Size at birth and glucose intolerance in a relatively genetically homogeneous, high–birth weight population[1–3]

Bryndis E Birgisdottir, Ingibjorg Gunnarsdottir, Inga Thorsdottir, Vilmundur Gudnason, and Rafn Benediktsson

ABSTRACT

Background: The results of epidemiologic studies have linked birth size to adult glucose intolerance.

Objective: We investigated this association in a genetically homogeneous population with higher birth weights and a lower prevalence of type 2 diabetes than previously studied.

Design: The subjects were 2362 men and 2286 women aged 33–65 y. Size at birth was obtained from the National Archives of Iceland. Data for adult anthropometry, fasting blood glucose, and blood glucose after an oral glucose load came from the randomized prospective Reykjavík Study.

Results: Postchallenge glucose concentrations were inversely related to birth weight and length in men and inversely related to birth weight and ponderal index in women ($P < 0.001$). This association was mainly found among those within the highest one-third of adult body mass index values. In men, the prevalence of dysglycemia was lower with increasing weight ($P = 0.04$) and length ($P = 0.003$) at birth but there was no relation of dysglycemia to ponderal index. For women, there was no linear trend for dysglycemia in relation to size at birth but the relation with birth length was U shaped.

Conclusions: Greater birth weight and length appear to offer a protective effect against glucose intolerance. Adult overweight or obesity enhances the risk associated with low birth weight and length. Because the population studied has higher birth weights and a lower prevalence of type 2 diabetes than are found in neighboring countries, it is possible that decreasing the number of low–birth weight infants might help to stem the increasing prevalence of type 2 diabetes worldwide. *Am J Clin Nutr* 2002;76:399–403.

KEY WORDS Newborns, adults, birth weight, body height, blood glucose, type 2 diabetes, impaired glucose tolerance, dysglycemia, Reykjavík Study

INTRODUCTION

Many epidemiologic studies have found an association between reduced size at birth [birth weight, birth length, and ponderal index (in kg/m^3)] and impaired glucose tolerance and type 2 diabetes mellitus, ie, dysglycemia (1–5). Although this relation seems to exist throughout the normal birth weight spectrum, it appears to be exaggerated at the lower end of the birth weight range.

The most popular hypothesis for explaining these observations is that inadequate nutrition permanently programs the endocrine systems involved in nutritional homeostasis (6). This has caused scientists to focus on lifestyle and nutritional factors as well as on maternal nutritional status before and during pregnancy (6–8).

Iceland is geographically isolated and has a small, relatively genetically homogeneous population (9). The birth weights of Icelandic children are among the highest in the world (10–13), in contrast with the groups previously used in studying this subject. Furthermore, the prevalence of type 2 diabetes is lower in Iceland than in the genetically related nations of Scandinavia (14), despite a higher prevalence of obesity (15). The aim of this study was to investigate the relation between size at birth and adult glucose intolerance in Icelanders.

SUBJECTS AND METHODS

Study population

The study population was a subcohort of the randomly selected participants in the ongoing prospective Reykjavík Study (16), including those born in the greater Reykjavík area in 1914–1935 who were still living in Reykjavík in 1967 ($n = 6120$). Complete midwives' birth records for 78.9% of the individuals were available at the National Archives of Iceland; of these, 180 were excluded: 53 twins, 8 persons with type 1 diabetes, and 119 persons who were > 65 y of age. The current analysis thus includes 4648 subjects aged 33–65 y. Ethical approval was granted by The Icelandic Data Protection Commission and The National Bioethics Committee, and the subjects gave written, informed consent.

Collection of birth data

Midwives' birth records included sex, birth weight (kg), crown-heel length (cm), and whether a birth was a singleton. Ponderal index was calculated. Preterm births were not identified

[1] From the Unit for Nutrition Research (BEB, IG, and IT) and the Department of Medicine (RB), Landspitali-University Hospital, Reykjavík, Iceland; the Department of Food Science (BEB, IG, and IT) and the Faculty of Medicine (RB), University of Iceland, Reykjavík; and The Icelandic Heart Association, Reykjavík (VG and RB).

[2] Supported by the Icelandic Research Council and the Research Fund of the University of Iceland.

[3] Address reprint requests to BE Birgisdottir, Unit for Nutrition Research, PO Box Nyja-Gardi, University of Iceland, 101 Reykjavík, Iceland. E-mail: beb@hi.is.

Received April 30, 2001.

Accepted for publication August 1, 2001.

The American Journal of Clinical Nutrition

Downloaded from ajcn.nutrition.org by guest on December 18, 2016

TABLE 1
Birth and adult size and adult blood glucose values in a cohort of participants in the Reykjavík Study[1]

	Men	Women
Birth weight (kg)	3.82 ± 0.6 [2345]	3.68 ± 0.5[2] [2273]
Birth length (cm)	52.7 ± 2.5 [2356]	52.1 ± 2.3[2] [2281]
Ponderal index (kg/m^3)	26.1 ± 3.4 [2340]	26.1 ± 3.3 [2269]
Adult weight (kg)	82.3 ± 12.5 [2355]	67.8 ± 11.4[2] [2278]
Adult height (cm)	177.7 ± 6.5 [2360]	164.8 ± 5.6[2] [2284]
Adult BMI (kg/m^2)	26.0 ± 3.6 [2355]	25.0 ± 4.0[2] [2277]
Fasting glucose (mmol/L)	4.6 ± 0.8 [2348]	4.4 ± 0.6[2] [2284]
90-Min glucose (mmol/L)	5.6 ± 2.0 [2331]	5.7 ± 1.6[2] [2264]

[1] $\bar{x}$ ± SD; *n* in brackets.
[2] Significantly different from men, $P < 0.001$.

clearly in the birth records. All newborns were therefore included in the study.

Collection of adult data

The Reykjavík Study measured capillary whole-blood glucose (from the ear lobe) after the subjects had fasted for 10 h and 90 min after an oral intake of 50 g glucose. Glucose was measured as previously described (14). Weight and height were recorded. Information was collected by questionnaire about prior diagnoses of type 1 or 2 diabetes, education, and current regular physical activity. Subjects were classified as having type 2 diabetes if they reported so, if fasting glucose values were ≥6.1 mmol/L, or if 90-min glucose values were ≥11.1 mmol/L (14). Impaired glucose tolerance was defined as fasting glucose <6.1 mmol/L and 90-min glucose ≥7.8–11.0 mmol/L. *Dysglycemia* is used here as a collective term including impaired glucose tolerance and type 2 diabetes.

Statistical analysis

Means and SDs were used to describe the basic data. The Student's *t* test was used to compare these data for men and women. Blood glucose distributions were skewed and thus log transformed for analysis. For analysis of the trend in blood glucose values across the range of birth weight, length, and ponderal index, linear regression was used. In those analyses, individuals claiming to be diabetic were excluded ($n = 50$) because medication might have affected their glucose values. Adult body mass index (BMI; in kg/m^2) values were divided into approximate thirds and linear regression analysis performed within each to analyze the trend in blood glucose values within each BMI category.

For testing significance between odds ratios across quartiles of birth size, logistic regression was used. The reference group for birth weight was >3.75–4.0 kg and for birth length >52–54 cm (the third-quartile groups). Trend analysis for dysglycemia across quartiles of birth size was done with continuous birth size variables, with the use of logistic regression. For all analyses that used linear or logistic regressions, data were adjusted for age at examination and year of arrival at the clinic. Year of birth correlated (Kendall correlation) negatively with birth weight ($r = -0.046$, $P < 0.001$) and positively with birth length ($r = 0.13$, $P < 0.001$) and was adjusted for. Data were also tested after adjustment for educational status (elementary school, junior high, college or university degree) as a proxy for social class and for current regular physical activity (as a yes or no question regarding regular physical activity in the questionnaire). $P < 0.05$ was considered statistically significant. The statistical software used was SPSS for WINDOWS, version 9 (SPSS Inc, Chicago).

RESULTS

Anthropometry on subjects at birth and as adults and blood glucose values are shown in **Table 1**. Men were heavier and taller than women, at birth as well as in adulthood ($P < 0.001$), although their ponderal indexes at birth were not significantly different ($P = 0.416$). The mean (±SD) age of the subjects was 50 ± 7 y. The prevalence of dysglycemia was 11.8% for men and 8.9% for women. The prevalence of type 2 diabetes was 3.4% for men and 2.2% for women.

For fasting glucose values, an inverse relation with birth weight was found after adjustment for current BMI in men ($P = 0.007$). This relation was found for length at birth for men both before ($P = 0.018$) and after ($P = 0.012$) adjustment for BMI. For women, the only significant trend found was with birth weight after adjustment for BMI ($P = 0.036$). No such association was observed for ponderal index.

For 90-min blood glucose values, an inverse relation with birth weight and length was found (**Tables 2** and **3**). Linear regression for birth weight and length and 90-min glucose values for underweight women (BMI <20; $n = 145$) showed that these variables were responsible for the trend in the lowest one-third of BMI values ($P < 0.001$); there was no association for the rest of the lowest third, for either birth weight ($P = 0.272$) or length ($P = 0.095$). Ponderal index was inversely related to 90-min glucose in women ($P = 0.003$) but not in men ($P = 0.299$). When the range of BMI values was split into thirds, the trend for ponderal index held only for women in the middle ($P = 0.036$) and highest ($P = 0.006$) categories of BMI.

The risk of developing dysglycemia in relation to categories of birth weight was estimated with odds ratios, with the use of the third category as the reference group (>3.75–4.0 kg; **Figure 1**). As shown, the group with the highest birth weight always had the lowest relative odds ratio, although this difference was not statistically significant. For men, there was a significant trend toward a lower prevalence of dysglycemia with increasing birth weight, both before ($P = 0.04$) and after ($P = 0.018$) adjustment for BMI, as well as with length, both before ($P = 0.003$) and after ($P = 0.003$) adjustment for BMI, but this was not the case for women. The relation with length at birth in women was U shaped, and each category was significantly different from the reference group (Figure 1). No association was found between dysglycemia and ponderal index, in either the odds ratio or trend values. Adjustment for educational status and regular physical activity did not affect the results.

Calculating the risk of dysglycemia with increasing BMI, with the use of the lowest one-third of BMI values as the reference, gave odds ratios of 1.5 ($P = 0.03$) and 2.3 ($P = 0.002$) in the middle and highest BMI groups, respectively, for men, and 1.0 ($P = 0.275$) and 1.6 ($P = 0.007$) in the middle and highest BMI groups, respectively, for women.

DISCUSSION

The results of the present study confirm the previously observed inverse association between weight and length at birth and adult glucose intolerance (4, 5, 7, 17). Dividing the subjects into approximate thirds according to adult BMI showed that the association is mainly found among subjects who become overweight or obese later in life, as previously suggested (4, 8).

When odds ratios are used for comparison, it is evident that the association between birth weight and adult dysglycemia seen in this study is weak. For example, the odds ratio for the lowest category in relation to the reference category was 1.1–1.2 in this study; others have published odds ratios of 1.8–6.4 and even 12.1 (1–5). The birth weights of children in Iceland are exceptionally

The American Journal of Clinical Nutrition
Downloaded from ajcn.nutrition.org by guest on December 18, 2016

TABLE 2
Birth weight, adult BMI, and geometric mean concentration of blood glucose 90 min after an oral glucose challenge in a cohort of participants in the Reykjavík Study[1]

	Birth weight (kg)					
	≤3.45 (*n* = 500 M, 649 F)	>3.45–3.75 (*n* = 637 M, 720 F)	>3.75–4.0 (*n* = 527 M, 461 F)	>4.0 (*n* = 625 M, 404 F)	Regression coefficient (95% CI)[2]	*P* for trend
Men						
BMI (kg/m^2)						
All (*n* = 2289)	5.4	5.5	5.3	5.1	−0.27 (−0.19, −0.41)	<0.001
≤24.5 (*n* = 787)	5.0	5.3	5.2	5.0	−0.05 (0.17, −0.27)	0.434
>24.5 to ≤27.0 (*n* = 705)	5.4	5.5	5.1	5.0	−0.42 (−0.20, −0.64)	<0.001
>27.0 (*n* = 793)	5.9	5.8	5.6	5.2	−0.48 (−0.26, −0.70)	<0.001
Women						
BMI (kg/m^2)						
All (*n* = 2234)	5.7	5.5	5.5	5.4	−0.26 (−0.15, −0.37)	<0.001
≤23.0 (*n* = 759)	5.6	5.4	5.3	5.3	−0.23 (−0.01, −0.45)	0.008
>23.0 to ≤26.0 (*n* = 755)	5.6	5.5	5.5	5.3	−0.20 (0.02, −0.42)	0.051
>26.0 (*n* = 711)	5.9	5.6	5.8	5.5	−0.33 (−0.11, −0.44)	0.01

[1] Geometric $\bar{x}$.
[2] Not calculated on a logarithmic scale.

high, among the highest in the world (10–13) and higher than in comparable studies (1–5, 7, 17, 18). This might suggest that because the relation between birth weight and dysglycemia seems to be steepest at the lower end of the international birth weight scale, one would not see as clear a difference between those with the lowest birth weight and the reference group in a population that has been well nourished over a long period and that has high birth weights. It is thus remarkable to find a relation at all between fetal growth and adult dysglycemia, especially given the relative adult obesity (15) and low prevalence of diabetes in Iceland (14).

A noteworthy finding is the decreasing 90-min blood glucose values observed with increasing birth weight and length in women who are thin as adults (BMI < 20). This might be an index of relative insulin deficiency rather than insulin resistance in this subgroup.

A consistently low prevalence of dysglycemia in those with very high birth weights was seen in all analyses using odds ratios, a pattern that has been seen in most (1, 2, 4, 5) but not all (3) studies. The increased prevalence of type 2 diabetes that has been observed with very high birth weights has been attributed in part to gestational diabetes, resulting in large babies prone to diabetes later in life. In Iceland the prevalence of gestational diabetes is low (19), making this an unlikely explanation for the high birth weight.

The data used in this study are from the 30 000-subject longitudinal Reykjavík Study carried out by the Icelandic Heart Association in 1967–1997. The population invited to participate in the study were randomly selected groups of males and females born in 1907–1935 and with legal residence in the greater Reykjavík area. In our study, we included those born in Reykjavík in 1914–1935 because midwives' records before that time did not include anthropometric measurements. Iceland is an ideal location for epidemiologic studies because of its geographical isolation and the relatively genetically homogeneous nature of its small population. The Reykjavík Study is unique because the participation rate was very high and information on an exceptionally large

TABLE 3
Birth length, adult BMI, and geometric mean concentration of blood glucose 90 min after an oral glucose challenge in a cohort of participants in the Reykjavík Study[1]

	Birth length (cm)					
	≤50 (*n* = 433 M, 646 F)	>50–52 (*n* = 680 M, 689 F)	>52–54 (*n* = 720 M, 586 F)	>54 (*n* = 467 M, 321 F)	Regression coefficient (95% CI)[2]	*P* for trend
Men						
BMI						
All (*n* = 2300)	5.6	5.4	5.3	5.1	−0.06 (−0.03, −0.09)	<0.001
≤24.5 (*n* = 791)	5.2	5.1	5.1	5.0	−0.03 (0.02, −0.08)	0.272
>24.5 to ≤27.0 (*n* = 709)	5.5	5.4	5.2	5.0	−0.07 (−0.02, −0.12)	0.009
>27.0 (*n* = 795)	6.0	5.6	5.6	5.2	−0.09 (−0.03, −0.15)	0.001
Women						
BMI						
All (*n* = 2242)	5.6	5.5	5.5	5.5	−0.03 (0, −0.06)	0.053
≤23.0 (*n* = 763)	5.6	5.4	5.4	5.2	−0.05 (−0.005, −0.095)	0.017
>23.0 to ≤26.0 (*n* = 757)	5.6	5.4	5.4	5.6	−0.01 (0.04, −0.06)	0.717
>26.0 (*n* = 713)	5.7	5.7	5.7	5.6	−0.01 (0.04, −0.06)	0.803

[1] Geometric $\bar{x}$.
[2] Not calculated on a logarithmic scale.

The American Journal of Clinical Nutrition

Downloaded from ajcn.nutrition.org by guest on December 18, 2016

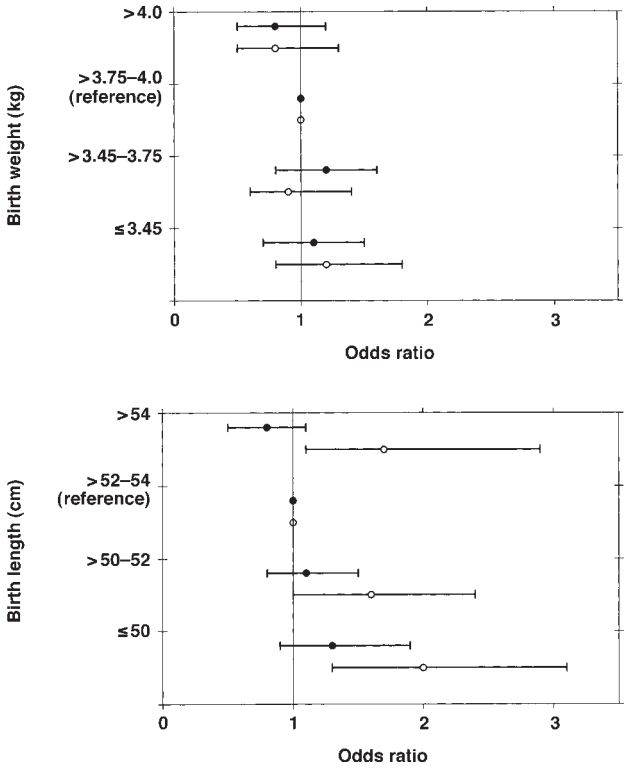

FIGURE 1. Odds ratios and 95% CIs for dysglycemia, ie, type 2 diabetes or impaired glucose tolerance, by quartiles of birth weight and length adjusted for BMI. ●, men; *P* for trend = 0.018 (top) and 0.003 (bottom); ○, women; *P* for trend = 0.091 (top) and 0.225 (bottom).

number of factors was collected. The study provided valuable information about the health status of Icelanders.

The large birth sizes in Iceland might be explained by nutritional factors, such as a high-protein diet, especially from milk and fish, throughout the century (20–22). n–3 Fatty acid consumption, mainly from cod liver oil, which was still consumed by one-half the population in 1990, may be of particular importance because it may not only affect fetal development but also prolong gestation (21, 23), resulting in newborns of higher birth weight. Icelandic women are tall; the mean BMI of women of childbearing age at the time of the study was 24.4 (24), and they gain considerable weight during pregnancy (on average 15 kg; 11). All these factors relate to size at birth. The high birth weight in Iceland may contribute to the lower incidence of type 2 diabetes than is found in Scandinavia, which cannot be explained by lower BMIs in Iceland than in the Scandinavian countries (14, 15).

Genes also influence fetal growth and disease, and some researchers suggest that individual susceptibility to diabetes is primarily genetically determined (25). The same genetic influences are hypothesized to alter both intrauterine growth and adult dysglycemia, for example, by a mutation in the glucokinase gene (25, 26).

The strongest association found in the present study was between dysglycemia and length at birth, which has been seen in other studies (1, 18). It was suggested that genetic influences affect length more than they do weight (27, 28). However, body length has been increasing in Iceland and many other countries during the past century, which strongly implies a nutritional rather than a genetic cause. The relative importance of environment and genetics to fetal growth cannot be determined from the data of the present study, although genetic homogeneity (9) minimizes possible confounding by genetic admixture. The predisposition of smaller children to type 2 diabetes and vascular disease is thus likely to be the result of both genetic and environmental factors (26), the interaction of which needs further study (25). The most popular hypothesis to explain the epidemiologic observations is that inadequate nutrition permanently programs the endocrine systems involved in nutritional homeostasis (6). It is known that several maternal factors influence birth weight, such as heredity (25) and the mother's own fetal and childhood growth, body composition before pregnancy, weight gain during pregnancy, and diet before and during pregnancy (6). The main causes of intrauterine malnutrition are poor maternal nutrition, placental insufficiency (poor transfer capacity), and impaired fetal use of nutrients (29). It was shown in animal studies that if mothers are undernourished during pregnancy the offspring show persistent changes in insulin secretion and in responsiveness to the hormone (8). For example, low-protein manipulations in rat pregnancy elicit different programming effects on the developing cardiovasculature as well as reducing the birth weight of the pups. The balance of nutrients might be a critical determinant of the long-term health effects of maternal malnutrition in pregnancy (30). It is important to do epidemiologic studies on the association between size at birth and later diseases in different areas with different populations and dietary habits, because this can yield valuable indications about the mechanism behind the association.

It was suggested that postnatal change in size might be of equal importance in programming for future diseases (31). This view is supported by studies showing that the path of growth through childhood modifies the risk of adult disease (1, 32, 33). This seems plausible, but more studies are needed to get a clear picture of the role of events during both fetal and childhood development, as well as other influences throughout life, that may contribute to future diseases. The sex difference found in the study might thus be caused by the different growth patterns of girls and boys in utero (6) and by endocrinologic differences between men and women later in life (1). This should be studied further because it might be important for future recommendations.

In conclusion, a protective effect of increased birth weight and length with regard to glucose intolerance was seen in a population with higher average birth size than was previously investigated. Adult overweight and obesity enhanced the risk of low birth weight and length. Because the population studied had a lower prevalence of type 2 diabetes despite a higher prevalence of obesity than is found in neighboring countries, measures aimed at decreasing the number of low–birth weight infants might to some extent offset the risk associated with adult obesity and help in the battle against the increasing prevalence of type 2 diabetes worldwide.

We thank Orn Olafsson, Helgi Sigvaldason, and Nikulas Sigfusson for their valuable help in data preparation and calculations and the employees at the National Archives of Iceland for their assistance.

REFERENCES

1. Forsén T, Eriksson J, Tuomilehto J, Reunanen A, Osmond C, Barker D. The foetal and childhood growth of persons who develop type 2 diabetes. Ann Intern Med 2000;133:176–82.
2. Carlsson S, Persson PG, Alvarsson M, et al. Low birth weight, fam-

The American Journal of Clinical Nutrition

Downloaded from ajcn.nutrition.org by guest on December 18, 2016

ily history of diabetes and glucose intolerance in Swedish middle-aged men. Diabetes Care 1999;22:1043–7.
3. Rich-Edwards JW, Colditz GA, Stampfer MJ, et al. Birth weight and the risk for type 2 diabetes mellitus in adult women. Ann Intern Med 1999;130:278–84.
4. Lithell HO, McKeigue PM, Berglund L, Mohsen R, Lithell UB, Leo DA. Relation of size at birth to non-insulin dependent diabetes and insulin concentrations in men aged 50–60 years. BMJ 1996;312: 406–10.
5. Phipps K, Barker DJP, Hales CN, Fall CHD, Osmond C, Clark PMS. Foetal growth and impaired glucose tolerance in men and women. Diabetologia 1993;36:225–8.
6. Godfrey KM, Barker DJ. Foetal nutrition and adult disease. Am J Clin Nutr 2000;71(suppl):1344S–52S.
7. Mi J, Law C, Zhang KL, Osmond C, Stein C, Barker D. Effects of infant birth weight and maternal body mass index in pregnancy on components of the insulin resistance syndrome in China. Ann Intern Med 2000;132:253–60.
8. Ravelli ACJ, Van der Meulen JHP, Michels RPJ, et al. Glucose tolerance in adults after prenatal exposure to famine. Lancet 1998;351: 173–7.
9. Helgason A, Sigurdarottir S, Gulcher JR, Ward R, Stafansson K. mtDNA and the origin of the Icelanders: deciphering signals of recent population history. Am J Hum Genet 2000;66:999–1016.
10. Atladottir H, Thorsdottir I. Energy intake and growth of infants in Iceland—a population with high frequency of breast-feeding and high birth weight. Eur J Clin Nutr 2000;54:695–701.
11. Thorsdottir I, Birgisdottir BE. Different weight gain in women of normal weight before pregnancy: postpartum weight and birth weight. Obstet Gynecol 1998:92:377–83.
12. Meeuwisse G, Olausson PO. Increasing birth weight in the Nordic countries; a growing proportion of neonates weigh over four kg. Lakartidningen 1998;95:5488–92.
13. Olsen SF, Joensen HD. High liveborn birth weights in the Faroes: a comparison between birth weight in the Faroes and in Denmark. J Epidemiol Community Health 1985;39:27–32.
14. Vilbergsson S, Sigurdsson G, Sigvaldason H, Hreidarsson AB, Sigfusson N. Prevalence and incidence of NIDDM in Iceland: evidence for stable incidence among males and females 1967–1991—the Reykjavík Study. Diabet Med 1997;14:491–8.
15. Thorgeirsdottir H. Per capita supply of food in Iceland 1956–1995 and changes in the prevalence of overweight and obesity in men and women aged 45–64 in Reykjavík 1975–1994. MSc thesis. University of Iceland, Reykjavík, 1999.
16. Sigurdsson E, Thorgeirsson G, Sigvaldason H, Sigfusson N. Prevalence of coronary heart disease in Icelandic men 1968–1986. The Reykjavík Study. Eur Heart J 1993;14:584–91.
17. Robinson S, Walton RJ, Clark PM, Barker DJP, Hales CN, Osmond C. The relation of foetal growth to plasma glucose in young men. Diabetologia 1992;35:444–6.
18. Fall CHD, Stein CE, Kumaran K, et al. Size at birth, maternal weight and type 2 diabetes in South India. Diabet Med 1998;15: 220–7.
19. Hreidarsson AB, Geirsson RT, Helgason T. Diabetes mellitus in Iceland: prevalence, organization of services, pregnancy outcome and long-term complications. Diabetes Nutr Metab 1993;6: 333–4.
20. Olsen SF, Grandjean P, Weihe P, Videro T. Frequency of seafood intake in pregnancy as a determinant of birth weight: evidence for a dose dependent relationship. J Epidemiol Community Health 1993; 47:436–40.
21. Steingrimsdottir L. Nutrition in Iceland. Scand J Nutr 1993;37:10–2.
22. Petridou E, Stoikidou M, Diamantopoulou M, Mera E, Dessypris N, Trichopoulos D. Diet during pregnancy in relation to birth weight in healthy singletons. Child Care Health Dev 1998;24: 229–42.
23. Olsen SF. Further on the association between retarded foetal growth and adult cardiovascular disease. Could low intake of marine diets be a common cause? J Clin Epidemiol 1994;47:565–9.
24. Statistical Bureau of Iceland. Hagskinna. Sögulegar hagtölur um Ísland. (Icelandic historical statistics.) Reykjavík, Iceland: Statistical Bureau of Iceland, 1997 (in Icelandic).
25. McCarthy M. Weighing in on diabetes risk. Nat Genet 1998;19: 209–10.
26. Hattersley AT, Beards F, Ballantyne E, Appleton M, Harvey R, Ellard S. Mutations in the glucokinase gene of the fetus result in reduced birth weight. Nat Genet 1998;19:268–70.
27. Leger J, Limoni C, Collin D, Czernichow P. Prediction factors in the determination of final height in subjects born small for gestational age. Pediatr Res 1998;43:808–12.
28. Sorensen HT, Sabroe S, Rothman KJ, et al. Birth weight and length as predictors for adult height. Am J Epidemiol 1999;149: 726–9.
29. Henriksen T, Lande B, Clausen T, Gronn M, Salvesen K. Intrauterine nutrition. Tidsskr Nor Lægeforen 1998;118:3162–5.
30. Langley-Evans SC. Fetal origins of adult disease. Br J Nutr 1999; 81:5–6.
31. Lucas A, Fewtrell MS, Cole TJ. Foetal origins of adult disease—the hypothesis revisited. BMJ 1999;319:245–9.
32. Ong KKL, Ahmed ML, Emmett PM, Preece MA, Dunger DB. Association between postnatal catch-up growth and obesity in childhood: prospective cohort study. BMJ 2000;320:967–71.
33. Yajnik C. Interactions of perturbations in intrauterine growth and growth during childhood on the risk of adult-onset disease. Proc Nutr Soc 2000;59:257–65.

The American Journal of Clinical Nutrition

Downloaded from ajcn.nutrition.org by guest on December 18, 2016