanner stage	Race	Girls			Boys		
		n	Ht (cm)	Cross-sectional area (cm ²)	n	Ht (cm)	Cross-sectional area (cm ²)
I	Black	8	1.73 ± 1.53	6.31 ± 0.95	8	1.74 ± 0.08	7.51 ± 0.96
	White	8	1.88 ± 0.14	6.55 ± 0.59	8	1.81 ± 0.15	7.73 ± 1.09
II	Black	8	2.03 ± 0.16 ^a	7.32 ± 0.78	8	1.77 ± 0.11 ^a	8.47 ± 1.14
	White	8	2.10 ± 0.14	7.59 ± 0.51	8	1.93 ± 0.18	8.45 ± 1.19
III	Black	8	2.18 ± 0.16	7.79 ± 0.59	8	2.07 ± 0.12	9.38 ± 0.71
	White	8	2.21 ± 0.18	7.78 ± 0.96	8	2.13 ± 0.15	9.39 ± 0.40
IV	Black	8	2.21 ± 0.14	7.89 ± 1.28	8	2.10 ± 0.21 ^a	9.65 ± 1.20
	White	8	2.25 ± 0.14	8.09 ± 1.41	8	2.30 ± 0.15	9.46 ± 1.14
V	Black	8	2.28 ± 0.17	8.03 ± 1.19	8	2.50 ± 0.13	10.60 ± 1.34
	White	8	2.32 ± 0.12	8.27 ± 0.70	8	2.54 ± 0.24	10.56 ± 1.50
All	Black	40	2.09 ± 0.25	7.47 ± 1.13	40	2.04 ± 0.31 ^b	9.12 ± 1.50
	White	40	2.15 ± 0.23	7.66 ± 1.04	40	2.14 ± 0.31	9.12 ± 1.44

^a *P* = 0.02.^b *P* = 0.003.

sulfate, androstenedione, and estradiol levels increased with pubertal status, whereas sex hormone-binding globulin levels decreased. These biochemical indexes also correlated with age and anthropometric parameters, including CT measurements of bone size in the axial and appendicular skeletons. Variations in the material density of cortical bone were not accounted for by differences in any of the sex steroids measured ($r = -0.09$ to 0.19). After adjusting for Tanner stage, there were also no correlations between apparent cancellous bone density and sex hormone levels.

CT measurements

Table 4 shows CT values for vertebral heights and vertebral cross-sectional areas in black and white children at dif-

ferent Tanner stages. The heights of the vertebral bodies were significantly greater in white girls than in black girls at Tanner stage II ($P = 0.02$), in white boys than in black boys at Tanner stages II and IV (for both, $P = 0.02$), and when all Tanner stages were considered together ($P = 0.003$). There were, however, no significant differences in the cross-sectional areas of the vertebral bodies of black and white children at any Tanner stage or when all Tanner stages were considered together.

Figure 1 shows the mean values for apparent cancellous bone density in black and white children at different Tanner stages. Both pubertal status and race influenced cancellous bone density in the vertebrae. The mean density of cancellous bone did not differ among subjects in Tanner stage I, II, or

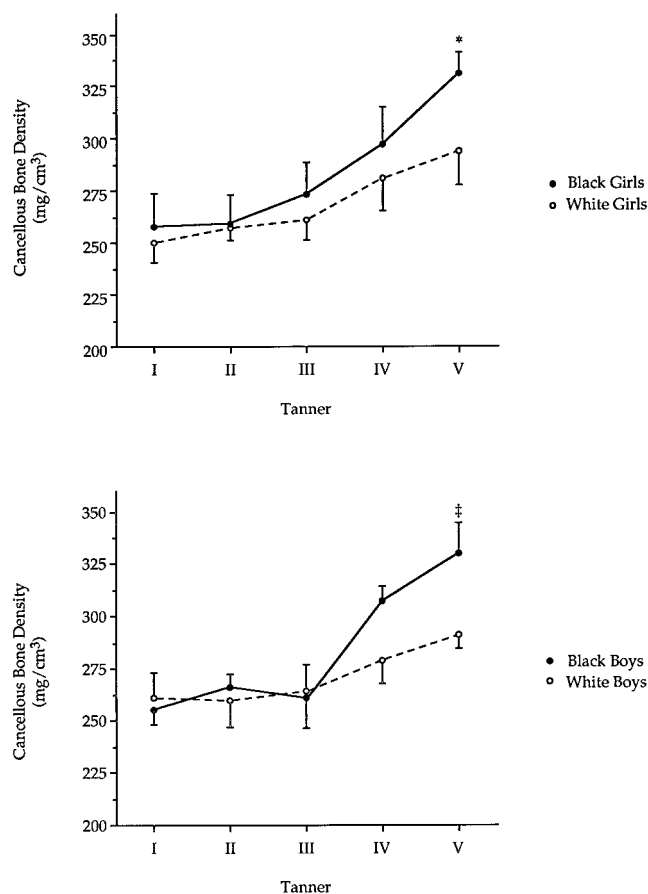


FIG. 1. Vertebral cancellous bone density in black and white girls and boys at each stage of sexual development. Values are the mean \pm SE. *, $P = 0.05$; ‡, $P = 0.007$.

III in either racial group, but increased linearly in all children from Tanner stages III-V. This increase during the final stages of puberty was substantially greater in black than in white children. At Tanner stage V, the mean vertebral bone density was 9.8% higher in black girls and 11.7% higher in black boys than that in their matched white counterparts. A linear fit over Tanner stages III, IV, and V yielded significant differences ($P = 0.004$) between black ($101.83 + 18.66 \times$ Tanner stage; standard error of the estimate = 22.14) and white ($128.78 + 8.74 \times$ Tanner stage; standard error of the estimate = 19.79) children.

In contrast to the findings for cancellous bone density in the vertebral bodies, values for the material density of cortical bone at the midshaft of the femur were similar for black and white children. Moreover, these measurements were remarkably constant and were not influenced by age, gender, pubertal status, or any of the anthropometric measurements (Fig. 2). On the average, the values for material cortical bone density were 8 times higher than those for apparent cancellous bone density.

Table 5 shows the mean CT values for femoral length and for the cross-sectional and cortical bone areas at the midshaft of the femurs in black and white children at different Tanner stages. There were significant racial differences in the lengths of the femurs, regardless of gender. Overall, black children had longer femurs than their matched white counterparts

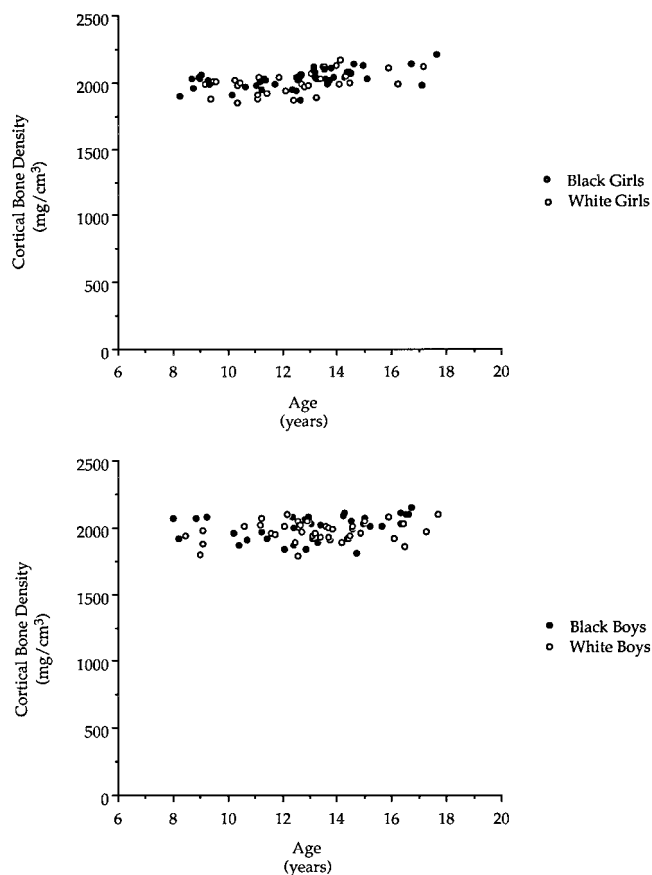


FIG. 2. Femoral cortical bone density in black and white girls and boys.

($P = 0.002$ and $P = 0.0001$ for girls and boys, respectively). These racial differences were also present at Tanner stage V in girls ($P = 0.04$) and at Tanner stages I, III, and V in boys ($P = 0.009-0.02$).

The cross-sectional area at the midshaft of the femurs was significantly greater in black children when subjects from all Tanner stages were considered together ($P = 0.008$ for girls and $P = 0.004$ for boys); on the average, values were 3% and 8.4% greater in black girls and boys, respectively. Values for femoral cross-sectional area correlated strongly with all anthropometric parameters in both black and white children, including measurements of femoral length. To establish whether racial differences in the cross-sectional areas and the lengths of the femurs were determined by the same moderator factor, the results from 10 pairs of black and white children were evaluated. Even after subjects were matched for cross-sectional area, skeletal age, Tanner stage and weight, the femoral lengths were greater in black than in white children ($P = 0.002$).

In contrast to the findings for femoral length and cross-sectional area, CT values for cortical bone area at the midshaft of the femur were similar in black and white children regardless of the level of sexual development (Table 5). Body weight and height were the primary determinants of the area of cortical bone at the midshaft of the femur regardless of race or gender. A multiple regression model accounting for chronological age, skeletal age, Tanner stage, sitting height, sur-

TABLE 5. CT bone measurements in the femurs of 80 matched pairs of black and white children

Tanner stage	Race	Girls				Boys			
		n	Length (cm)	Cross-sectional area (cm ²)	Cortical bone area (cm ²)	n	Length (cm)	Cross-sectional area (cm ²)	Cortical bone area (cm ²)
I	Black	8	37.2 ± 1.2	3.33 ± 0.43	2.44 ± 0.32	8	40.5 ± 1.8 ^a	3.64 ± 0.48	2.65 ± 0.27
	White	8	37.0 ± 2.3	3.21 ± 0.29	2.58 ± 0.23	8	36.6 ± 2.4	3.61 ± 0.44	2.71 ± 0.31
II	Black	8	42.8 ± 3.6	4.33 ± 0.34	3.35 ± 0.34	8	43.1 ± 3.2	4.41 ± 0.62	3.18 ± 0.47
	White	8	40.9 ± 2.7	4.14 ± 0.46	3.24 ± 0.53	8	41.1 ± 3.8	4.18 ± 0.56	2.95 ± 0.44
III	Black	8	43.5 ± 2.0	4.78 ± 0.47	3.66 ± 0.50	8	47.0 ± 2.1 ^a	5.64 ± 0.67	3.96 ± 0.40
	White	8	42.9 ± 1.5	4.26 ± 0.56	3.39 ± 0.40	9	44.5 ± 1.9	5.17 ± 0.61	3.91 ± 0.40
IV	Black	8	43.2 ± 2.5	5.10 ± 0.43	3.69 ± 0.31	8	47.6 ± 3.4	6.12 ± 1.17	4.59 ± 0.54
	White	8	42.3 ± 1.5	4.75 ± 0.68	3.75 ± 0.38	8	45.8 ± 3.8	5.54 ± 0.72	4.33 ± 0.70
V	Black	8	44.9 ± 2.3 ^b	5.27 ± 0.43	3.89 ± 0.50	8	50.3 ± 2.3 ^c	7.24 ± 1.18	4.63 ± 0.72
	White	8	43.2 ± 1.2	4.90 ± 0.63	3.80 ± 0.47	8	46.2 ± 1.5	6.44 ± 0.81	4.70 ± 0.38
All	Black	40	42.4 ± 3.62 ^d	4.58 ± 0.80 ^e	3.43 ± 0.63	40	45.7 ± 4.32 ^f	5.41 ± 1.53 ^g	3.80 ± 0.92
	White	40	41.4 ± 3.10	4.31 ± 0.78	3.35 ± 0.59	40	42.9 ± 4.54	4.99 ± 1.18	3.72 ± 0.90

^a $P = 0.02$, black vs. white children.

^b $P = 0.04$, black vs. white children.

^c $P = 0.009$, black vs. white children.

^d $P = 0.002$, black vs. white children.

^e $P = 0.008$, black vs. white children.

^f $P = 0.0001$, black vs. white children.

^g $P = 0.004$, black vs. white children.

face area, and body mass index in addition to weight and height did not substantially improve the predictive power of a model accounting for weight and height alone.

Discussion

The objective of this study was to examine the possible effects of race on skeletal growth in black and white children at different stages of sexual development. We found that race has significant and differential effects on the density and the size of the bones in the axial and appendicular skeletons. In the axial skeleton, race influenced the apparent density of cancellous bone, but not the cross-sectional area of the vertebral bodies. In contrast, in the appendicular skeleton, race influenced the cross-sectional areas of the femurs, but not the material density of cortical bone. These variant effects of race were equally manifested in girls and boys. Our results also corroborate previous studies indicating that there are significant racial differences in the lengths of the axial and appendicular skeletons (16, 17). Even after matching for height, black children had shorter sitting heights and greater leg length ratios than white children. Concordantly, CT values for vertebral height were lower and those for femoral length were greater in black children. As Tanner stage, anthropometric parameters, and dietary intake were similar in black and white children, our results cannot be attributed to differences in sexual maturity, body habitus, or calcium intake. Although black children have been reported to have more advanced skeletal age than white children of comparable chronological age (30), no significant differences in skeletal age were observed between black and white children in this study. Thus, our findings cannot be ascribed to variations in skeletal maturation. Lastly, the subjects were recruited from a limited geographic region, and any bias introduced by the method of selection would apply equally to both groups.

Our findings in the axial skeleton using quantitative CT

complement existing evidence showing that in girls, cancellous bone density in the vertebrae increases in the late stages of puberty, regardless of race, and that the magnitude of this increase is greater in black girls (21, 31). The results of this study also demonstrate similar patterns of increase in cancellous bone density in boys. Because of the limited resolution of CT scanners, we were unable to determine whether the differences in CT values in cancellous bone density during the later stages of puberty were a reflection of a greater increase in the number, the thickness, or the degree of mineralization of the trabeculae (14). Recent histomorphometric observations in adults would suggest however, that the structural basis for the higher cancellous bone density in blacks compared to whites is due to greater trabecular thickness (32).

In vitro studies indicate that the compressive strength of the vertebrae is mainly determined by the density of cancellous bone and its cross-sectional area (33–35). Although race influenced vertebral bone density, we found that values for cross-sectional area of the vertebral bodies were similar in black and white children at all stages of sexual development. Thus, our results suggest that racial differences in vertebral bone strength and the incidence of fractures in the axial skeleton of older subjects are a manifestation of early racial differences in the density of vertebral bone rather than in the size of the vertebrae.

In the appendicular skeleton, CT values for material density of cortical bone in black and white children were remarkably similar and constant. Neither race, pubertal status, age, gender, height, nor weight influenced these measurements. These data contradict the common belief that during the adolescent growth spurt, bone formation transiently outstrips mineral deposition, and there is a temporary decrease in bone density (36). It should be stressed that due to the thickness and the relative lack of porosity of the femoral cortex, CT values for cortical bone density reflect the true

density of the bone and the amount of collagen and mineral in a given amount of bone (22). Values for cortical bone density in this study were 8 times higher than cancellous bone density values, a finding consistent with histomorphometric studies, indicating an equivalent difference in the porosities of these two forms of bone (37).

In contrast to the findings in the axial skeleton, race influenced the cross-sectional area of the bones in the appendicular skeleton. Although values for femoral cross-sectional area increased with height, weight, and other anthropometric parameters in all children, this measurement was substantially greater in black children. On the average, the cross-sectional area was 3% and 8.4% greater in black girls and boys, respectively. We were not able to define the exact time when these racial differences first appeared, as only small, nonsignificant differences were seen in prepubertal children. Studies with larger samples sizes will be needed to determine whether there are any racial differences in the cross-sectional area of the bones in the appendicular skeleton before puberty.

Although race had significant effects on femoral length and cross-sectional area, CT values for cortical bone area at the midshaft of the femur were similar in black and white children regardless of the level of sexual development. Previous comparative studies of cortical bone in the appendicular skeleton using radiogrammetry have yielded conflicting results. Although the long bones in black subjects were consistently shown to have greater diaphyseal width than those in white subjects, some investigators found their cortex to be thicker, whereas others reported it to be thinner (7, 38, 39). Using CT, we found greater cross-sectional area and similar cortical bone area in black children compared to white children, which would manifest as reduced cortical thickness in a two-dimensional representation. Because the same amount of cortical bone placed further from the center of the bone results in a bone of greater strength (40), the structural basis for the advantage of blacks in the appendicular skeleton is probably the consequence of the greater cross-sectional size of their long bones.

The mechanisms by which race has a differential effect on the size of the bones in the axial and appendicular skeletons are unknown. It should be stressed, however, that the growth of the femur and that of the vertebrae result from two different processes that are probably regulated by different means. In the femur, growth in bone length occurs by endochondral bone formation at the growth plates, whereas increases in bone width occur by apposition of subperiosteal bone. In the vertebrae, growth occurs by endochondral ossification, which commences in the central area of the cartilage anlage and expands toward the periphery in all directions. Previous observations during the treatment of children with hypopituitarism suggest that longitudinal growth in the axial skeleton, indicated by sitting height, is relatively more dependent on sex hormones, whereas growth in the appendicular skeleton, indicated by the difference between standing and sitting heights, is primarily under the control of GH (41). However, in this study, we found no significant differences in the serum levels of GH, growth factors, or sex steroids between black and white children that would explain the discrepant effect of race on

vertebral and femoral size. Moreover, as racial differences in femoral length and vertebral height were present even in subjects with similar cross-sectional areas, it is unlikely that the length and the width of the bones are under the same controls.

The factors responsible for the rapid increase and racial differences in cancellous bone density that occur during puberty are also unknown. It should be noted that after adjusting for Tanner stage, there were no correlations between sex steroid levels and values for cancellous bone density. Regardless of the mechanisms, it is commonly thought that the greater accumulation of bone in black subjects is due to better renal calcium handling (shown by lower urinary calcium excretion in blacks) (42–44) and skeletal resistance to bone resorption by PTH (42, 45) (shown by lower serum levels of osteocalcin, bone-specific alkaline phosphatase, and urinary hydroxyproline). In addition, relatively higher PTH levels may promote optimal renal hydroxylation of 25-hydroxyvitamin D and, hence, maintain normal levels of 1,25-dihydroxyvitamin D and adequate intestinal calcium absorption. However, several studies in adults and the current study in children found no significant differences in the serum levels of calcium-regulating hormones and bone turnover markers between black and white subjects (46, 47).

In summary, the structural basis for the racial influences on bone growth differs in axial and appendicular skeletons. In the axial skeleton, these differences are based on greater cancellous bone density, whereas in the appendicular skeleton, they are founded on greater bone size. As skeletal mass in adulthood is the result at least in part of the amount of bone gained during growth, the skeletal advantages of black children described herein are likely to be important determinants of the greater skeletal resistance to fractures later in life.

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References

1. Cummings SR, Kelsey JL, Nevitt NC, O'Dowd KJ. 1985 Epidemiology of osteoporosis and osteoporotic fractures. *Epidemiol Rev.* 7:178–208.
2. Melton LJ, Riggs BL. 1987 Epidemiology of age-related fractures. In: Avioli LV, eds. *The osteoporotic syndrome: detection, prevention, and treatment*, 2nd ed. Orlando: Grune and Stratton; 1–30.
3. Riggs BL, Melton III LJ. 1987 Involutional osteoporosis. *N Engl J Med.* 314:1676–1686.
4. Heaney RP, Matkovic V. 1995 Inadequate peak bone mass. In: Riggs BL, Melton III LJ, eds. *Osteoporosis: etiology, diagnosis, and management*, 2nd ed. Philadelphia: Lippincott-Raven; 115–131.
5. Trotter M, Peterson RR. 1970 Weight of the skeleton during postnatal development. *Am J Phys Anthropol.* 33:313–324.
6. Arnold JS, Bartley MH, Tont SA, Jenkins DP. 1966 Skeletal changes in aging and disease. *Clin Orthop.* 49:17–38.
7. Garn SM, Nagy JM, Sandusky ST. 1972 Differential sexual dimorphism in bone diameters of subjects of European and African ancestry. *Am J Anthropol.* 37:127–130.
8. Specker BL, Brazzerol W, Tsang RC, Levin R, Search J, Steichen J. 1987 Bone mineral content in children 1 to 6 years of age: detectable sex differences after 4 years of age. *Am J Dis Child.* 141:343–344.
9. DePriester JA, Cole TJ, Bishop NH. 1991 Bone growth and mineralization in children aged 4 to 10 years. *Bone Miner.* 12:57–65.
10. Bell NH, Shary J, Stevens J, Garza M, Gordon L, Edwards J. 1991 Demonstration that bone mass is greater in black than in white children. *J Bone Miner Res.* 6:719–723.
11. Li J-Y, Specker BL, Ho ML, Tsang RC. 1989 Bone mineral content in black and

- white children 1 to 6 years of age. Early appearance of race and sex differences. *Am J Dis Child.* 143:1346–1349.
12. Southard RN, Morris JD, Mahan JD, et al. 1991 Bone mass in healthy children: measurement with quantitative DXA. *Radiology.* 179:735–738.
 13. Moro M, van der Meulen MCH, Kiratli BJ, Marcus R, Bachrach LK, Carter DR. 1996 Body mass is the primary determinant of mid-femoral bone acquisition during adolescent growth. *Bone.* 19:519–526.
 14. Genant HK, Engelke K, Fuerst T, et al. 1996 Noninvasive assessment of bone mineral and structure: state of the art. *J Bone Miner Res.* 11:707–730.
 15. Carter DR, Brouxsein ML, Marcus R. 1992 New approaches for interpreting projected bone densitometry data. *J Bone Miner Res.* 7:137–145.
 16. Tanner JM. 1978 Physical growth and development. In: Forfar JO, Arnell CC, eds. *Textbook of pediatrics.* 2nd ed. Edinburgh: Churchill Livingstone; 249–303.
 17. Hamill PVV, Johnston FE, Lemeshow S. 1973 Body weight, stature and sitting height: white and Negro youths 12–17 years. In: U.S. Department of Health, Education and Welfare; Vital and health statistics series 11 no. 126. Rockville: DHEW Publications HRA; 74–1608.
 18. Hamill PVV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. 1979 Physical growth: National Center for Health Statistics percentiles. *Am J Clin Nutr.* 32:607–629.
 19. Vaughan III VC, Litt IF. 1987 Developmental pediatrics: assessment of growth and development. In: Behrman RE, Vaughan III VC, eds. *Nelson textbook of pediatrics,* 13th ed. Philadelphia: Saunders; 24–33.
 20. Greulich WW, Pyle SI. 1950 Radiographic atlas of skeletal development of the hand and wrist. Stanford: Stanford University Press; 191.
 21. Gilsanz V, Roe TF, Mora S, Costin G, Goodman WG. 1991 Changes in vertebral bone density in black girls and white girls during childhood and puberty. *N Engl J Med.* 325:1597–1600.
 22. Hangartner T, Gilsanz V. 1996 Evaluation of cortical bone by computed tomography. *J Bone Miner Res.* 11:1518–1525.
 23. Gilsanz V, Boechat MI, Roe TF, Loro ML, Sayre JW, Goodman WG. 1994 Gender differences in vertebral body sizes in children and adolescents. *Radiology.* 190:673–677.
 24. Dyson ED, Jackson CK, Whitehouse WJ. 1970 Scanning electron microscope studies of human trabecular bone. *Nature.* 225:957–959.
 25. Gong JK, Arnold JS, Cohn SH. 1964 Composition of trabecular and cortical bone. *Anat Rec.* 149:325–331.
 26. Cann CE. 1991 Why, when and how to measure bone mass: a guide for the beginning user. In: Frey GD, Yester MV, eds. *Expanding the role of medical physics in nuclear medicine.* Colchester: American Physics Institute; 25–79.
 27. Kalender WA. 1991 Effective dose values in bone mineral measurements by photon absorptiometry and computed tomography. *Osteoporosis Int.* 2:82–87.
 28. Dixon WJ, Massey FJ. 1983 Introduction to statistical analysis. New York: McGraw-Hill; 129–130.
 29. Morrison DF. 1990 Multivariate statistical methods. New York: McGraw-Hill; 255–256.
 30. Garn SM, Sandusky ST, Nagy JM, McCann MB. 1927 Advanced skeletal development in low-income Negro children. *J Pediatr.* 80:965–969.
 31. Gilsanz V, Gibbens DT, Roe TF, et al. 1988 Vertebral bone density in children: effect of puberty. *Radiology.* 166:847–850.
 32. Han ZH, Palnitkar S, Sudhaker Rao D, Nelson D, Parfitt AM. 1997 Effects of ethnicity and age or menopause on the remodeling and turnover of iliac bone: implications for mechanisms of bone loss. *J Bone Miner Res.* 12:498–508.
 33. Biggemann M, Hilweg D, Brinckmann P. 1988 Prediction of the compressive strength of vertebral bodies of the lumbar spine by quantitative computed tomography. *Skeletal Radiol.* 17:264–269.
 34. Brinckmann P, Biggemann M, Hilweg D. 1989 Prediction of the compressive strength of human lumbar vertebrae. *Spine.* 6:606–610.
 35. Einhorn TA. 1992 Bone strength: the bottom line. *Calcif Tissue Int.* 51:333–339.
 36. Kleerekoper M, Tolia K, Parfitt AM. 1981 Nutritional, endocrine, and demographic aspects of osteoporosis. *Orthop Clin North Am.* 12:547–558.
 37. Snyder W. 1975 Report of task group on reference man. Oxford: Pergamon Press; 62–98.
 38. Bloom RA, Pogrund H. 1982 Humeral cortical thickness in female Bantu: its relationship to the incidence of femoral neck fracture. *Skeletal Radiol.* 8:59–62.
 39. Solomon L. 1979 Bone density in ageing Caucasian and African populations. *Lancet.* 2:1326–1330.
 40. Seeman E. 1997 From density to structure: growing up and growing old on the surfaces of bone. *J Bone Miner Res.* 12:1–13.
 41. Tanner JM, Whitehouse RH, Hughes PCR, Carter BS. 1976 Relative importance of growth hormone and sex steroids for the growth at puberty of trunk length, limb length, and muscle width in growth hormone-deficient children. *J Pediatr.* 89:1000–1008.
 42. Bell NH, Greene A, Epstein S, Oexmann MJ, Shaw S, Shary J. 1985 Evidence for alteration of the vitamin D-endocrine system in blacks. *J Clin Invest.* 76:470–473.
 43. Buyamba-Kabangu JR, Fagard R, Lijnen P, Bouillon R, Lissens W, Amery A. 1987 Calcium, vitamin D-endocrine system, and parathyroid hormone in black and white males. *Calcif Tissue Int.* 41:70–74.
 44. Meier DE, Luckey MM, Wallenstein S, Clemens TL, Orwoll ES, Waslien CL. 1991 Calcium, vitamin D, and parathyroid hormone status in young white and black women: association with racial differences in bone mass. *J Clin Endocrinol Metab.* 72:703–710.
 45. Kleerekoper M, Nelson DA, Peterson EL, et al. 1994 Reference data for bone mass, calciotropic hormones, and biochemical markers of bone remodeling in older (55–75) postmenopausal white and black women. *J Bone Miner Res.* 9:1267–1276.
 46. Meier DE, Luckey MM, Wallenstein S, Clemens TL, Orwoll ES, Waslien CL. 1991 Calcium, vitamin D, and parathyroid hormone status in young white and black women: association with racial differences in bone mass. *J Clin Endocrinol Metab.* 72:703–710.
 47. Ettinger B, Sidney S, Cummings SR, et al. 1997 Racial differences in bone density between young adult black and white subjects persist after adjustment for anthropometric, lifestyle, and biochemical differences. *J Clin Endocrinol Metab.* 82:429–434.