0021-972X/01/$03.00/0
The Journal of Clinical Endocrinology & Metabolism

Vol. 86, No. 1
*Printed in U.S.A.*

# Intrauterine Programming of Adult Body Composition*

CATHARINE R. GALE, CHRISTOPHER N. MARTYN, SAMANTHA KELLINGRAY, RICHARD EASTELL, AND CYRUS COOPER

*Medical Research Council Environmental Epidemiology Unit (University of Southampton), Southampton General Hospital (C.R.G., C.N.M., S.K., C.C.), Southampton, United Kingdom S016 6YD; and Osteoporosis Center, Northern General Hospital (R.E.), Sheffield, United Kingdom S5 7AU*

**ABSTRACT**

Epidemiological studies suggest an association between weight in infancy and the risk of osteoporosis in later life. The extent to which this reflects environmental influences on skeletal growth and metabolism before birth or during the first year of postnatal life remains uncertain. We therefore examined the association between birth weight and adult body composition (bone, lean, and fat mass) in a cohort of 143 men and women, aged 70–75 yr, who were born in Sheffield, UK, and still lived there. The subjects underwent assessment of body composition by dual energy x-ray absorptiometry. Neonatal anthropometric information included birth weight, birth length, head size, and abdominal circumference. There were significant ($P < 0.01$) positive associations between birth weight and adult, whole body, bone, and lean mass among men and women. These were mirrored in significant ($P < 0.03$) associations between birth weight and bone mineral content at the lumbar spine and femoral neck. Associations between birth weight and whole body fat were weaker and not statistically significant. The associations of birth weight with whole body bone mineral and lean mass remained statistically significant after adjustment for age, sex, and adult height. They also remained significant after adjustment for cigarette smoking, alcohol consumption, dietary calcium intake, and physical inactivity. These data are in accord with previous observations that anthropometric measures in infancy are associated with skeletal size in adulthood. The presence of these relationships at birth adds to the evidence that bone and muscle growth may be programmed by genetic and/or environmental influences during intrauterine life. (*J Clin Endocrinol Metab* **86:** 267–272, 2001)

OSTEOPOROSIS, DEFINED as a reduction in bone mass that predisposes to fracture, constitutes a major public health problem (1). The bone mass of an individual in later life depends upon both the growth and mineralization of the skeleton during the first 2 decades of life and the subsequent loss of bone, which commences during the fourth decade. A substantial proportion of the variance in peak bone mass found in the general population cannot be explained by known genetic factors (2) or by childhood environmental determinants such as diet (3) and exercise (4). Recent epidemiological studies suggest that part of this residual variation might be explained by patterns of growth in infancy (5, 6). The mechanism underlying this association is believed to be the programming of a range of metabolic and endocrine systems that control the skeletal growth trajectory during childhood and adolescence; programming is the term used for persisting changes in structure and function caused by environmental stimuli during critical periods of early development (7–9). Such endocrine programming would be likely to influence the development of other body compartments, such as fat and muscle. However, studies to date have not used dual energy x-ray absorptiometry (DXA) to relate birth weight to body composition. Furthermore, the importance of disproportionate intrauterine growth in endocrine programming remains uncertain; most evidence relates to gross measures of birth size such as birth weight, rather than incorporating indexes such as head and abdominal circumference at birth. We therefore examined the relationship between neonatal anthropometry and adult body composition in a cohort of men and women born in Sheffield between 1922 and 1926, who are still resident in the city.

## Subjects and Methods

We studied 143 men and women who had been born at the Jessop Hospital for Women in Sheffield between 1922 and 1926 and who had been traced and found to still be resident in the city during 1996/1997. They were selected from a group of 322 men and women who had been previously included in a study of cardiovascular risk factors (10). Of these, 212 (89%) agreed to a home interview, and 143 (69% of those visited at home) attended the Osteoporosis Center, Northern General Hospital (Sheffield, UK), for assessment of body composition. This group of people was unique in that detailed anthropometric information about them at the time of their birth, including weight, length, head size, abdominal and chest girths, and placental weight, had been recorded by the midwife. These midwife records had been preserved. After obtaining permission from their general practitioners, the men and women were interviewed at home; details were obtained about their cigarette smoking, alcohol consumption, dietary calcium intake, and physical activity. The women also provided information about age at menopause.

All 143 subjects underwent assessments of bone density and body composition by DXA using a Hologic, Inc., QDR 4,500A instrument (Waltham, MA). Measurements were made of bone mineral content (BMC), bone area, and bone mineral density (BMD) at the lumbar spine, proximal femur, and whole body. We used these measurements to calculate bone mineral apparent density at the lumbar spine and femoral neck using the method of Carter *et al.* (11). We also made measurements of body composition (whole body fat and lean mass). Measurement precision, expressed as coefficient of variation, was 1.0% for lumbar spine BMD and 3.0% for femoral neck BMD.

We explored the relation between birth weight, adult bone mineral, and body composition measurements and potential confounding variables using ANOVA, partial correlation coefficients, and multiple linear

Received June 21, 2000. Revision received September 18, 2000. Rerevision received October 3, 2000. Accepted October 3, 2000.

Address all correspondence and requests for reprints to: Prof. Cyrus Cooper, Medical Research Council Environmental Epidemiology Unit (University of Southampton), Southampton General Hospital, Southampton, United Kingdom SO16 6YD. E-mail: cc@mrc.soton.ac.uk.

* This work was supported by the Medical Research Council and the Gatsby Charitable Foundation.

regression. Variables with a skewed distribution were normalized by log transformation.

The study was approved by the North Sheffield local research ethics committee, and all subjects gave written informed consent.

## Results

The anthropometric, bone mineral, and body composition measurements of the 143 study subjects are shown in Table 1. The mean birth weight of the men was 3391 ± 520 g (±SD), and that of the women was 3226 ± 438 g. There was little difference between the sexes in head or abdominal circumference at birth. When the 143 subjects were contrasted with the 322 born at Jessop Hospital over the study period and included in the initial cardiovascular study, there were no statistically significant differences in terms of birth weight or head or abdominal circumference between the 2 groups.

Table 2 shows mean bone mineral measurements in men and women, adjusted for age, according to recorded weight at birth. Among men, there were consistent, strong positive associations between birth weight and bone area at the lumbar spine (r = 0.28; $P = 0.004$), femoral neck (r = 0.37; $P < 0.001$), and whole body (r = 0.46; $P < 0.001$) after adjusting for age. Thus, men in the highest third of the distribution of birth weight had 6.4% greater spine bone area, 7.3% greater femoral neck bone area, and 9.5% greater whole body bone area than their counterparts in the lowest third of the distribution of birth weight. Slightly weaker, but nevertheless statistically significant, positive associations were also observed between birth weight and BMC at the spine, femoral neck, and whole body. In the smaller number of women studied, bone area tended to be greater in those who had been heavier at birth, but only the association between birth weight and whole body bone area reached statistical significance. There were significant positive associations between birth weight and both BMC and BMD at the lumbar spine, femoral neck, and whole body. Among the neonatal anthropometric measures recorded, birth weight showed the strongest and most consistent associations with bone area and BMC. Patterns for head circumference and abdominal circumference, which were strongly collinear with birth weight, were similar. However, the ratio of head circumference to abdominal circumference (a measure of brain-sparing when the developing fetus is exposed to late intrauterine adversity) was not predictive of bone size or density.

Figure 1 illustrates the relationship between birth weight and whole body BMC, lean mass, and fat mass in the men and women separately after adjustment for age. In both sexes, birth weight was positively associated with bone and lean mass (BMC in men: r = 0.31; $P = 0.002$; BMC in women: r = 0.45; $P = 0.004$; lean mass in men: r = 0.50; $P < 0.001$; lean mass in women: r = 0.46; $P = 0.003$). In men, birth weight was also positively associated with whole body fat (r = 0.19; $P = 0.06$); there was a similar trend in women, but it was not statistically significant.

The relationships between body composition and birth weight were little altered and remained statistically significant after further adjustment for known lifestyle and medical determinants of bone loss (cigarette smoking, alcohol consumption, physical inactivity, reduced dietary calcium intake, and menopausal age in women). There were associations between birth weight and adult height (r = 0.37; $P < 0.001$) and weight (r = 0.36; $P < 0.001$) after age and sex adjustment. The association of birth weight with adult body mass index was less pronounced (r = 0.19; $P = 0.026$). We therefore examined the extent to which relationships between birth weight and adult measures of body composition remained after further adjustment for height and weight (Table 3). Whole body lean mass ($P = 0.002$) retained a positive association with birth weight after adjustment for age, sex, height, and weight. Birth weight was also a predictor ($P < 0.05$) of bone mineral content at the lumbar spine, proximal femur, and whole body after adjustment for age, sex, and adult height. When weight was introduced as a covariate, these relationships became nonsignificant.

The relationship of birth weight to adult whole body fat mass appeared less marked than that to lean mass and bone mineral (Fig. 1); it also altered direction when adjustment was made for adult weight (Table 3). We therefore examined the effect of the simultaneous association between birth weight and adult weight on whole body fat mass. The predominant determinant of adult fat mass was adult weight. However, in each third of the distribution of adult weight, there was a tendency (not statistically significant) for whole body fat mass to be greater among subjects of low birth weight. The data therefore point to opposing trends for birth weight and adult weight with adult fat mass.

**TABLE 1.** Neonatal anthropometry and bone mineral and body composition measurements in men and women

| | Men (n = 102) | Women (n = 41) |
|---|---|---|
| Birth wt (kg) | 3.39 (0.52) | 3.23 (0.44) |
| Head circumference (cm) | 34.6 (1.8) | 34.3 (1.8) |
| Abdominal circumference (cm) | 30.8 (2.5) | 30.3 (2.4) |
| Adult ht (m) | 1.68 (0.07) | 1.56 (0.06) |
| Adult wt (kg) | 75.4 (11.7) | 66.9 (11.9) |
| Whole body | | |
| Total BMC (kg) | 2.47 (0.35) | 1.77 (0.31) |
| Total fat (kg) | 19.62 (6.5) | 28.16 (7.9) |
| Total lean mass (kg) | 50.15 (5.2) | 35.36 (4.3) |
| Lumbar spine BMD (g/cm$^2$) | 1.06 (0.17) | 0.89 (0.16) |
| Femoral neck BMD (g/cm$^2$) | 0.81 (0.13) | 0.69 (0.10) |

Values are means (±SD).

## Discussion

We traced 143 men and women born in Sheffield between 1922–1926, whose birth weight and neonatal anthropometry were recorded. Birth weight was a significant predictor of BMC at the lumbar spine, femoral neck, and whole body of these men and women some 7 decades later. These relationships were independent of known adult lifestyle determinants of bone loss such as physical inactivity, low dietary calcium intake, and cigarette smoking. They also remained after adjustment for age, sex, and adult height. Parallel relationships between birth weight and whole body lean mass were observed, but a substantially weaker association was present for whole body fat. These data suggest that genetic and/or intrauterine environmental factors that influence the fetal growth trajectory and are reflected in birth weight have long-term consequences on body composition, particularly

**TABLE 2.** Bone mineral measurements according to birth weight in men and women after adjustment for age

| | Site | Measure | Birth wt (kg) | | | $P$ for trend[a] |
|---|---|---|---|---|---|---|
| | | | <3.15 | 3.15–3.64 | >3.64 | |
| Men | Lumbar spine | Area ($cm^2$) | 67.07 | 70.31 | 71.43 | 0.004[b] |
| | | BMC (g) | 69.61 | 75.28 | 78.23 | 0.012[c] |
| | | BMD ($g/cm^2$) | 1.03 | 1.07 | 1.09 | 0.109 |
| | | BMAD ($g/cm^2$) | 0.12 | 0.13 | 0.13 | 0.501 |
| | Femoral neck | Area ($cm^2$) | 5.54 | 5.65 | 5.85 | <0.001[b] |
| | | BMC (g) | 4.40 | 4.65 | 4.73 | 0.024[c] |
| | | BMD ($g/cm^2$) | 0.79 | 0.82 | 0.81 | 0.351 |
| | | BMAD ($g/cm^2$) | 0.34 | 0.35 | 0.34 | 0.780 |
| | Whole body | Area ($cm^2$) | 2095.87 | 2188.20 | 2276.68 | <0.001[b] |
| | | BMC (g) | 2357.53 | 2476.51 | 2575.32 | 0.002[b] |
| | | BMD ($g/cm^2$) | 1.12 | 1.13 | 1.13 | 0.416 |
| Women | Lumbar spine | Area ($cm^2$) | 55.33 | 55.37 | 58.62 | 0.086 |
| | | BMC (g) | 46.52 | 48.64 | 56.41 | 0.003[b] |
| | | BMD ($g/cm^2$) | 0.84 | 0.87 | 0.96 | 0.004[b] |
| | | BMAD ($g/cm^2$) | 0.11 | 0.12 | 0.13 | 0.011[c] |
| | Femoral neck | Area ($cm^2$) | 4.85 | 4.72 | 4.96 | 0.249 |
| | | BMC (g) | 3.14 | 3.18 | 3.72 | 0.004[b] |
| | | BMD ($g/cm^2$) | 0.65 | 0.67 | 0.75 | 0.011[c] |
| | | BMAD ($g/cm^2$) | 0.30 | 0.31 | 0.34 | 0.014[c] |
| | Whole body | Area ($cm^2$) | 1819.94 | 1744.99 | 1938.39 | 0.019[c] |
| | | BMC (g) | 1696.98 | 1654.61 | 1972.22 | 0.007[b] |
| | | BMD ($g/cm^2$) | 0.94 | 0.95 | 1.01 | 0.025[c] |

[a] $P$ values calculated from linear regression.
[b] $P < 0.01$.
[c] $P < 0.05$.

bone and muscle mass in late adulthood, which influence fracture risk in later life.

Our study was based on 143 participants who agreed to attend a hospital clinic (44%) from among 322 people invited to take part in the study. They were not a representative sample of all people born in Sheffield at the time, because they were born in the hospital when most births took place at home and because they continued to live in the city in which they were born. However, in the statistical analyses all comparisons were made within the group who participated. We do not think that nonresponse or our inability to follow-up all members of the original cohort will have biased the results unless relationships between birth measurements and body composition in adult life differ in nonresponders or in people who have died or moved away. Furthermore, the distribution of body mass index and prevalence of cigarette smoking in these men and women are similar to estimates derived from British population samples of comparable age, such as the General Household Survey (12, 13). We used DXA to estimate whole body bone mineral, lean, and fat mass. This technique has rapidly become a standard method for the noninvasive assessment of body composition. Measurements of bone and soft tissue are highly reproducible (14–16), and they have been extensively validated both *in vivo* and *in vitro* (17–19). The technique is highly sensitive to the age-related decline in muscle mass (20, 21) as well as to the accumulation of central fat in postmenopausal women (21, 22).

Evidence has now accumulated that the risk of osteoporosis might be modified by environmental influences during early life. Several epidemiological studies have confirmed that infants who are light at 1 yr of age have lower adult bone mineral content at the lumbar spine and proximal femur (5, 6, 23, 24). This relationship has been documented in young adulthood as well as in cohorts aged 60–70 yr, in which fracture incidence rates are substantially higher. Finally, a recent Finnish cohort study has demonstrated a direct association between low birth length, poor childhood growth, and later risk of hip fracture (25). These epidemiological studies suggest a discordance between the environmental influences acting on bone growth and mineralization. Weight at 1 yr has tended to predict bone size and total mineral content much better than volumetric assessments of BMD (5, 6).

In previous studies the relationship of weight in infancy to adult bone mass was stronger for weight at 1 yr than for birth weight (6, 26). There are two explanations for this pattern. First, the major genetic and/or environmental influences programming skeletal growth might be timed during early postnatal life; second, these environmental influences act during intrauterine life, but their effects only become apparent when body size begins to track during the first year of postnatal life. In previous cohorts (6), we have been able to pursue environmental determinants of adult bone mass that might act during the months following birth; for example, type of infant nutrition or exposure to infections during childhood and infancy. Neither of these exposures resulted in significant deficits in bone mineral that persisted through to later life. The Sheffield cohort reported here provides some of the highest quality information available on neonatal anthropometry. The data clearly demonstrate that birth weight bears a positive association with adult bone mass, even after adjusting for adult body height. Our findings are consistent with those of an Australian cohort study (27), in which birth

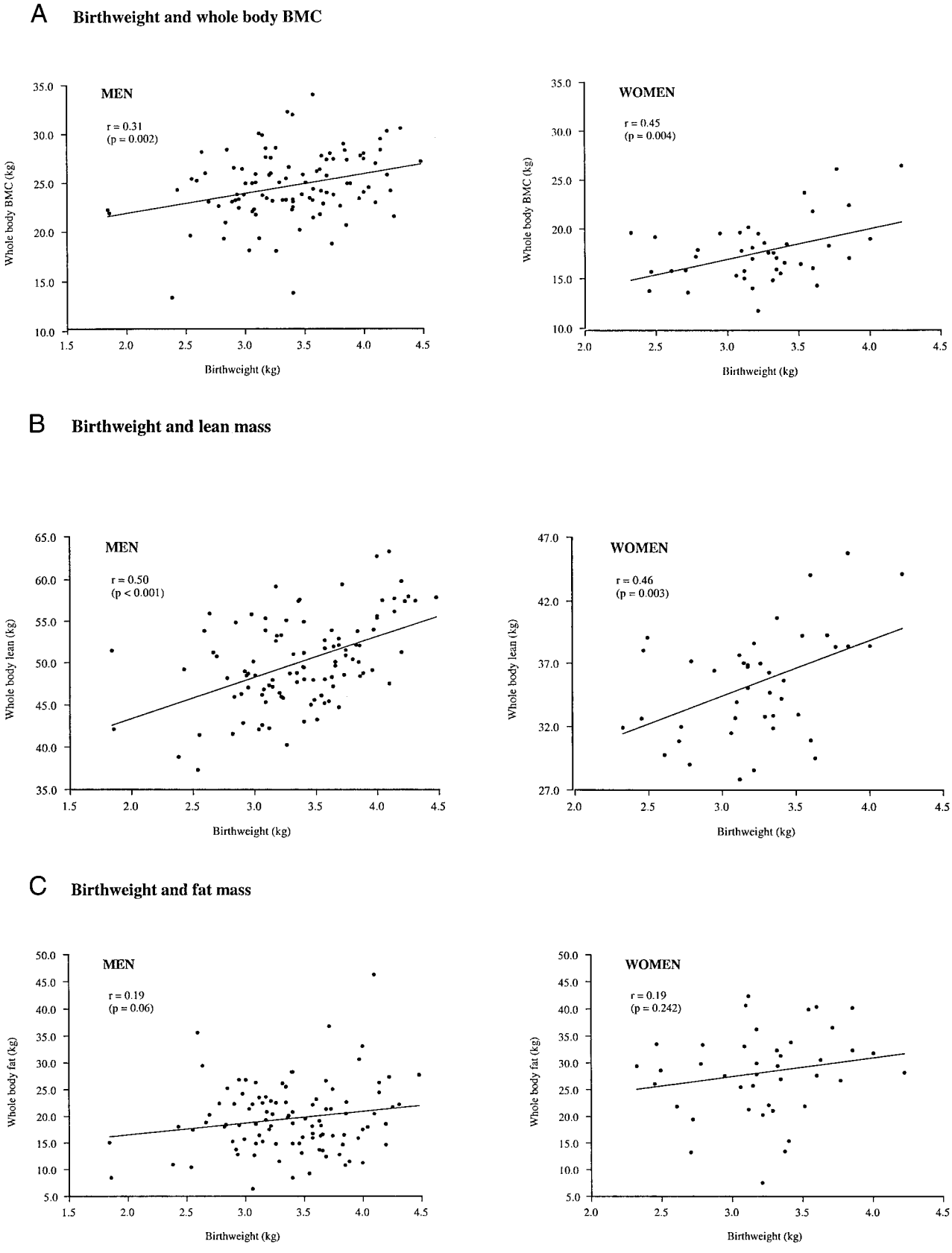


FIG. 1. The relationship between birth weight and whole body BMC (A),) whole body lean mass (B), and whole body fat mass (C) after adjustment for age in men and women.

**TABLE 3.** Bone mineral measurements according to birth weight after adjustment for age, sex, and adult height and weight

| Measure | Birth wt (kg) | | | *P* for trend[a] |
|---|---|---|---|---|
| | <3.15 | 3.15–3.64 | >3.64 | |
| Adjusted for age, sex and height | | | | |
| Whole body BMC (kg) | 22.25 | 22.71 | 23.21 | 0.029[b] |
| Femoral neck BMC (g) | 4.11 | 4.28 | 4.34 | 0.039[b] |
| Lumbar spine BMC (g) | 65.25 | 68.36 | 69.44 | 0.040[b] |
| Whole body total lean mass (kg) | 43.08 | 44.31 | 51.62 | <0.001[c] |
| Whole body total fat (kg) | 22.16 | 21.36 | 23.14 | 0.179 |
| Adjusted for age, sex, and weight | | | | |
| Whole body BMC (kg) | 22.18 | 22.78 | 23.16 | 0.035 |
| Femoral neck BMC (g) | 4.05 | 4.14 | 4.54 | 0.184 |
| Lumbar spine BMC (g) | 65.00 | 68.60 | 69.03 | 0.058 |
| Whole body total lean mass (kg) | 44.64 | 45.97 | 47.43 | <0.001[c] |
| Whole body total fat (kg) | 23.42 | 22.15 | 20.55 | <0.001[c] |
| Adjusted for age, sex, height, and weight | | | | |
| Whole body BMC (kg) | 22.43 | 22.85 | 22.79 | 0.244 |
| Femoral neck BMC (g) | 4.15 | 4.31 | 4.24 | 0.353 |
| Lumbar spine BMC (g) | 65.94 | 68.88 | 67.79 | 0.214 |
| Whole body total lean mass (kg) | 45.02 | 46.08 | 46.88 | 0.002[c] |
| Whole body total fat (kg) | 23.09 | 22.05 | 21.03 | 0.003[c] |

[a] *P* values calculated from linear regression.
[b] $P < 0.05$.
[c] $P < 0.01$.

weight was found to be a predictor of total body bone mass at age 8 yr. They are also in accord with follow-up studies of premature infants (28), who appear to have deficits in bone size and mineral content during later childhood. We therefore conclude that genetic and/or environmental influences during intrauterine life explain at least in part the previously observed associations between weight at 1 yr and adult bone mass.

It is difficult to disentangle the influences of the genome and intrauterine environment on birth weight. In a family study performed over 4 decades ago, Penrose (29) suggested that 62% of the variation in birth weight between individuals was the result of the intrauterine environment, 20% was the result of maternal genes, and 18% was the result of fetal genes. These estimates are concordant with the modest heritability of birth weight (~10%) observed in a recently published twin study from The Netherlands (30). Finally, a study of babies born after ovum donation (31) showed that although their birth weights were strongly related to the birth weights of the recipient mother, they were unrelated to the weight of the female donors. Coupled with animal studies (32–34), these findings suggest that birth size is controlled at least in part by the intrauterine environment rather than by the genetic inheritance from both parents.

There have been no previously published reports of the relationship between birth size and adult body composition measured by DXA; our results point to a significant association between birth weight and adult muscle mass. Indeed, around 25% of the variation in whole body lean mass among men and women, aged 70–74 yr, in this cohort was explained by birth weight. This relationship was much more pronounced than that between birth weight and whole body fat mass and remained highly statistically significant after adjusting for age, adult height, and adult weight. Early growth retardation in animal models leads to permanent reductions in the mass of muscle (35–38), which has been postulated to explain the link between impaired fetal growth and glucose intolerance. Data obtained in human studies are scant. A recent study of young children reported that birth weight was associated with increased lean tissue in the upper arm, as assessed by upper arm muscle-bone area, but that fatness in the upper arm was less affected (39). A study of 191 men, aged 17–22 yr (40), reported that thigh muscle-bone area in adulthood was strongly correlated with birth weight, but not with thigh sc fat area, and that the relationship between birth size and adult body mass index was markedly attenuated by adjusting for the muscle-bone measurement. Finally, 2 studies have evaluated the relationship between birth weight and muscle mass or strength in later adulthood. The first of these (41) examined the relationship between birth weight and muscle mass, as estimated by urinary creatine excretion, among 217 men and women, aged 50 yr. Adult muscle mass was predicted by low birth weight and small head circumference, but not by thinness at birth. The second explored the relationship between birth weight, weight at 1 yr, and adult grip strength among 717 British men and women, aged 60–74 yr. Strong positive associations were found between both measures of weight in infancy and adult grip strength, such that subjects in the lowest fifth of the distribution of birth weight had 12% lower grip strength than those in the highest fifth of the distribution, after adjusting for age, sex, socioeconomic status, and adult height (42). Our results support these observations and suggest that one manifestation of metabolic programming might be the allocation of cells during critical early periods to different body compartments (fat, muscle, and bone). Furthermore, our data suggest that adult bone and muscle mass are more closely interrelated in individuals than either compartment is with adult fat mass. Although this discordance between the development of bone and muscle, on the one hand, and fat, on the other, might stem from different environmental determinants in later life (for example, physical activity), our data suggest differential metabolic programming as an alternative explanation.

In summary, this cohort study suggests that low birth

weight is associated with lower adult bone and muscle mass, even after adjusting for adult height. These data add to the evidence that the risk of osteoporosis in later life might be programmed by genetic and/or environmental influences during gestation. The genetic and environmental programming of the skeletal growth trajectory and any concomitant adverse effect on age-related bone loss require further study so that current strategies to prevent osteoporosis may be enhanced.

## Acknowledgments

We thank the participants for their time; the staff of the Medical Records Department at Jessop Hospital for Women (Sheffield, UK), who allowed us to use the birth records; and the staff at the National Health Service Central Register (Southport, UK), and at the Sheffield Family Health Services Authority who helped to trace the participants. Kate Ellis, Karen Cusick, and Élaine Langley performed the fieldwork; Graham Wield processed the data. The manuscript was prepared by Gill Strange.

## References

1. **Cooper C, Melton LJ.** 1996 Magnitude and impact of osteoporosis and fractures. In: Marcus R, Feldman D, Kelsey J, eds. Osteoporosis. San Diego: Academic Press; 419–434.
2. **Ralston S.** 1998 Do genetic markers aid in risk assessment? Osteop Int. 8(Suppl 1):S37–S42.
3. **Cadogan J, Eastell R, Jones N, Barker M.** 1997 Milk intake and bone mineral acquisition in adolescent girls: randomised controlled intervention. Br Med J. 315:1255–1260.
4. **Friedlander AL, Genant HK, Sadowski S, Byl NN, Gluer CC.** 1995 A two year programme of aerobics and weight training enhances bone mineral density of young women. J Bone Miner Res. 10:574–585.
5. **Cooper C, Cawley MID, Bhalla A, Egger P, Ring F, Morton L, Barker D.** 1995 Childhood growth, physical activity and peak bone mass in women. J Bone Miner Res. 10:940–947.
6. **Cooper C, Fall C, Egger P, Hobbs R, Eastell R, Barker D.** 1997 Growth in infancy and bone mass in later life. Ann Rheum Dis. 56:17–21.
7. **Fall C, Hindmarsh P, Dennison E, Kellingray S, Barker D, Cooper C.** 1998 Programming of growth hormone secretion and bone mineral density in elderly men: an hypothesis. J Clin Endocrinol Metab. 83:135–139.
8. **Dennison E, Hindmarsh P, Fall C, Kellingray S, Barker D, Phillips D, Cooper C.** 1999 Profiles of endogenous circulating cortisol and bone mineral density in healthy elderly men. J Clin Endocrinol Metab. 84:3058–3063.
9. **Barker DJP.** 1998 Mothers, babies and health in later life, 2nd Ed. Edinburgh: Churchill Livingstone.
10. **Martyn CN, Gale CR, Jespersen S, Sheriff SB.** 1998 Impaired fetal growth and atherosclerosis of carotid and peripheral arteries. Lancet. 352:173–178.
11. **Carter DR, Bouxsein ML, Marcus R.** 1992 New approaches for interpreting projected bone densitometry data. J Bone Miner Res. 7:137–145.
12. **Thomas M, Goddard E, Hickman M, Hunter P.** 1994 General household survey, 1992. London: OPCS Social Service Division, HMSO.
13. **Egger P, Duggleby S, Hobbs R, Fall C, Cooper C.** 1996 Cigarette smoking and bone mineral density in the elderly. J Epidemiol Commun Health. 50:47–50.
14. **Heymsfield SB, Wang ZM, Baumgartner RN, Ross R.** 1997 Human body composition: advances in models and methods. Annu Rev Nutr. 17: 527–558.
15. **Mazess RB, Barden HS, Bisek JMP, Hanson HA.** 1990 Dual-energy x-ray absorptiometry for total-body and regional bone-mineral and soft-tissue composition. Am J Clin Nutr. 51:1106–1112.
16. **Slosman DO, Casez JP, Pichard C, et al.** 1992 Assessment of whole-body composition with dual energy x-ray absorptiometry. Radiology. 185:593–598.
17. **Madsen OR, Beck Jensen JE, Sorensen OH.** 1997 Validation of a dual energy x-ray absorptiometer: measurement of bone mass and soft tissue composition. Eur J Appl Physiol. 75:554–558.
18. **Hildreth HG, Johnson RK, Goran MI, Contompasis SH.** 1997 Body composition in adults with cerebral palsy by dual energy x-ray absorptiometry, bioelectrical impedance analysis, and skin-fold anthropometry compared with 18O isotope-dilution technique. Am J Clin Nutr. 66:1436–1442.
19. **Pintauro SJ, Nagy TR, Duthie CM, Goran MI.** 1996 Cross-calibration of fat and lean measurements by dual energy x-ray absorptiometry to pig carcass analysis in the pediatric body weight range. Am J Clin Nutr. 63:293–298.
20. **Abbassi AA, Mattson DE, Duthie EH, Wilson C, Sheldahl L, Sasse E, Rudman IW.** 1998 Predictors of lean body mass and total adipose mass in community-dwelling elderly men and women. Am J Med Sci. 351:188–193.
21. **Martini G, Valenti R, Giovani S, Nuti R.** 1997 Age-related changes in body composition of healthy and osteoporotic women. Maturitas. 27:25–33.
22. **Horber FF, Gruber B, Thomi F, Jensen EX, Jaeger P.** 1997 Effect of sex and age on bone mass, body composition and fuel metabolism in humans. Nutrition. 13:524–534.
23. **Duppe H, Cooper C, Gardsell P, Johnell O.** 1997 The relationship between childhood growth, bone mass and muscle strength in male and female adolescents. Calcif Tissue Int. 60:405–409.
24. **Jones G, Riley M, Dyer T.** 1999 Maternal smoking during pregnancy, growth, and bone mass in prepubertal children. J Bone Miner Res. 14:146–151.
25. **Cooper C, Eriksson JG, Forsén T, Osmond C, Tuomilehto J, Barker DJP.** 1999 Childhood growth trajectory is a strong determinant of later risk of hip fracture: a prospective study [Abstract]. Calcif Tissue Int. 64(Suppl 1):S38.
26. **Hamed HM, Purdie DW, Ramsden CS, Carmichael B, Steel SA, Howey S.** 1993 Influence of birthweight on adult bone mineral density. Osteop Int. 3:1–2.
27. **Jones G, Couper D, Riley M, Goff C, Dwyer T.** 1997 Determinants of bone mass in prepubertal children: antenatal, neonatal and current influences [Abstract]. J Bone Miner Res. 12(Suppl 1):S145.
28. **Fewtrell MS, Prentice A, Jones SC, et al.** 1999 Bone mineralisation and turnover in preterm infants at 8–12 years of age: the effect of early diet. J Bone Miner Res. 14:810–820.
29. **Penrose LS.** 1954 Some recent trends in human genetics. Caryologia. 6(Suppl):521–530.
30. **van Baal CG, Boomsma DI.** 1998 Aetiology of individual differences in birthweight of twins as a function of maternal smoking during pregnancy. Twin Res. 1:123–130.
31. **Brooks AA, Johnson MR, Ster PJ, Pawson ME, Abdalla HI.** 1995 Birthweight: nature or nurture? Early Hum Dev. 42:29–35.
32. **Lush JL, Hetzer HO, Culbertson CC.** 1934 Factors affecting birthweights of swine. Genetics. 19:329–343.
33. **Cawley RH, McKeown T, Record RG.** 1954 Parental stature and birthweight. Ann Hum Genet. 6:448–456.
34. **Roberts DF.** 1986 The genetics of human growth. In: Falkner F, Tanner JM, eds. Human growth. New York: Plenham Press; vol 3:113–143.
35. **Winick M, Noble A.** 1966 Cellular response in rats during malnutrition at various ages. J Nutr. 89:300–306.
36. **Fleagle JG, Samonds KW, Hegsted DM.** 1975 Physical growth of sebus albifrons monkeys (during protein or calorie deficiency). Am J Clin Nutr. 28:246–253.
37. **McCance RA, Widdowson EM.** 1961 Nutrition and growth. Proc R Soc Lond B 156:326–337.
38. **Barac-Nieto M, Spurr GB, Lotero H, Maksud MG.** 1978 Body composition in chronic undernutrition. Am J Clin Nutr. 31:23–40.
39. **Hediger ML, Overpeck MD, Kuczmarski RJ, McGlynn A, Maurer KR, Davis WW.** 1998 Muscularity and fatness of infants and young children born small- or large-for-gestational age [Abstract]. Pediatrics. 102:E60.
40. **Kahn HS, Venkat KMN, Williamson DF, Valdez R.** 2000 Relation of birthweight to lean and fat thigh tissue in young men. Int J Obesity. 24:667–672.
41. **Phillips DIW.** 1995 Relation of fetal growth to adult muscle mass and glucose tolerance. Diabet Med. 12: 686–690.
42. **Aihie Sayer A, Cooper C, Evans JR, Rauf A, Wormald RPL, Osmond C, Barker DJP.** 1998 Are rates of aging determined in utero? Age Ageing. 27: 579–583.