Published in final edited form as:

Placenta. 2011 October ; 32(10): 783–787. doi:10.1016/j.placenta.2011.07.031.

The lifespan of men and the shape of their placental surface at birth

D.J.P. Barker^{a,b,c,*}, C. Osmond^b, K.L. Thornburg^a, E. Kajantie^{d,e}, and J.G. Eriksson^{e,f,g,h,i}

^aHeart Research Center, Oregon Health and Science University, Portland, OR 97201-3098, USA

^bMRC Lifecourse Epidemiology Unit (University of Southampton), Southampton General Hospital, Southampton SO16 6YD, UK ^cChair of Fetal Programming, King Saud University, Saudi Arabia

^dHospital for Children and Adolescents, Helsinki University Central Hospital, Helsinki, Finland

^eNational Institute for Health and Welfare, Department of Chronic Disease Prevention, Helsinki, Finland

^fUniversity of Helsinki, Department of General Practice and Primary Health Care, University of Helsinki, Finland

^gVasa Central Hospital, Sandviksgatan 2-4, 65130 Vasa, Finland

^hFolkhälsan Research Centre, Helsinki, PB 63, 00014 Helsingfors Universitet, Finland ⁱUnit of General Practice, Helsinki University Central Hospital, Finland

Abstract

Background—Tall men generally lead longer lives than short men. Within the Helsinki Birth Cohort, however, there is a group of boys among whom being tall when they entered school was associated with reduced lifespan. These boys had birthweights and maternal heights above the median for the cohort; but they tended to be lighter at birth than their mother's body mass index (weight/height²) in pregnancy predicted. We suggested that, while they had grown rapidly in utero, their growth had faltered at some point; and their tallness at age seven was the result of a resumption during infancy of their rapid growth trajectory. We here examine the size and shape of their placentas at birth to gain further insight into their path of fetal growth.

Methods—We examined all cause mortality in the 1217 men who had birthweights and maternal heights above the median for the cohort. Their birth measurements included placental weight and the length and breadth of the placental surface.

Results—Shorter length of the placental surface was associated with increased mortality ($p = 0.002$). There was no similar trend with the breadth. Mortality rose as the difference between the length and breadth decreased, that is as the surface became rounder. The hazard ratio was 1.10 (1.03–1.18, $p = 0.007$) for every cm decrease in the difference. Among men with a round placental surface (length-breadth difference 2 cm or less) increased mortality was associated with lower birthweight ($p = 0.03$ or 0.005 allowing for mother's body mass index) and shorter gestation, but not with lower head circumference or length.

Copyright © 2011 Published by Elsevier Ltd. All rights reserved.

*Corresponding author. MRC Lifecourse Epidemiology Unit (University of Southampton), Southampton General Hospital, Southampton SO16 6YD, UK. Tel.: +44 (0) 23 80777624; fax: +44 (0) 23 80704021. djparker@gmail.com (D.J.P. Barker).

Conflicts of interest

None declared.

Conclusion—Reduced lifespan among men is associated with a particular path of early growth. After rapid growth in early gestation, associated with tall maternal stature, soft tissue growth falters in mid-gestation. Rapid growth resumes in late gestation and continues through infancy.

Keywords

Lifespan; Fetal growth; Placental surface; Childhood height

1. Introduction

In modern societies taller people generally lead longer lives than shorter people [1–6]. Tall stature is the product of good nutrition in utero and during childhood combined with the absence of recurrent infection, which diverts nutrients away from growth [7]. We have previously examined the relation between height at seven years, the age of school entry in Finland, and mortality from all causes among men in the Helsinki Birth Cohort who were born during 1934–1944 [8]. Boys who were tallest at seven years of age lived five years longer than those who were shortest. There was, however, a subgroup of boys among whom tall stature was associated with a reduced lifespan. These boys had birthweights above the median for the cohort, 3470 g. They tended, however, to be lighter at birth than their mother's body mass index (weight/height²) in pregnancy predicted [8]. We therefore suggested that, while they had grown rapidly in utero and achieved birthweights above the median, their growth had faltered at some point during gestation. During the first two years after birth (infancy) the boys grew rapidly in height, so that at seven years they were taller than their birth weights and birth lengths predicted [8]. The lifespan of these boys was unrelated to their growth in height between two and seven years of age. We suggested that their tallness at age seven was the result of a resumption during infancy of a rapid growth trajectory following growth faltering in utero.

The mothers of the boys among whom tall stature at seven years was associated with reduced lifespan were tall, with heights above the median for the cohort, 160 cm. Tall mothers generally have larger babies than short mothers because their babies grow more rapidly [9,10]. It is more difficult for babies that are growing rapidly to sustain their growth trajectory if the flow of nutrition is reduced. In these circumstances babies that are growing slowly may not need to reduce their growth [11].

In Helsinki in the past the placenta was not only routinely weighed at birth but the length and breadth of its surface were measured because it was recognised that the surface tends to be oval rather than round [12]. In this paper we examine how these measurements are related to all cause mortality among the subgroup of boys for whom tall stature at seven years was associated with a reduced lifespan. Our objective was to gain further insights into the boys' path of intrauterine growth. We have previously shown that, within the Helsinki Birth Cohort, the surface of placentas from pregnancies complicated by preeclampsia tended to be more oval than those from normal pregnancies [12]. Preeclampsia was associated with reduced breadth of the surface but not with reduced length. On this basis we postulated that the surface is aligned along two axes, and that the growth of tissue along the two axes is controlled by different influences. Tissue along the axes may also have different functions.

We proposed that the growth of tissue along the length follows the rostro-caudal growth of the fetus, while tissue along the breadth serves as a nutrient sensor.

2. Methods

The Helsinki Birth Cohort includes 6975 men who were born in the city during 1934–1944. They were born in either the University Central Hospital or in the Maternity Hospital. Details of their birth records have been described [13]. They include the mother's height and weight in late pregnancy and the date of her last menstrual period. The weight, head circumference and length of the newborn baby are recorded. The birth records also include the weight of the placenta, together with the length and breadth of its surface, which were measured to the nearest centimeter [12,14]. The length was taken as the maximal diameter of the surface and the breadth as the diameter that bisected it at right angles. The length and breadth were measured because, in the past, it was recognized that the placental surface tends to be oval rather than round. We used the difference between the length and breadth as an indicator of ovality. On school entry, which in Finland occurred at seven years, each child's height and weight was recorded.

We used the father's occupation to define the mother's social class [14,15]. Based on a classification from Statistics Finland fathers were grouped into upper and lower middle class and manual workers. The men's own occupations, recorded at successive 5-year censuses from 1970 to 2000, were obtained from Statistics Finland, who grouped them into four categories – higher official, lower official, self-employed, and manual worker [15]. We used the highest category attained. Using the personal identification number assigned to each Finnish citizen we identified all deaths among the men during 1971–2007. All deaths in Finland are recorded in the national mortality register.

2.1. Statistical methods

The end points for our survival analysis were deaths from all causes. Men were censored in the analysis when they migrated from Finland or survived to the end of 2007. We used a Cox proportional hazards model to calculate the hazard ratios for death stratified by year of birth. To determine the statistical significance of trends measurements were analysed as continuous variables although they are presented in the tables as groups. Interaction terms were calculated by introducing the product of terms into the regression equation.

3. Results

In our previous analysis [8] we identified a subgroup of boys among whom tall stature at age seven years was associated with a reduced lifespan. These boys had birthweights above the median for the cohort, 3470 g, and their mothers' heights were also above the median, 160 cm. The correlation coefficient between maternal height and birth weight was 0.17. Table 1 is taken from this published analysis [8]. Among boys with birth weight and mother's height above the median all cause mortality rates were highest among those who were tallest (Table 1). Among all other boys mortality was highest in those who were the shortest, the difference between the shortest and tallest group being equivalent to eight years of life.

Our analyses now focus on the 1217 boys with birthweight and mother's height above the median. Table 2 shows their maternal size, birth size, length of gestation, placental size, childhood height, and the numbers of deaths among them. All cause mortality was unrelated to maternal size or birth size. Shorter gestation, however, was associated with increased mortality ($p = 0.03$). Shorter length of the placental surface was also associated with increased mortality ($p = 0.002$). There was no similar trend with the breadth, although length and breadth were highly correlated ($r = 0.54$). In a simultaneous regression increased mortality was associated with shorter length ($p = 0.001$), but not with breadth ($p = 0.2$). These results were unchanged if length of gestation was added to the regression. Mortality rose as the difference between the length and breadth decreased, that is as the surface became rounder. The hazard ratio was 1.10 (1.03–1.18, $p = 0.007$) for every cm decrease in the difference.

We found that the effect of the difference between placental length and breadth on mortality interacted with the effect of height at age seven years. In Table 3 the men are divided into two groups according to whether their placental surface was round or oval. 62 percent of the men had a round surface, defined by a length-breadth difference of 2 cm or less. This was the most even division of the men using placental surface shape. In Table 3 height at age seven is re-categorized into five groups, rather than the six used in Table 1, to accommodate smaller numbers of men in the subgroups. Whereas among men in whom the placental surface was oval all-cause mortality was unrelated to height at seven years, among men in whom the surface was round mortality increased with tallness. This was a statistically significant interaction.

We examined which birth measurements predicted all cause mortality among the men who had round placentas. Mortality was not associated with maternal height, weight or body mass index. Increased mortality was associated, however, with lower birth-weight ($p = 0.03$ or 0.005 allowing for mother's body mass index) and shorter gestation ($p = 0.02$), but not with head circumference ($p = 0.9$), length ($p = 0.3$) or ponderal index ($p = 0.2$). Birth weight was positively correlated with height at age two years (correlation coefficient = 0.25). In a simultaneous regression, however, increased mortality was associated with lower birthweight ($p = 0.008$) but greater height at age two years ($p = 0.04$). Height at seven years was strongly correlated with height at two years ($r = 0.69$) and in a simultaneous regression increased mortality was associated with lower birthweight ($p = 0.006$) and greater height at seven years ($p < 0.001$). The effect of short gestation on mortality was confined to men born at 38 weeks or earlier among whom the hazard ratio was 1.7 (1.1–2.5, $p = 0.01$) in comparison to men born later.

We examined the causes of death associated with tallness at age seven years among men who had round placentas. Among these men the hazard ratio for cardiovascular deaths was 1.84 (0.96–3.50) per 10 cm increase in height at age seven years, while the ratio for non-cardiovascular deaths was 1.73 (1.07–2.82). The strongest association with any single cause of death was with stroke, for which the hazard ratio was 7.41 (1.67–32.8).

3.1. Socio-economic status

Low mother's social class and low socio-economic status in adult life were both associated with increased all cause mortality ($p < 0.001$ for both). The trends in all cause mortality with height at age 7 years among men with round placentas (Table 3) were little changed by adjusting for either of these indicators of socioeconomic status. Among these men the hazard ratio for all cause mortality in those who were classified as higher officials was equivalent to 7.6 years longer lifespan than in those who were manual workers. In comparison, those who were 117 cm or less in height at age seven years had hazard ratios for all cause mortality equivalent to 6.6 years longer lifespan than in those who were more than 126 cm (Table 3).

4. Discussion

We have previously identified a group of men among whom tall stature in early childhood was associated with a reduced lifespan [8]. Their birth weights and mothers' heights were above the median. We have now further characterized their early life phenotype by their having a placental surface that tends to be round because of reduced growth of the length in relation to the breadth.

On the basis of studies of pregnancies complicated by preeclampsia we have postulated that the surface of the placenta is aligned along two axes, and that the growth of tissue along the two axes is controlled by different influences [12]. We suggested that the growth of tissue along the length follows the rostro-caudal growth of the fetus, while tissue along the breadth serves as a nutrient sensor. Studies of fetal programming support the idea that tissue along the two axes has different functions, and that their growth is differently controlled. The occurrence of four common disorders of later life, coronary heart disease, chronic heart failure, hypertension and lung cancer, is related to the size of the breadth of the placental surface at birth but not to the length [14,16–19]. Among nine-year old children in South India blood pressure levels were more strongly related to the breadth than to the length [20]. Among men born around the period of war-time famine in Holland a small placental breadth predicted hypertension in those who were not in utero during the famine [18]. In contrast, among those who were in utero during the famine hypertension was predicted by a large breadth. This is evidence that the function of tissue along the breadth of the placental surface responds to changes in maternal diet. It is consistent with other evidence that the placenta can compensate for maternal malnutrition by expansion of its surface along the breadth [14].

On the basis of our hypothesis that the growth of tissue along the length follows the rostro-caudal growth of the fetus [12], we suggest that the association between short length of the placental surface and reduced lifespan indicates that the growth of the fetus faltered at some stage of gestation. We found that, within the phenotype we have described, lower birthweight predicted reduced lifespan but lower head circumference and length did not. This suggests that, for the fetus, a consequence of growth faltering was reduced soft tissue mass at birth. We also found that reduced lifespan was associated with premature delivery. This could also be associated with growth faltering.

A recent study of serial ultrasounds of more than 4000 babies identified a group of neonates, around 10% of the sample, who were delivered, on average, one week early [21]. These babies grew rapidly until 22 weeks after which growth of their soft tissues, measured by the abdominal circumference, slowed while rapid brain and skeletal growth were sustained. After 28 weeks soft tissue growth rebounded and the fetus grew rapidly to be delivered, on average, one week early. The authors of the study attribute this early delivery to the accelerated growth in late gestation. We speculate that the phenotype described in our study was the result of a similar path of growth. The birthweights of boys with the phenotype we have described were above the median for the cohort, indicating a rapid fetal growth trajectory, which we attribute to the mothers' tall stature [9,10]. Babies with the phenotype had an early delivery and reduced soft tissue mass at birth.

Reduced lifespan was associated with low maternal socioeconomic status. There were well-documented food scarcities in Finland during the time when the boys were born [22]. These would have been more severe among women of low socioeconomic status. Maternal malnutrition is known to have a greater effect on fetuses that are growing rapidly [11]. We suggest that the food scarcity led to slowing of the fetuses' soft tissue growth in mid-gestation. The authors of the serial ultrasound study proposed that the rebound in soft tissue growth in late gestation was associated with placental compensation. Under our hypothesis this compensation would depend on tissue along the breadth of the surface. We hypothesise that the phenotype we have described was the result of a similar period of accelerated growth in late gestation, and that this accelerated growth led to early delivery and was continued through infancy leading to tallness at seven years.

Among men with the phenotype tallness at age seven years was associated with increased mortality from both cardiovascular and non-cardiovascular causes. The strongest association with a single cause of death was with stroke. In our previous publication we described how the men with the phenotype were taller at age seven years than their size at birth predicted, which suggested that their rapid growth was compensatory [8]. The ability to mount rapid compensatory growth following growth faltering is common in animals and familiar to farmers [23]. If energy is allocated to rapid growth the allocation to some other developmental activity must be reduced. Compensatory growth has a wide range of physiological and metabolic costs that include premature death.

5. Limitations of the study

The placental measurements in our study were made during routine obstetric practice 70 years ago. Routine measurements of the placental diameters ceased in Helsinki in the 1970s. We have discussed the simple procedures used with people who worked as midwives at that time. The quality of the measurements was not routinely checked, just as there are no routine checks of other clinical measurements, such as blood pressure. The mothers were weighed in late gestation and we are not able to distinguish the effects of pre-pregnancy body mass from those of weight gain in pregnancy. The people in our study may not be representative of all people now living in Helsinki, although at birth their social class distribution was similar to that in the city as a whole [13].

6. Conclusion

We have previously identified a group of men among whom tall stature in childhood was associated with a reduced lifespan. Their birth weights and mothers' heights were above the median. We now find that within this group reduced lifespan is associated with a round placental surface at birth as a result of reduced growth of the length in relation to the breadth. Reduced lifespan was also associated with reduced soft tissue mass at birth and preterm delivery. We suggest that a particular path of early growth leads to reduced lifespan. Rapid growth in early gestation is followed by faltering of soft tissue growth in mid-gestation and accelerated compensatory growth in late gestation that continues through infancy.

Acknowledgments

Funding

The study was supported by grants from the National Institute of Aging, the Academy of Finland, British Heart Foundation, Finnish Medical Society Duodecim, Finska Läkaresällskapet, Foundation for Pediatric Research, Jalmari and Rauha Ahokas Foundation, Juho Vainio Foundation, Päivikki and Sakari Sohlberg Foundation, Signe and Ane Gyllenberg Foundation, Yrjö Jahnsson Foundation and the Edwards Endowment.

References

1. Waaler HT. Height, weight and mortality. The Norwegian experience. *Acta Med Scand Suppl.* 1984; 679:1–56. [PubMed: 6585126]
2. Hebert PR, Rich-Edwards JW, Manson JE, Ridker PM, Cook NR, O'Connor G, et al. Height and incidence of cardiovascular disease in male physicians. *Circulation.* 1993; 88:1437–43. [PubMed: 8403290]
3. Davey Smith G, Hart C, Upton M, Hole D, Gillis C, Watt G, et al. Height and risk of death among men and women: aetiological implications of associations with cardiorespiratory disease and cancer mortality. *J Epidemiol Comm Health.* 2000; 54:97–103.
4. McCarron P, Okasha M, McEwen J, Smith GD. Height in young adulthood and risk of death from cardiorespiratory disease: a prospective study of male former students of Glasgow University, Scotland. *Am J Epidemiol.* 2002; 155:683–7. [PubMed: 11943683]
5. Langenberg C, Shipley MJ, Batty GD, Marmot MG. Adult socioeconomic position and the association between height and coronary heart disease mortality: findings from 33 years of follow-up in the Whitehall Study. *Am J Public Health.* 2005; 95:628–32. [PubMed: 15798120]
6. Sunder M. Toward generation XL: anthropometrics of longevity in late 20th century United States. *Econ Hum Biol.* 2005; 3:271–95. [PubMed: 15921967]
7. Tanner, JM. *Fetus into man.* 2. Ware:Castlemead; 1989.
8. Barker DJP, Kajantie E, Osmond C, Thornburg KL, Eriksson JG. How boys grow determines how long they live. *Am J Hum Biol.* 2011; 23:412–6. [PubMed: 21448906]
9. McCance RA, Widdowson EM. The determinants of growth and form. *Proc Roy Soc Lond B.* 1974; 185:1–17. [PubMed: 4149051]
10. Cawley RH, McKeown T, Record RG. Parental stature and birthweight. *Ann Hum Genet.* 1954; 6:448–56.
11. Harding JE. The nutritional basis of the fetal origins of adult disease. *Int J Epidemiol.* 2001; 30:15–23. [PubMed: 11171842]
12. Kajantie E, Thornburg K, Eriksson JG, Osmond C, Barker DJ. In preeclampsia, the placenta grows slowly along its minor axis. *Int J Dev Biol.* 2010; 54:469–73. [PubMed: 19876819]
13. Barker DJP, Osmond C, Forsén TJ, Kajantie E, Eriksson JG. Trajectories of growth among children who have coronary events as adult. *N Engl J Med.* 2005; 353:1802–9. [PubMed: 16251536]

14. Barker DJ, Thornburg KL, Osmond C, Kajantie E, Eriksson JG. The surface area of the placenta and hypertension in the offspring in later life. *Int J Dev Biol.* 2010; 54:525–30. [PubMed: 19876839]
15. Barker DJP, Forsén T, Uutela A, Osmond C, Eriksson JG. Size at birth and resilience to effects of poor living conditions in adult life: longitudinal study. *Brit Med J.* 2001; 323:1273–6. [PubMed: 11731388]
16. Eriksson JG, Kajantie E, Thornburg JG, Osmond C, Barker DJP. Mother's body size and placental size predict coronary heart disease in men. *Eur Heart J.* 2011 [epub].
17. Barker DJP, Gelow J, Thornburg K, Osmond C, Kajantie E, Eriksson JG. The early origins of chronic heart failure; impaired placental growth and initiation of insulin resistance in childhood. *Eur J Heart Fail.* 2010; 12:819–25. [PubMed: 20504866]
18. van Abeelen AFM, de Rooij SR, Osmond C, Painter RC, Veenendaal MVE, Bossuyt PMM, et al. Sex-specific effects of famine on the placental programming of hypertension. *Placenta.* 2011 Jul 9. [Epub ahead of print].
19. Barker DJ, Thornburg KL, Osmond C, Kajantie E, Eriksson JG. The prenatal origins of lung cancer. II. The placenta. *Am J Hum Biol.* 2010; 22:512–6. [PubMed: 20309992]
20. Winder NR, Krishnaveni GV, Hill JC, Karat CL, Fall CHD, Veena SR, et al. Placental programming of blood pressure in Indian children. *Acta Paed.* 2011; 100:653–60.
21. Lampl M, Kusanovic JP, Erez O, Gotsch F, Espinoza J, Goncalves L, et al. Growth perturbations in a phenotype with rapid fetal growth preceding preterm labor and term birth. *Am J Hum Biol.* 2009; 21:782–92. [PubMed: 19298010]
22. Pesonen AK, Raikkonen K, Heinonen K, Kajantie E, Forsen T, Eriksson J. Depressive symptoms in adults separated from their parents as children: a natural experiment during World War II. *Am J Epidemiol.* 2007; 2007(166):1126–33. [PubMed: 17875582]
23. Metcalfe NB, Monaghan P. Compensation for a bad start: grow now, pay later? *Trends Ecol Evol.* 2001; 16:254–60. [PubMed: 11301155]

Table 1

Hazard ratios for all causes of death in men according to their height at age seven years, divided by median birthweight and mother's height.

Height at age seven (cm)	Boys with birthweight and mother's height above the median		All other boys	
	Deaths/men	HR (95% CI)	Deaths/men	HR (95% CI)
114	3/23	0.5 (0.2–1.7)	127/381	2.1 (1.5–2.9)
–117	17/70	0.9 (0.5–1.5)	151/600	1.5 (1.1–2.1)
–120	38/203	0.7 (0.5–1.0)	206/859	1.4 (1.1–1.9)
–123	61/288	0.8 (0.6–1.2)	178/827	1.4 (1.0–1.8)
–126	69/325	0.9 (0.6–1.2)	106/517	1.3 (0.9–1.8)
>126	72/308	1.0 (baseline)	57/345	1.0 (baseline)
HR per 10 cm		1.32 (1.00–1.75)		0.67 (0.58–0.78)
p for trend		0.05		<0.0001

HR = hazard ratio; CI = confidence interval.

Table 2

Characteristics of 1217 men with birth weight above the median (3470 g) and mother's height above the median (160 cm).

	Mean	St Dev	Missing values
Mother			
Height (cm)	165.1	3.4	0
Weight in pregnancy (kg)	72.5	8.1	14
Body mass index (kg/m ²)	26.6	3.0	14
Baby			
Birth weight (g)	3873	307	0
Head circumference (cm)	36.0	1.3	10
Length (cm)	51.8	1.5	6
Ponderal index (kg/m ³)	27.9	2.1	6
Gestation (days)	282	11	36
Placenta			
Weight (g)	708	114	2
Length (cm)	20.2	2.0	3
Breadth (cm)	17.7	2.0	2
Length – breadth (cm)	2.5	1.9	3
Child			
Height at age two years (cm)	88.3	2.9	1
Height at age seven years (cm)	123.1	4.4	0
Adult			
No of deaths	260		

Table 3

Hazard ratios for all causes of death according to height at age seven years and the shape of the placental surface.

Height at age seven (cm)	Shape of the placental surface (length-breadth difference)			
	Oval (- 3 cm)		Round (- 2 cm)	
	Deaths/men	HR (95% CI)	Deaths/men	HR (95% CI)
117	10/36	1.0 (baseline)	10/56	1.0 (baseline)
-120	14/77	0.6 (0.3–1.5)	24/126	1.1 (0.5–2.3)
-123	24/108	0.9 (0.4–1.8)	36/179	1.1 (0.6–2.3)
-126	25/129	0.7 (0.3–1.6)	44/195	1.4 (0.7–2.8)
>126	18/116	0.6 (0.3–1.3)	54/192	1.8 (0.9–3.6)
HR per 10 cm		0.77 (0.47–1.26)		1.76 (1.24–2.51)
p for trend		0.3		0.002
p for interaction			0.01	

HR = hazard ratio; CI = confidence interval.