Age-, Sex-, and Menopause-Related Changes of Vertebral and Peripheral Bone: Population Study Using Dual and Single Photon Absorptiometry and Radiogrammetry

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Vertebral and peripheral bone mass have been measured with single and dual photon absorptiometry and radiogrammetry in 146 male and 220 female volunteers ranging in age from 20 to 85 yr. One hundred four subjects with interfering diseases, treatment, or x-ray manifestations of lumbar osteoarthritis were excluded for purposes of this study. Patterns of age-related bone gain and diminution differed between sexes and measuring sites. The effect of menopause on the peripheral and vertebral skeleton also differed. Men, at all measured sites, have more bone than women. In the fifth decade, however, women's lumbar bone mineral content was almost equal to the value found in men. Bone loss associated with aging was more marked in women than in men and started, for the lumbar spine, at about the age of 25 yr in both women and men and, for the peripheral bones, at the age of 55 in women and 65 in men. Bone loss in the spine in women was not linear. Women in the fifth and sixth decade, who still had menstruation, differed significantly from those who had not menstruated for at least the last 6 mo. Bone diminution at menopause was twice as great in the lumbar spine than elsewhere in the peripheral skeleton, 15% versus 7%. Of the 25% total bone loss of the spine during adult life in women, 60% was lost within 10 yr after menopause. Estrogen deficiency, not aging, is the predominant cause of bone loss in the spine. For the peripheral skeleton, there is a two-component decrease, a rapid loss induced by the menopause superimposed on a slower age-related loss. Although there was a significant correlation between peripheral and vertebral bone mass indices, it was clear that observations made at one site will not necessarily reflect changes observed at another site.

During the last two decades, several noninvasive methods of quantifying bone mass at the appendicular and axial skeleton have been developed. In the 1960s radiogrammetry of cortical bone, in the 1970s single photon absorptiometry of the radius, trabecular, and cortical area, and in the 1980s dual photon absorptiometry of the spine, have become firmly established for the investigation of age-related bone loss and metabolic bone diseases. Much information has been published in both clinical and basic fields for each technique separately, but no populations study in Europe has been published using the three techniques at the same time in the same individual. The purpose of this study is to provide normal data for a European (Belgian) population and to compare information gained by three different techniques on peak bone mass, age-related changes, and the effect of the menopausal state.

MATERIALS AND METHODS

Subjects

Three hundred sixty-six normal volunteers (146 M and 220 F) had bone mass measurements. Their age ranged from 20 to 85 yr. All normal subjects were volunteers recruited by a newspaper and broadcast appeal for a family and twin study on bone mass. All were white, gave their informed consent, and were living in an area within 100 km of our institution. Sixty-six of them were twins. Ninety-six percent of the twins knew their zygosity; 53% were monozygotic and 47% were dizygotic. Forty-two percent of the twins were males

and 58% females. Seventy-nine percent of the twins were younger than 40 yr. They were ambulatory, had a history taken by a physician for back pain, fractures, menopausal state, hormone treatment, and surgical or medical therapy at present and in the past. For gross evaluation of spine disorders, especially osteoporosis and osteoarthritis, a postero-, anterior, and lateral x-ray of the lumbar spine was done for all those above the age of 40 yr, and in those with a history of back pain below the age of 40 yr. All those with an x-ray Kellgren (1) grade 3 and more for spondylosteo-arthritis and vertebral fracture, were eliminated. In two male subjects 60 and 50 yr old, one vertebral crush fracture in the lumbar spine was detected. In none of the female subjects were crush fractures seen. A total 104 individuals (40 M and 64 F) had to be discarded from the study for the following reasons: hysterectomy and ovarectomy, thyroid disease, tumorectomy, corticosteroids, treatment for osteoporosis, gout, rheumatoid arthritis, algoneurodystrophy, congenital abnormalities of skeleton, epilepsy, Crohn's disease, sacroiliitis, gastrectomy, diabetes mellitus, and spondylosteoarthritis grade 3.

The breakdown of the subjects regarding age and sex groups according to disease and spondylarthritis of the spine is shown in Table 1. In the fourth and fifth decade, one-third had to be eliminated and from the sixth decade onwards almost half had to be eliminated.

In the premenopausal group, 48% of the proponents had taken a contraceptive pill during periods varying from 6 mo to 20 yr. The mean duration of contraceptive use was 6.3 yr. In the postmenopausal group, 5 had had estrogen substitution for 2 yr and ten patients had been taking contraceptive pills before the onset of menopause. The mean number of pregnancies in the third decade was 0.3, in the fourth 2.1, in the fifth 2.4, and in the sixth 2.5.

Bone Mass Measurements

Radiogrammetry. Semi-automatic measurements with a 0.01-mm readout of periosteal (D) and endosteal (d) width of the second metacarpal at midshaft were made on posteroanterior hand radiographs of all subjects by a single observer as described by Dequeker (2). The length of the second metacarpal of the right hand was measured with a millimeter ruler.

An estimate of the cross-sectional cortical area was calculated by substracting the square of the endosteal diameter from the square of the periosteal diameter (D^2-d^2), assuming a cylindrical model and omitting the constant $\pi/4$. The metacarpal index is the percent ratio of cortical area of the metacarpal to the square of periosteal diameter $\dfrac{D^2-d^2}{D^2}$. The reproducibility of the method is 3.1% (3).

Single photon absorptiometry radius. Measurements of bone mineral content were also made at the lower third of the radius and at the distal radius, respectively, at 8 cm and 3 cm from the distal end on the left arm, with use of the single photon absorptiometry technique Norland Cameron Bone Mineral Analyser Model 189, as described by Cameron and Sorenson (4). This method utilizes a monochormatic beam from a iodine-125 source. The forearm is wrapped in tissue equivalent material to give a constant soft-tissue thickness, and is transversly scanned. Four linear scans are made at each site and the results are averaged. In our laboratory, replicate scans made on the same patients at different times had a coefficient of variation of 1.8 for the 8 cm site and of 3.4 for the distal radius. In 12 normal adults, the mean difference in BMC/width 8 cm between dominant and nondominant arm was +2% for the dominant arm.

Dual photon absorptiometry lumbar spine. Bone mineral content (BMC) of the axial skeleton was determined by dual photon absorptiometry, as described by Krølner and Nielsen (5).

The dual photon absorption technique for measuring bone mineral content is based on measurements of radiation transmission of two separate photon energies through a medium consisting of two different materials,

TABLE 1
Breakdown in Age and Sex Groups of Subjects Eliminated for Diseases or for Spondylosteoarthritis Grade 3 or More

Males				Females			
Proponents	Diseases	Spondylosteoarthritis	% Excluded	Proponents	Diseases	Spondylosteoarthritis	% Excluded
20–29	1	0	4.2	20–29	4	0	13
n = 24				n = 32			
30–39	3	1	14	30–39	9	0	21
n = 29				n = 43			
40–49	10	2	35	40–49	7	4	21
n = 34				n = 53			
50–59	4	7	38	50–59	14	6	36
n = 29				n = 56			
60–69	5	2	37	60–69	8	5	59
n = 19				n = 22			
70–84	2	3	45	70–85	2	5	50
n = 11				n = 14			

bone and soft tissue. The dichromatic beam from a gadolinium-153 source has photon electric peaks at 44 and 100 keV.

BMC of the spine was assessed from scans of the L_2 to L_4 region using Novo BMC Lab 22a. Total bone mineral content is calculated by summing up BMC values within the region of interest L_2-L_4 and is expressed after calibration in units of grams hydroxyapatite (gHA) and in areal density (gHA/cm^2). The latter has been calculated by Novo Software Calc lc. The reproducibility of the measurements of the lumbar spine gHA was in young adults 1.8% and in osteoporosis cases 3% (6) and for the area density (gHA/cm^2) expression 2.4% in adult volunteers.

RESULTS

Because there were no systematic differences between the results obtained for weight, length, and bone mass measured in twins and the other volunteers, the results will be reported for the whole population.

The results representing means, standard deviations, and coefficients of variation for height, weight, cortical area of the second metacarpal, and BMC at the radius 3 cm and 8 cm from the distal end, and BMC lumbar spine L_2-L_4 according to age are listed in Table 2 for women and in Table 3 for men.

Men exceed women in amount of bone at the four levels measured throughout the age range 20 to 85 yr.

The age period when peak bone mass is attained and the age-related changes for the four measuring sites in women and in men are shown in Figs. 1A and B, respectively. In men, peak bone mass for all measuring sites is reached in the third decade. The maximum mean bone mass value at the spine in women is reached in the third decade, but the maximum value at the peripheral skeleton is 10 yr later.

An age-related loss in mean bone mass was observed at all measuring sites in men as well as in women, but the overall pattern was not the same. In women, a lower average bone mass was found from the third decade onwards at the lumbar spine while at the cortical site of the radius and the metacarpal, a marked lower bone mass was only observed from the fifth decade onwards and from the radius trabecular area in the sixth decade.

In men, the reduction in average bone amount was most marked at the trabecular bone measurement sites as the lumbar spine and radius distal end. For the lumbar spine, the average bone mineral content in the fifth decade in men was almost equal to the average of the same age for women and was significantly lower (p <0.05) compared with the preceding decade mean. Thereafter, there was no further age-related loss of lumbar bone mass in men.

The average height is significantly higher in the

TABLE 2
Decade Specific Means, Standard Deviations and CV for Height, Weight, Peripheral and Axial Absolute Bone Mass Parameters in Females

Age groups	Height (cm)	Weight (kg)	Cortical area second metacarpal (mm^2)	BMC Radius g/cm Trabec. site 3cm	BMC Radius g/cm Cortical site 8cm	Lumbar BMC L_2-L_4 gHA
20–29						
Mean 24.4 ± 2.8	166.2 ± 4.3	56.3 ± 6.3	55.9 ± 5.1	1.052 ± 0.150	0.918 ± 0.104	48.1 ± 7.1
n = 28	CV = 2.6	CV = 11.2	CV = 9.1	CV = 14.2	CV = 11.3	CV = 14.8
30–39						
Mean 35.2 ± 2.9	161.3 ± 5.1*	57.0 ± 6.6	59.8 ± 10.2	1.071 ± 0.158	0.945 ± 0.108	46.4 ± 6.7
n = 34	CV = 3.2	CV = 11.6	CV = 17.1	CV = 14.7	CV = 11.4	CV = 14.4
40–49						
Mean 44.6 ± 2.8	162.3 ± 5.1	64.3 ± 10.4*	57.4 ± 8.9	1.089 ± 0.249	0.926 ± 0.139	46.2 ± 5.9
n = 42	CV = 3.1	CV = 16.2	CV = 15.5	CV = 23	CV = 15.0	CV = 12.8
50–59						
Mean 54.5 ± 3.1	158.9 ± 5.7†	64.4 ± 9.1	58.8 ± 7.8	1.086 ± 0.158	0.904 ± 0.093	40.9 ± 7.8†
n = 36	CV = 3.6	CV = 14.1	CV = 13.3	CV = 14.5	CV = 10.3	CV = 19.1
60–69						
Mean 63.5 ± 2.7	160.1 ± 7.0	70.1 ± 7.3	53.3 ± 3.2	0.953 ± 0.185	0.828 ± 0.156	38.6 ± 6.7
n = 9	CV = 4.4	CV = 10.4	CV = 6.0	CV = 19.4	CV = 18.8	CV = 17.4
70–85						
Mean 72.4 ± 3.6	158.3 ± 5.7	63.3 ± 10.5	43.4 ± 7.9	0.693 ± 0.142	0.672 ± 0.135	38.9 ± 12.0
n = 7	CV = 3.6	CV = 16.6	CV = 18.2	CV = 20.5	CV = 19.9	CV = 30.1

*p < 0.001, Student's t-test comparison with preceding decade.
†p < 0.01
‡p < 0.05

TABLE 3

Decade Specific Means, Standard Deviations, and CV for Height, Weight, Peripheral and Axial Absolute Bone Mass Parameters in Males

| Age groups	Height (cm)	Weight (kg)	Cortical area 2nd metacarpal (mm²)	BMC Radius g/cm Trabec. site 3cm	BMC Radius g/cm Cortical site 8cm	Lumbar BMC L_2–L_4 gHA
20–29						
Mean 25.3 ± 2.7	179.7 ± 5.5	74.0 ± 10.3	74.9 ± 12.4	1.536 ± 0.236	1.252 ± 0.142	60.4 ± 9.6
n = 23	CV = 3.1	CV = 13.9	CV = 16.6	CV = 15.4	CV = 11.3	CV = 15.9
30–39						
Mean 35.1 ± 3.4	174.7 ± 5.2†	77.2 ± 10.9	72.6 ± 10.2	1.575 ± 0.318	1.261 ± 0.163	52.6 ± 9.2†
n = 25	CV = 3.0	CV = 14.1	CV = 14.0	CV = 20.2	CV = 12.9	CV = 17.5
40–49						
Mean 44.0 ±2.9	71.3 ± 4.7*	74.1 ± 9.5	67.6 ± 9.8	1.461 ± 0.231	1.192 ± 0.115	47.5 ± 8.7
n =22	CV = 2.7	CV = 12.8	CV = 14.5	CV = 15.8	CV = 9.6	CV = 18.3
50–59						
Mean 54.1 ±3.1	171.3 ± 5.0	77.0 ± 8.5	73.1 ± 12.8	1.458 ± 0.290	1.195 ± 0.142	50.2 ± 10.4
n = 18	CV = 2.9	CV = 11.0	CV = 16.8	CV = 19.9	CV = 11.9	CV = 20.7
60–69						
Mean 64.2 ±2.8	169.8 ± 5.8	73.9 ± 9.5	74.9 ± 3.3	1.436 ± 0.215	1.238 ± 0.186	49.5 ± 5.6
n = 12	CV = 3.4	CV = 12.9	CV = 4.4	CV = 15.0	CV = 15.0	CV = 11.3
70–84						
Mean 76.7 ± 6.6	169.8 ± 10.2	65.3 ± 9.6	65.7 ± 7.2	1.239 ± 0.221	1.199 ± 0.120	52.2 ± 23.5
n = 6	CV = 6.0	CV = 14.6	CV = 10.9	CV = 16.9	CV = 10.1	CV = 45.1

*p < 0.05.
†p < 0.01.
‡p < 0.001, Student's t-test comparison with preceding decade.

younger generation, third decade and fourth decade, compared to the older age groups. In premenopausal women and in men a significant positive correlation between height and all bone mass measurements, except cortical area second metacarpal in men, was found more so for the vertebral bone mineral content than for the peripheral bone mass indices (Table 4). In postmenopausal women, there is no significant correlation between bone mass and height, but a strong correlation with weight.

Lumbar bone mineral content is significantly correlated with the measurements made at the peripheral skeleton in men and women, except for cortical area of the second metacarpal in premenopausal women. The
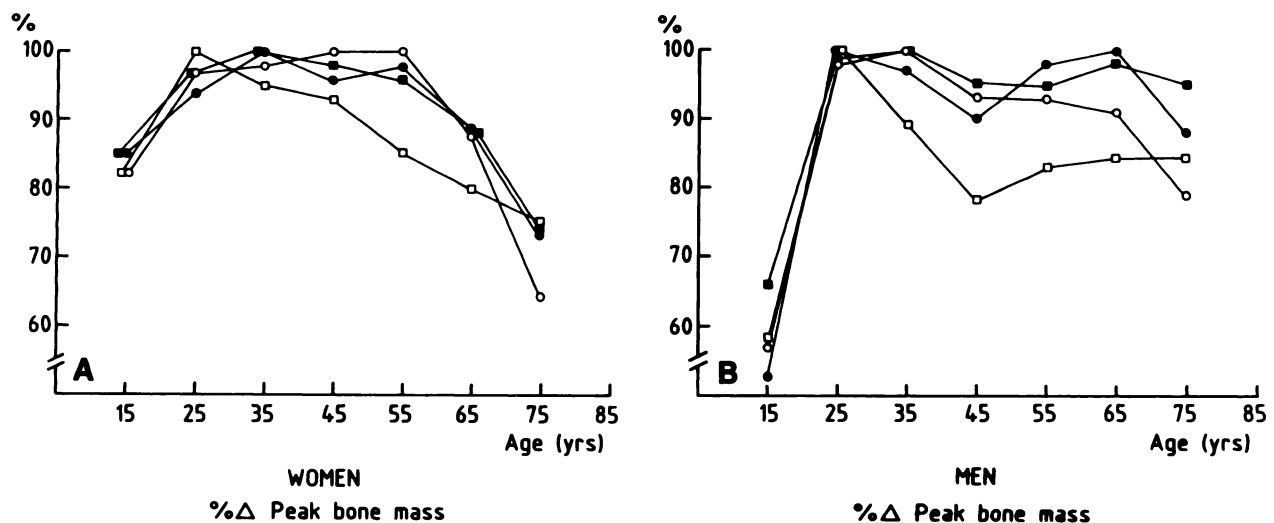
FIGURE 1

A, B: Peak bone mass and age-related changes in men and women D²-d² (mm²)—BMC radius (g/cm)—BMC Lumbar L_2-L_4 (gHA). A: (●) D²-d² metacarpal II; (O) BMC radius 3 cm; (■) BMC radius 8 cm; (□) BMC₍c₎ lumbar L_2-4. B: (●) Cortical area metacarpal II; (O) BMC radius 3 cm; (■) BMC radius 8 cm; (□) BMC₍c₎ lumbar L_2-4

TABLE 4
Intercorrelation Matrix Lumbar BMC, Radius BMC 3cm and 8cm, Cortical Area Second Metacarpal, Weight and Height in Men, Pre- and Postmenopausal Women

	Men age-range 20–85 yr (N=99)				
	Radius 3cm	Radius 8cm	Cortical area	Weight	Height
Lumbar BMC	0.416§	0.365§	0.267*	0.330‡	0.477§
Radius BMC 3cm	1.000	0.684§	0.184	0.421§	0.397§
Radius BMC 8cm		1.000	0.102	0.138	0.321†
Cortical area 2mc			1.000	0.158	0.267*
Weight				1.000	0.345‡
Height					1.000

	Premenopausal women age-range 20–56 yr (N=94)				
	Radius 3cm	Radius 8cm	Cortical area	Weight	Height
Lumbar BMC	0.456§	0.460§	0.190	0.260*	0.478§
Radius BMC 3cm	1.000	0.590§	0.171	0.330†	0.294†
Radius BMC 8cm		1.000	0.267*	0.176	0.291†
Cortical area 2mc			1.000	0.119	0.058
Weight				1.000	0.295†
Height					1.000

	Postmenopausal women age-range 45–80 yr (N=36)				
	Radius 3cm	Radius 8cm	Cortical area	Weight	Height
Lumbar BMC	0.662§	0.655‡	0.441*	0.593‡	0.091
Radius BMC 3cm	1.000	0.837§	0.565†	0.291	−0.089
Radius BMC 8cm		1.000	0.482†	0.565‡	0.239
Cortical area 2mc			1.000	0.498†	0.185
Weight				1.000	0.206
Height					1.000

* $p < 0.05$.
† $p < 0.01$.
‡ $p < 0.001$.
§ $p < 0.0001$.

correlation between vertebral and peripheral bones are weaker in the premenopausal than in the postmenopausal group.

Because there is a well-known significant correlation between bone mass and a skeletal size parameter (length), it is useful to report data when comparing different skeletal size groups in relation to a skeletal size parameter. Table 5 summarizes the mean values, standard deviations, and coefficients of variation for the lumbar bone mineral content related to area, radius BMC divided by width, and percent cortical area according to age, respectively, for women and men.

The overall age-related pattern of bone mass remains the same as for the absolute bone mass measurements. The difference between the sexes are, however, reduced and in the youngest age group even reversed, with males having a relatively lower bone mass (% cortical thick-ness and lumbar bone density) than females in the younger age groups.

A considerable variability in CV is seen in the absolute amount of bone mass indices as well for trabecular as for cortical bone. This variability can be reduced by taking into account skeletal size parameters as is manifest in the relative bone indices, but there remains a large variability especially in women in the older age groups.

There is a tendency for an increase in CV value in the older age group and more so for the relative bone indices. The variability of bone mass for each sex and age group in larger than the variability in body length and approaches the variability values for body weight.

Effect of menopause. Table 6 shows the effect of menopause on bone mass values. The female population of the fifth and sixth decade have been split up in

TABLE 5
Decade Specific Mean, s.d., and CV from Relative Bone Mass Indices of Peripheral and Axial Skeleton in Males and Females

Age groups	% Cortical area second metacarpal	MALES BMC/W Radius g/cm² Trabecular site 3cm	Cortical site 8cm	Lumbar BMC/area L₂-L₄ gHA/cm²
20-29				
Mean 25.3 ± 2.7	81.7 ± 8.2	0.589 ± 0.070	0.782 ± 0.046	1.07 ± 0.12
n = 23	CV = 10.0	CV = 11.9	CV = 5.9	CV = 11.2
30-39				
Mean 35.1 ± 3.4	81.6 ± 8.8	0.583 ± 0.104	0.783 ± 0.062	0.96 ± 0.72[t]
n = 25	CV = 10.8	CV = 17.8	CV = 7.9	CV = 12.5
40-49				
Mean 44.0 ± 2.9	81.9 ± 8.1	0.561 ± 0.074	0.753 ± 0.060	0.93 ± 0.13
n = 22	CV = 9.9	CV = 13.2	CV = 8.0	CV = 13.9
50-59				
Mean 54.1 ± 3.1	78.1 ± 4.6	0.536 ± 0.068	0.735 ± 0.047	0.90 ± 0.15
n = 18	CV = 5.9	CV = 12.7	CV = 6.4	CV = 16.7
60-69				
Mean 64.2 ± 2.8	79.1 ± 4.5	0.560 ± 0.090	0.756 ± 0.063	0.94 ± 0.07
n = 12	CV = 5.7	CV = 16.1	CV = 8.3	CV = 7.5
70-84				
Mean 76.7 ± 6.6	72.4 ± 3.6	0.559 ± 0.110	0.739 ± 0.060	0.94 ± 0.32
n = 6	CV = 5.0	CV = 19.4	CV = 7.5	CV = 34.0
FEMALES				
20-29				
Mean 24.4 ± 2.8	86.9 ± 5.4	0.510 ± 0.053	0.710 ± 0.050	1.02 ± 0.09
n = 28	CV = 6.2	CV = 10.4	CV = 7.0	CV = 8.8
30-39				
Mean 35.2 ± 2.9	86.9 ± 6.3	0.520 ± 0.073	0.730 ± 0.045	0.99 ± 0.11
n = 34	CV = 7.2	CV = 14.0	CV = 6.2	CV = 11.1
40-49				
Mean 44.6 ± 2.8	80.6 ± 9.4[t]	0.530 ± 0.113	0.690 ± 0.064[t]	0.96 ± 0.11
n = 42	CV = 11.7	CV = 21.3	CV = 9.3	CV = 11.5
50-59				
Mean 54.5 ± 3.1	82.2 ± 5.1	0.490 ± 0.069	0.670 ± 0.060	0.89 ± 0.70[t]
n = 36	CV = 6.2	CV = 14.1	CV = 9.0	CV = 11.2
60-69				
Mean 63.5 ± 2.7	70.6 ± 11.6	0.440 ± 0.106	0.580 ± 0.090*	0.80 ± 0.12*
n = 9	CV = 16.4	CV = 24.1	CV = 15.5	CV = 7.9
70-79				
Mean 72.4 ± 3.6	61.9 ± 8.3	0.368 ± 0.075	0.520 ± 0.102	0.78 ± 0.13
n = 7	CV = 13.4	CV = 20.4	CV = 19.6	CV = 16.8

Student's t-test comparison with preceding decade.
* p < 0.05.
[t] p < 0.01.
[‡] p < 0.005.
[§] p < 0.001.

those who are in their menopause (no menstruation for the last 6 mo) and those who are still menstruating. Some could not be classified and are not included in the analysis because of irregular periods or insufficient information concerning their menopause. There is a significant difference in mean bone mineral content at the lumbar spine and radius between pre- and postmenopausal women.

The loss of bone mineral content at menopause is twice as high in the vertebral area than in the peripheral

cortical area, respectively, 15 and 8% over a period of 10 yr. When the effect of age on bone mass is evaluated in the total population and in pre- and postmenopausal women separately, it is clear that there is no significant age-associated loss of bone before the menopause in the peripheral and axial skeleton, with the exception of lumbar area density and cortical area, but that there is a marked age-associated loss in the postmenopausal women in the peripheral skeleton (Table 7). At the vertebral column there is some loss in the pre- and

TABLE 6
Effect of Menopause on Bone Mass Indices (Age Group 40–59 yr)

	Premenopause n = 42 Mean ± s.d.	Postmenopause n = 22 Mean ± s.d.	%Δ	P*
M̄ age	45.6 ± 4.1	55.0 ± 3.8		
Age range	40–56	45–59		
Height (cm)	162.2 ± 5.1	158.9 ± 5.0	−2.0	N.S.
Weight (kg)	64.7 ± 10.7	61.7 ± 10.1	−4.6	N.S.
Cortical area (mm²)	58.3 ± 9.0	54.6 ± 6.1	−6.3	N.S.
BMC Radius 3 cm	1.119 ± 0.217	1.019 ± 0.154	−8.9	N.S.
BMC Radius 8 cm	0.943 ± 0.115	0.873 ± 0.120	−7.4	p < 0.05
Lumbar BMC (gHA)	46.4 ± 6.6*	40.0 ± 6.9	−15.4	p < 0.001
% Cortical area	80.6 ± 9.1	81.7 ± 5.1	+1.3	N.S.
Radius 3 cm BMC/width	0.530 ± 0.111	0.476 ± 0.066	−10.2	p < 0.05
Radius 8 cm BMC/width	0.702 ± 0.056	0.658 ± 0.073	−6.3	p < 0.02
Lumbar BMC/area (gHA/cm²)	0.967 ± 0.099*	0.857 ± 0.090	−16.2	p < 0.001

* Student's t-test.

postmenopause in area density, while in the combined pre- and postmenopausal women group a highly significant bone loss was noted at the vertebral column. These data indicate that the bulk of loss in vertebral bone mineral content is related to menopause and that peripheral bone loss is mainly related to aging, starting after menopause.

In men the pattern is different. The aging effect is more marked in the vertebral column than in the peripheral skeleton.

DISCUSSION

In this cross-sectional population study of bone mass several interesting facts—besides normal values for an European population—were disclosed. We found different patterns of age-related bone gain and diminution between sexes and measuring sites, and a different effect of the menopause on the peripheral and the vertebral skeleton.

The "normal population" studied was selected from

TABLE 7
Correlation Between Age and Bone Mass Indices in Pre- and Postmenopausal Women and in Men

	Premenopause	Women postmenopause	Total	Men
Age range	20–56	45–80	20–80	20–85
Number	94	36	155	107
Cortical area 2 mc	0.141	−0.485[t]	−0.180	−0.077
Radius BMC 3 cm	0.165	−0.464[t]	−0.193*	−0.224
Radius BMC 8 cm	0.050	−0.472[t]	−0.300[‡]	−0.099
Lumbar BMC L₂-L₄	−0.181	−0.167	−0.427[§]	−0.298[t]
% Cortical area	−0.267*	−0.729[§]	−0.511[§]	−0.207
Radius BMC/W 3 cm	−0.084	−0.429[t]	−0.263[‡]	−0.131
Radius BMC/W 8 cm	−0.141	−0.569[‡]	−0.546[§]	−0.268[t]
Lumbar BMC/area	−0.251*	−0.456[t]	−0.512[‡]	−0.383[‡]

*p < 0.05.
[t]p < 0.01.
[‡]p < 0.001.
[§]p < 0.0001.

volunteers and from a twin population who participated in a study on heredity and bone mass. The results of the latter study will be reported separately (7). Both groups were recruited by advertising. The twins were included only after a statistical analysis was performed which showed that there was no systematic difference between them and the other volunteers in weight, height, and bone mass indices. The criteria for elimination included all conditions in the past and the present which might affect bone metabolism. In addition, an x-ray of the lumbar spine was obtained for all participants above the age of 40 yr in order to excluded asymptomatic spondylosteoarthritis or vertebral collapse case. Spondylosteoarthritis with osteophytes grade 3 and more (1) and apophyseal joint osteoarthritis affect seriously the BMC values of the lumbar spine. When those who have a spondylosteoarthritis grade more than 3 on x-ray are included, we observed elevation of the lumbar BMC (in females of 2.7% in the fifth, 2.9% in the sixth, 5% in the seventh, and 15% in the eight decade).

For these reasons, 28% of the population examined had to be eliminated. This high percentage might partially be explained by a bias in the volunteers to come for a free bone examination when they had some back problems in the past.

Women who were on or who had taken birth control pills were not excluded because of the wide spread use of these pills. Forty-eight percent of the premenopausal women had taken the anticonceptive pill. In the postmenopausal group only five subjects had had estrogen substitution for 2 yr. They were also included.

Although there is a clear difference in bone mass between the sexes, men having more bone than women, an unexpected finding was the significant lower mean lumbar bone mineral content in the fifth decade in men, approaching the mean value in women. This dip is also present when the results are exposed in mineral density (gHA/cm^2). The lower bone mass in males in the fifth decade is not due to a sampling bias (i.e., the inclusion of twins of heterogeneity within the group) because the CV is equal to that of the other decades, but is partially due to skeletal size differences, the younger age groups being taller. This does not explain, however, the low value especially at the lumbar spine in men compared with women in the fifth decade, since men had a significantly higher height than women in this decade, respectively 171,3 ± 4,7 cm vs. 162,3 ± 5,1 cm, p <0.001. A hypothetical explanation could be that a secular event, for example adolescence during war time, had a major influence on bone development in this age group. Why this secular event is only seen in man at the axial skeleton and not in women is not evident. Those born during and after the war are generally taller than those born before the second world

war, but this effect is seen in both sexes especially in the third decade.

A marked lower mean bone mineral value at the lumbar spine in men of the fifth decade compared with the fourth decade has also been reported in the study of Meier et al. (8), using a computed tomography technique. In this study, however, there was a continuous decrease from the age of 60 onwards after the early diminution of trabecular bone mass, while in our population no further loss with aging was observed at the lumbar spine in men.

The bone loss associated with aging is more marked in women than in men and apparently begins at age 25 yr in women and in men in the lumbar spine, and at the age of 55 in women and of 65 in men for the peripheral bones. Because the study is cross-sectional, no firm conclusions on linearity or nonlinearity of bone loss with aging can be made. Although there are significant differences in skeletal size, height, and weight between the decades, the so-called skeletal size corrected indices did not change the overall pattern of bone loss with aging.

There is a lot of controversy in the literature concerning the bone loss at the axial skeleton. Some authors (9–11) found a linear decrease of spinal bone mineral content in women starting at premenopause in accordance with patterns demonstrated in iliac crest biopsies (12–14). Others found a loss only after the age of 40–50 yr in women (15,16).

From our data it is now clear that the discrepancy is a matter of statistics and lack of definition of the menopausal state of the women investigated.

In our overall analysis a linear loss of bone mineral content at the lumbar spine in adult women from the age of 20 yr was evident and similar to the rate observed by Riggs et al. (10). However, from the inspection of the decade mean values it was already clear that there was an acceleration of this decrease in bone mineral content between the fifth and sixth decade, the only age period where the decade difference became significant, p <0.05. Because temporal variability of menopause could obscure the effect of the menopause on bone diminution in the usual cross-sectional study, the female population between 40 and 59 yr old was split up in those who were already in their menopause (no menstruation the last 6 mo) and those who had regular menstruation. Now a highly significant effect of the menopause could be established and bone diminution at menopause appeared to be twice as great in the lumbar spine than elsewhere in the peripheral skeleton, 15% vs. 7% in 10 yr. This rapid loss the first years after the menopause is in agreement with the 3 to 6% loss over 5 yr found in a longitudinal study of Krølner and Nielsen (15) in women with a natural menopause, using dual photon absorptiometry and in agreement with the

5 to 10% annual loss in the study of Cann et al. (17), using computed tomography of the lumbar spine to follow changes for 2 yr following oophorectomy.

The significant age-related loss in bone mineral content at the spine found in the overall group is only marginally significant in lumbar area density, but not in gHA, when only pre- or postmenopausal women are evaluated, indicating that trabecular bone loss does indeed occur at menopause and at a rate several times greater than that occurring either earlier or later. These findings are in accordance with the finding of Richelson et al. (18) comparing bone mineral data in oophorectomized, perimenopausal, and postmenopausal women.

Although there is a more rapid menopause-induced loss of compact bone in the peripheral skeleton, this is imposed upon an underlying age-related slower loss, since in the postmenopausal group a highly significant correlation with age was found in contrast to what was seen in the spine.

The present data in females suggest that, for the spine, estrogen deficiency and not aging is the predominant cause of bone loss and that for the peripheral skeleton there is a two-component decrease, a rapid menopause-induced loss superimposed on an underlying age related slower loss.

An interesting finding of this study is also the difference in age and sex when peak bone mass is attained at the different measuring sites. The age period when peak bone mass is reached can give information on pathophysiological mechanisms of bone development. There is a clear sex difference regarding the time that peak bone mass is reached between vertebral and peripheral measuring sites. In men, peak bone mass for all measuring sites is reached at the age of 25 yr. The time peak bone mass is reached at the peripheral skeleton in women differs from that in men. The maximum mean bone mass value of the spine in women is reached at age 25 yr, but the maximum mean value at the peripheral skeleton occurs 10 yr later, indicating a differential development pattern between sites and sex which might be related to the child-bearing period and its hormonological consequences.

In addition to the aforementioned different effects of menopause on vertebral and peripheral skeleton, it is of particular interest to note that in comparison with previous epidemiologic studies (19,20) the mean age when major diminution of bone mass starts in the peripheral skeleton has been delayed by 5 to 10 yr— bone diminution now begins at 55 yr, while previously it was 45 to 50 yr.

This observation of retarded postmenopausal bone loss in the peripheral skeleton might be a reflection of a change in life style, for example, generalized use of the contraceptive pill in the last 15 yr as seen in our population characteristics. This might explain why, in view of the previous discussion, the menopausal effect

on bone in present cross-sectional studies is seen from age 55 yr and up instead of 45 yr and above. Although this epidemiologic change in lifestyle has not yet been reflected in the frequency of symptomatic osteoporosis, it is possible that in the next 20 yr a change (diminution) in femoral neck fracture, a mainly cortical bone failure, might be evident. The opposite is true at the present time (21), and may be explained by a secular effect of the World War II. In this study, we found that males born before the World War II had low bone mineral content and density.

The cumulative diminution of bone mass between peak value and old age for the lumbar spine in women is 25% and in men 16% over an age range of 50 yr (25-75 yr), respectively, 0.5 and 0.3% per yr. For the peripheral cortical bones, the loss was 25% in women and 10% in men over an age span of 20 yr (55-75 yr) in women and 10 yr (65-75 yr) in men, corresponding to 1.25% in women and 1% in men per yr.

The cumulative loss of bone in the spine of 25% in women is considerably lower than the diminution in bone mineral content found by Riggs et al. (10); 46% in women but similar to that found in men (14%). This difference in women may be due to a larger group of contraceptive pill users in our female population. We have previously shown in cross-sectional and longitudinal studies that the use of the contraceptive pill retards bone loss (22,23).

If the latter observation has something to do with skeletal size differences between populations, its effect is not clear at the present time. The bone mineral content values in the paper of Riggs et al. (10) are expressed in density values and not in absolute values as is the case in our study. From the intercorrelation studies it is clear that skeletal size has an influence on bone mass values not only in the peripheral skeleton but even more on the vertebral bone mineral content especially in the younger premenopausal age groups.

Although there is a significant correlation between peripheral and vertebral absolute bone mass indices, more so in the postmenopausal than in the premenopausal group, it is clear from the different remodeling behavior of the bone in time of reaching peak value and around the menopause, that observations made at one site will not necessarily reflect changes observed at an other site. For cross-sectional and certainly for longitudinal evaluation measurements of bone by a single method at a single site will no longer suffice.

REFERENCES

1. Kellgren JH: Atlas of standard radiographs of arthritis. In *The Epidemiology of Chronic Rheumatism, Vol. II*, Blackwell, Oxford, 1963
2. Dequeker J: Quantitative radiology: radiogrammetry of cortical bone. *Br J Radiol* 49:912-920, 1976
3. Dequeker J: Precision of the radiogrammatic evalua-

tion of bone mass at the metacarpal bone. In *Non-Invasive Bone Measurements: Methodological Problems*, Dequeker J, Johnston CC, eds. Washington, Oxford Press, 1982, pp 27–32

4. Cameron JH, Dorenson J: Measurements of bone mineral in vivo: An improved method. *Science* 142:230–232, 1964

5. Krølner B, Nielsen P: Measurement of bone mineral content (BMC) of the lumbar spine I. Theory and application of a new two-dimensional dual-photon attenuation method. *Scand J Clin Lab Invest* 40:653–663, 1980

6. Dequeker J, Geusens P, Wielandts L, et al: Lumbar BMC skeletal size monogram. In *Osteoporosis I*, Christiansen C, Arnaud CD, Norden BEC, et al., eds. Copenhagen, 1984, pp 665–667

7. Dequeker J, Nijs J, Verstraeten A, et al: Genetic determinants of bone mineral content at the spine and radius: A twin study. *Bone:* in press

8. Meier DE, Orwall ES, Jones JM: Marked disparity between trabecular and cortical bone loss with age in healthy men. *Ann Intern Med* 101:605–612, 1984

9. Madsen M: Vertebral and peripheral bone mineral content by photon absorptiometry. *Invest Radiol* 12:185–188, 1977

10. Riggs BL, Wahner HW, Dunn WL et al: Differential changes in bone mineral density of the appendicular and axial skeleton with aging. *J Clin Invest* 67:328–335, 1981

11. Hansson T, Roos B: The influence of age, height, and weight on the bone mineral content of lumbar vertebrae. *Spine* 5:545–551, 1980

12. Dequeker J, Remans J, Franssen R, et al: Ageing patterns of trabecular and cortical bone and their relationship. *Calc Tiss Res* 7:23–30, 1971

13. Meunier P, Courpron P, Edouard C, et al: physiological senile involution and pathological rarefaction of bone. *Clin Endocrinol Metab* 2:239–256, 1973

14. Marius R, Kosek J, Pfefferbaum A, et al: Age-related loss of trabecular bone in premenopausal women: A biopsy study. *Calc Tiss Int* 35:406–409, 1983

15. Krølner B, Nielsen P: Bone mineral content of the lumbar spine in normal and osteoporotic women: Cross-sectional and longitudinal studies. *Clin Sci* 62:329–336, 1982

16. Tothill P, Smith MA, Sutton D: Dual photon absorptiometry of the spine with a low activity source of gadolinium 153. *Br J Radiol* 56:829–835, 1983

17. Cann CE, Genant HK, Ettinger B, et al: Spinal mineral loss in oophorectomized women. *J Am Med Ass* 244:2056–2059, 1980

18. Richelson LS, Wahner HW, Melton LJ III, et al: Relative contribution of aging and oestrogen deficiency to postmenopausal bone tiss. *N Engl J Med* 311:1273–1275, 1984

19. Dequeker J: Bone loss in normal and pathological conditions. PhD Thesis, Leuven University Press, Leuven, Belgium, 1972

20. Mazess RB: On aging bone loss. *Clin Orthop* 165:239–252, 1982

21. Lewis AF: Fracture of the neck of the femur: Changing incidence *Br Med J* 283:1217–1219, 1981

22. Dequeker J, De Muylder E, Ferin J: The effect of long-term lynestrend treatment on bone mass in cycling women. *Contraception* 15:717–723, 1977

23. Dequeker J, De Muylder E: Long-term progestogen treatment and bone remodelling in perimenopausal women: A longitudinal study. *Maturitas* 4:309–313, 1982