Original Contribution

Adult Blood Pressure and Climate Conditions in Infancy: A Test of the Hypothesis that Dehydration in Infancy Is Associated with Higher Adult Blood Pressure

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The authors hypothesized that individuals born in the early 20th century who experienced the hottest and driest summers during infancy would be more likely to have suffered severe infant diarrhea and dehydration, and consequently have had higher blood pressure in adulthood, than those who experienced cooler and wetter summers. In this context, these climate data act as an instrumental variable for the association of early-life dehydration with later blood pressure. For 3,964 randomly selected British women born between 1919 and 1940 and whose blood pressure was measured at age 60–79 years, a one standard deviation (1.3°C) higher mean summer temperature in the first year of life was associated with a 1.12-mmHg (95% confidence interval: 0.33, 1.91) higher adult systolic blood pressure, and a one standard deviation higher mean summer rainfall (33.9 mm) was associated with lower systolic blood pressure (−1.65 mmHg, 95% confidence interval: −2.44, −0.85). Equivalent results for diastolic blood pressure were 0.11 (95% confidence interval: −0.65, 0.86) and −0.32 (95% confidence interval: −0.71, 0.05). The climate variables were not associated with potential confounding factors such as socioeconomic position or lifestyle risk factors. These findings provide some evidence in favor of the hypothesis that dehydration in infancy is associated with higher adult blood pressure.

blood pressure; climate; dehydration; growth and development; infant

Abbreviations: CI, confidence interval; SD, standard deviation.

Animal studies suggest that severe dehydration in infancy results in greater sodium retention and a taste for salty foods throughout life (1). This developmental plasticity (2, 3) (i.e., the ability of environmental effects during sensitive early life periods to affect the mature phenotype) can be explained by natural selection over generations produced by the survival advantage associated with the ability to retain sodium and hence water in the face of severe dehydration (1). However, as with other examples of developmental plasticity in humans (2, 3), the ability to program the retention of sodium in response to an environmental forecast of dehydration may be associated with adverse health outcomes in contemporary populations, in this case by leading to sodium retention that persists into later life and leads to raised blood pressure (4).

The ALSPAC study found that hospital admission for dehydration in the first 6 months of life was associated with higher blood pressure at age 7 years (5). We know of no equivalent data for adults, and it is likely that experiencing severe diarrhea would be related to socioeconomic and other potential confounding factors that could generate a noncausal association with later blood pressure. We therefore decided to examine the association of an instrumental variable for diarrheal illness and dehydration in infancy with blood pressure in adulthood in a cohort study of British women.

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Rates of infant mortality and morbidity from diarrheal illnesses increased considerably during the summer months in the early decades of the 20th century in Britain (6–12). This summer diarrhea and its associated infant mortality occurred in epidemic proportions during the hottest and driest (compared with cooler and wetter) summers (6–12). Routine statistics from 30 towns (covering all of the regions included in the present study) in Britain demonstrate that 60–84 percent of infant mortality (deaths of infants less than 1 year of age) from diarrhea in the last decades of the 19th century and first decades of the 20th century occurred in the months July–September (6, 9). In an address to the Royal College of Physicians in 1902, Arthur Newsholme concluded that, "I would go so far as to say that, given two towns equally placed so far as social and sanitary conditions are concerned, their relative diarrhoeal mortality is proportional to the height of the temperature and the deficiency of rainfall of each town, particularly the temperature and rainfall of the third quarter (summer) of the year" (7. p. 170).

Thus, contemporary adults who experienced hot, dry summers during the first year of life are more likely than those who experienced cooler and wetter summers to have suffered infant diarrhea and dehydration. We obtained air temperature and rainfall data for geographic areas of Britain for the whole of the 20th century (13) and, in this study, tested the hypotheses that for women born in Britain between 1919 and 1940, 1) summer temperature in the first year of life is positively associated with adult blood pressure, and 2) summer rainfall in the first year of life is inversely associated with blood pressure.

In this paper, summer temperature and rainfall in the first year of life are used as instrumental variables (14) for being more likely to have experienced diarrhea and dehydration in infancy (bearing in mind that these study participants were born in the 1920s and 1930s when there were still large epidemics of severe diarrhea during hot, dry summers and that methods for preventing dehydration were less sophisticated than in contemporary times). Although this approach has the disadvantage of using an ecologic exposure, and hence we do not know exactly which women were exposed to diarrhea and dehydration, it has the advantage of being an exposure measurement unlikely to be confounded by the usual environmental factors that might explain any association with more direct measurements of infant diarrhea. For example, the use of hospital records of diarrhea or questions to parents will be confounded by socioeconomic and other factors associated with some parents seeking medical help or reporting certain illnesses. By contrast, it is difficult to imagine how socioeconomic position or other potential confounding factors could be associated with climate conditions in the first year of life. Thus, our climate data provide a suitable instrumental variable for the unconfounded association of dehydration during infancy with adult blood pressure (14).

MATERIALS AND METHODS

Study and participants

The British Women's Heart and Health Study included a sample of women aged 60–79 years randomly selected from general practitioner lists in 23 British towns. Full details of the study have been reported previously (15). A total of 4,286 women (60 percent of those invited) participated, and baseline data (self-completed questionnaire, research nurse interview, physical examination, and primary care medical record review) were collected between April 1999 and March 2001. Ethics committee approval was obtained to undertake the study.

Assessment of exposures, outcome, and covariates

Date of birth for each participant was initially obtained from her general practice medical records and was confirmed during the research nurse interview. Each participant was asked her town or city, county, and country of birth. For these analyses, we assumed that each woman remained in the same geographic location from birth to her third year of life. Monthly mean outdoor air temperature and rainfall data for each month, year, and place of residence for each participant during her first, second, and third years of life were obtained from the Climatic Research Unit at the University of East Anglia (16). Full details of these data and how we linked them to the British Women's Heart and Health Study data set have been reported previously (17).

For mean outdoor temperature and rainfall during summer months of participants' first year of life, we used July–September since summer epidemics of infant mortality due to diarrhea occurred during these months (6–9). The mean summer temperature during the first year of life for women born on or before August 31 of any year was calculated as the mean of the ambient temperatures (from the model described above) for the 3 months July–September in the place and year in which they were born. For women born after August 31, mean summer temperature was calculated similarly but was for July-September of the year after their birth year. To determine whether any association was specific to the first year of life, we also examined the associations between mean summer temperature and rainfall in the second and third years of life, with these being calculated in a way similar to that described above but by using the corresponding later years of temperature and rainfall data.

A Dinamap 1846SX vital sign monitor (GE Healthcare, Chalfont St. Giles, United Kingdom) was used to measure blood pressure. We corrected for the systematic overestimate of systolic blood pressure with this instrument (18). Right-arm measurements were taken twice in succession, with a 1-minute interval in between. The participant was seated, and the arm was supported on a cushion at chest level. Arm circumference was measured, and the appropriate cuff size was used. The mean of the two measurements was used for all analyses. Standing and seated height were measured, without shoes, using a Harpenden stadiometer (Holtain, Crymych, United Kingdom), recording to the nearest millimeter. Trunk length was calculated as the seated height minus the height of the stool on which the participant was seated (407 mm). Leg length was taken as the standing height minus the trunk length. Weight was measured in light clothing without shoes to the nearest 0.1 kg with Soehnle portable scales (Soehnle, Murrhardt, Germany).

In the questionnaire, participants were asked to report their father's occupation when they were children, their own occupation, and, where appropriate, the occupation of their spouse. These items were used to derive childhood and adulthood occupational social class. Participants were also asked whether the house they lived in as a child had a bathroom, whether it had a hot water supply, and whether the family had access to a car. They were asked how many siblings they had and their position in the family. This information enabled us to determine how many siblings they had at the time of their birth and, by extraction, during the first year of their lives.

Statistical analyses

Linear regression was used to assess the associations between our exposures and blood pressure. Logistic regression was used to evaluate the association with high blood pressure, defined as systolic blood pressure of ≥140 mmHg, diastolic blood pressure of ≥90 mmHg, or use of antihypertensive medication. In multivariable regression models, we adjusted for age, year of birth, childhood social class (I, II, III nonmanual, III manual, IV, or V), presence of a bathroom and hot water in the childhood home, family access to a car, number of siblings at birth, and season of birth (spring, summer, autumn, or winter). There was evidence of collinearity between having no bathroom in the childhood home and no hot water in the childhood home (85 percent of those women who reported not having a bathroom also reported not having hot water). Therefore, we present results from two multivariable models, one including no bathroom and all other variables and the other including no hot water and all other variables.

Evidence of statistical interactions was assessed by using F tests. We decided a priori to test for interactions between socioeconomic factors (father's occupational social class (manual vs. nonmanual), childhood home with a bathroom, childhood home with hot water, and number of siblings (two or fewer vs. more than two)) since it is plausible that the association would be greater for those from lower socioeconomic groups who may be less able to protect themselves from epidemics of diarrhea. We also decided a priori to test for an interaction between season of birth (spring or summer vs. autumn or winter) since infant mortality from diarrheal illnesses at the beginning of the 20th century was greater among those aged 6–12 months than among those younger than age 6 months, possibly because of a protective effect of breastfeeding (12, 19). Children born in autumn or winter would have been age 6 months or older in the summer of their first year of life, whereas those born in spring or summer would have been younger.

To take account of any possible effect of blood pressure treatment on the results, we conducted two sensitivity analyses. In one, the analyses were restricted to data for those women not taking blood pressure medication (75 percent of the whole sample); in the second, 5 mmHg was added to the on-treatment blood pressure measurement for those women (25 percent of the sample) using antihypertensives at the time of blood pressure assessment.

In all analyses, robust confidence intervals were estimated, which take into account the clustering between participants from the same towns. All analyses were conducted by using Stata version 8.0 software (Stata Corporation, College Station, Texas).

RESULTS

We were able to match 4,091 (95 percent) of the 4,286 respondents to the climate data. Of the remaining 5 percent ($n = 195$), 148 were born outside of Britain (while we did have climate data for other countries, the recorded place of birth given was too general (e.g., Africa, France) to make a reliable match for these respondents), and 47 did not provide details of their place of birth. Mean systolic and diastolic blood pressures did not differ between those for whom temperature data were versus were not available (systolic blood pressure: 147.2 (standard deviation (SD), 25.1) mmHg vs. 146.6 (SD, 25.9) mmHg, $p = 0.6$; diastolic blood pressure: 79.4 (SD, 11.8) mmHg vs. 80.2 (SD, 11.6) mmHg, $p = 0.4$). Of the 4,091 women for whom temperature data were available, 3,964 (97 percent) had two adequate measures of systolic and diastolic blood pressures, and all remaining analyses were based on these 3,964 women.

Mean summer temperature in the first year of life varied from 10.8°C to 18.1°C, with a mean of 14.7 (SD, 1.3) °C. Mean summer rainfall in the first year of life ranged from 22.7 mm to 198.7 mm, with a mean of 83.2 (SD, 33.9) mm. Mean summer temperature and mean summer rainfall were correlated: Pearson's correlation coefficient was −0.57 (95 percent confidence interval (CI): −0.60, −0.54). Table 1 shows the association of potential covariates with summer rainfall and temperature in the first year of life. As anticipated, indicators of socioeconomic position, trunk length, body mass index, and smoking were not associated with either summer temperature or summer rainfall in the first year of life. For those who experienced the hottest summers and driest summers in the first year of their lives, total height and leg length were shorter than for those experiencing the cooler and wetter summers. Year of birth was associated with systolic and diastolic blood pressures: with each more recent year of birth from 1919 to 1940, mean systolic and diastolic blood pressures decreased −1.27 (95 percent CI: −1.40, −1.12) mmHg and −0.31 (95 percent CI: −0.38, −0.25) mmHg, respectively. However, we found no association between year of birth and mean summer temperature or mean summer rainfall (for both, $p > 0.6$). Place of birth was not associated with systolic or diastolic blood pressure (for both, $p > 0.3$).

Table 2 shows the association of one standard deviation difference in mean summer temperature and mean summer rainfall during the first year of life with adult systolic and diastolic blood pressures. Mean summer temperature in the first year of life was positively associated with systolic blood pressure, and mean summer rainfall in the first year of life was inversely associated with systolic blood pressure. These associations were somewhat attenuated with adjustment for leg length (model 1), but adjustment for other potential covariates had no effect (models 2 and 3). In the fully adjusted models, a one standard deviation higher mean summer temperature in the first year of life was associated with a 1.12-mmHg (95 percent CI: 0.33, 1.91) higher systolic

TABLE 1.   Association of indicators of socioeconomic position, components of adult height, body mass index, and smoking with mean summer temperature and mean summer rainfall in the first year of life for 3,964 British women born between 1919 and 1940

	Prevalence (%) or means per quarter of mean summer temperature (°C) in the first year of life				p value
	Quarter 1: range, 10.8–13.7	Quarter 2: range, 13.8–14.6	Quarter 3: range, 14.7–15.7	Quarter 4: range, 15.8–18.1	
Father: manual social class (%)	77.5 (75.2, 79.8)*	78.1 (75.3, 80.5)	78.1 (75.3, 80.6)	77.7 (75.4, 78.1)	0.7
House during childhood: no bathroom (%)	38.1 (35.0, 41.4)	39.5 (36.7, 42.5)	39.8 (36.9, 42.7)	38.7 (36.8, 40.7)	0.1
House during childhood: no hot water (%)	35.7 (33.2, 38.4)	35.6 (33.1, 38.3)	34.9 (32.5, 37.5)	36.3 (33.8, 39.0)	0.7
No family access to a car during childhood (%)	83.2 (77.4, 89.5)	83.2 (77.4, 89.5)	81.7 (76.0, 87.8)	83.5 (77.7, 89.8)	0.8
≥4 siblings (%)	28.8 (25.9, 32.0)	28.5 (25.7, 31.7)	28.6 (25.7, 31.8)	28.6 (25.7, 31.8)	0.8
Adult: manual social class (%)	50.2 (47.0, 53.3)	55.3 (52.2, 58.3)	52.0 (48.9, 55.0)	50.0 (46.6, 52.7)	0.4
Ever smoked (%)	44.1 (41.0, 47.5)	43.8 (40.7, 47.0)	45.0 (41.9, 48.4)	44.7 (41.6, 48.1)	0.4
Adult height (mm)	1,590.7 (1,587.7, 1,593.8)	1,590.3 (1,587.3, 1,593.3)	1,583.7 (1,580.7, 1,586.8)	1,581.1 (1,578.2, 1,584.0)	<0.001
Adult leg length (mm)	760.3 (758.6, 761.9)	759.5 (757.9, 761.2)	755.0 (753.4, 756.7)	754.2 (752.7, 757.9)	<0.001
Adult trunk length (mm)	830.7 (829.5, 832.0)	831.5 (830.0, 833.0)	830.4 (829.2, 831.6)	829.3 (828.1, 830.4)	0.1
Adult body mass index (kg/m²)	27.5 (28.2, 26.8)	27.8 (27.7, 27.9)	27.4 (27.1, 27.6)	27.6 (27.4, 29.0)	0.3
	Prevalence (%) or means per quarter of mean summer rainfall (mm) in the first year of life				
	Quarter 1: range, 22.7–58.2	Quarter 2: range, 58.3–79.2	Quarter 3: range, 79.3–103.7	Quarter 4: range, 103.8–198.7	
Father: manual social class (%)	76.6 (73.7, 79.2)	76.4 (73.5, 79.0)	76.6 (73.6, 79.7)	77.6 (74.9, 79.8)	0.8
House during childhood: no bathroom (%)	41.2 (38.3, 44.1)	39.8 (36.8, 42.8)	36.3 (33.5, 39.2)	39.6 (36.6, 42.5)	0.7
House during childhood: no hot water (%)	35.1 (32.7, 37.7)	34.9 (32.5, 37.5)	34.4 (31.5, 37.4)	34.7 (31.8, 37.7)	0.4
No family access to a car during childhood (%)	82.2 (80.1, 84.7)	82.3 (80.1, 84.8)	82.3 (80.1, 84.8)	83.1 (80.6, 85.7)	0.8
≥4 siblings (%)	28.4 (25.6, 31.6)	28.7 (25.8, 31.9)	28.6 (25.7, 31.8)	28.9 (26.0, 32.1)	0.9
Adult: manual social class (%)	51.0 (47.9, 54.0)	50.4 (47.0, 53.2)	53.5 (50.3, 56.6)	51.2 (48.0, 54.3)	0.5
Ever smoked (%)	44.5 (41.0, 47.8)	44.0 (40.9, 47.3)	44.6 (41.5, 48.0)	45.2 (42.0, 48.6)	0.8
Adult height (mm)	1,579.6 (1,576.5, 1,582.6)	1,585.9 (1,583.0, 1,589.0)	1,587.4 (1,584.3, 1,590.4)	1,592.4 (1,587.7, 1,595.2)	<0.001
Adult leg length (mm)	753.6 (751.9, 755.2)	755.7 (754.0, 757.4)	758.2 (756.5, 759.8)	761.2 (759.6, 762.8)	<0.001
Adult trunk length (mm)	831.7 (829.5, 833.8)	829.1 (827.9, 830.3)	832.5 (831.3, 833.7)	829.7 (826.5, 830.9)	0.2
Adult body mass index (kg/m²)	27.6 (27.4, 27.8)	27.5 (27.3, 27.7)	27.7 (27.5, 27.9)	27.5 (27.3, 27.7)	0.9

* Values in parentheses, 95% confidence interval.

blood pressure, and a one standard deviation higher mean summer rainfall in the first year of life was associated with lower systolic blood pressure (−1.65 mmHg, 95 percent CI: −2.44, −0.85). Mean summer rainfall was weakly inversely associated with diastolic blood pressure. This association attenuated toward the null with adjustment for leg length; mean summer temperature during the first year of life was not associated with diastolic blood pressure. We found a positive association between mean summer temperature in the first year of life and high blood pressure (systolic blood pressure of ≥140 mmHg, diastolic blood pressure of ≥90 mmHg, or use of antihypertensive medication), which was robust to adjustment for potential covariates.

When both summer temperature and rainfall were included in the same regression model, there was evidence of collinearity, with the standard error for both regression co-

efficients increasing markedly. To assess the combined association of summer temperature and rainfall with blood pressure in adulthood, data for those subjects who experienced the hottest and driest summers in their infancy (i.e., those who were in both the top quarter of the distribution of mean summer temperature in the first year of life and the bottom quarter of the distribution of mean summer rainfall in the first year of life) were compared with those for all other subjects. In age-adjusted models, mean systolic blood pressure among these 532 (13 percent) women was 2.39 mmHg (95 percent CI: 0.09, 4.69) higher than among other subjects, whereas mean diastolic blood pressure was not markedly higher in this group (0.57 mmHg, 95 percent CI: −0.49, 1.65). With adjustment for leg length, the association with systolic blood pressure attenuated somewhat (2.17 mmHg, 95 percent CI: –0.13, 4.47).

TABLE 2. Association of mean summer temperature and mean summer rainfall in the first year of life with systolic and diastolic blood pressures measured at age 60–79 years for 3,964 British women born between 1919 and 1940

	Mean difference in blood pressure or odds ratio of high blood pressure per 1 SD* of mean summer temperature† and mean summer rainfall‡ in the first year of life			
	Age adjusted	Model 1§	Model 2¶	Model 3#
Mean difference in systolic blood pressure (mmHg)				
Per SD mean summer temperature	1.25 (0.46, 2.04)**	1.11 (0.32, 1.90)	1.12 (0.32, 1.91)	1.12 (0.33, 1.91)
Per SD mean summer rainfall	−1.72 (−2.52, −0.92)	−1.63 (−2.43, −0.83)	−1.63 (−2.43, −0.83)	−1.65 (−2.44, −0.85)
Mean difference in diastolic blood pressure (mmHg)				
Per SD mean summer temperature	0.19 (−0.56, 0.94)	0.11 (−0.64, 0.86)	0.11 (−0.64, 0.86)	0.11 (−0.65, 0.86)
Per SD mean summer rainfall	−0.39 (−0.76, −0.01)	−0.33 (−0.70, 0.05)	−0.32 (−0.71, 0.06)	−0.32 (−0.71, 0.05)
Odds ratio of high blood pressure††				
Per SD mean summer temperature	1.10 (1.02, 1.18)	1.06 (0.99, 1.14)	1.06 (0.99, 1.14)	1.06 (0.99, 1.14)
Per SD mean summer rainfall	0.85 (0.79, 0.91)	0.91 (0.85, 0.97)	0.91 (0.85, 0.97)	0.91 (0.85, 0.97)

* SD, standard deviation.
† 1 SD = 1.3°C.
‡ 1 SD = 33.9 mm.
§ Adjusted for age and leg length.
¶ The same as model 1, but also adjusted for year of birth, father's occupational social class, childhood house with no bathroom, no family access to a car during childhood, number of siblings, adult occupational social class, smoking, and body mass index.
# The same as model 2, but adjusted for childhood house with no hot water instead of no bathroom.
** Values in parentheses, 95% confidence interval.
†† Systolic blood pressure of ≥140 mmHg, diastolic blood pressure of ≥90 mmHg, or use of antihypertensive medication.

The associations of climate with blood pressure were similar in different socioeconomic groups (for all statistical interactions, $p > 0.4$). Associations did not differ statistically between those born in autumn and winter months (October–March) versus summer and spring months (April–September) (table 3). We found no association between mean summer temperature or rainfall in the second or third year of life and adult systolic blood pressure (data not shown).

With adjustment for other covariates, living in a house with no bathroom during childhood was associated with higher systolic blood pressure (2.09 mmHg, 95 percent CI: 0.41, 3.76), as was living in a house with no hot water as a child (1.43 mmHg, 95 percent CI: −0.28, 3.15) and having four or more siblings (2.83 mmHg, 95 percent CI: 1.18,

4.48). With adjustment for other covariates, a one standard deviation greater leg length was associated with lower systolic blood pressure (−1.09 mmHg, 95 percent CI: −1.91, −0.27). Other childhood characteristics were not associated with systolic blood pressure, and none of the childhood characteristics were associated with diastolic blood pressure.

The results of both sensitivity analyses used to deal with a possible influence of blood pressure treatment on these outcomes did not alter the association substantively. Results tended to increase slightly. For example, when analyses were restricted to women who were not using blood pressure medications, the adjusted (equivalent to model 3) change in mean systolic blood pressure for a one standard deviation higher mean summer temperature in the first year of life was

TABLE 3. Association of mean summer temperature and mean summer rainfall in the first year of life with systolic blood pressure, stratified by season of birth, for 3,964 British women born between 1919 and 1940

	Age-adjusted mean difference in systolic blood pressure (mmHg) per 1 SD* of mean summer temperature in first year of life	Age-adjusted mean difference in systolic blood pressure (mmHg) per 1 SD of mean summer rainfall in first year of life
Spring or summer months (April–September)	1.07 (−0.06, 2.21)†	−1.60 (−2.76, −0.45)
Autumn or winter months (October–March)	1.42 (0.32, 2.53)	−1.83 (−2.95, −0.73)
p value‡	0.67	0.77

* SD, standard deviation.
† Values in parentheses, 95% confidence interval.
‡ Test for interaction or difference in the association between the two strata (spring or summer months vs. autumn or winter months).

1.19 mmHg (95 percent CI: 0.34, 2.05), and the adjusted change in systolic blood pressure for a one standard deviation higher mean summer rainfall in the first year of life was −1.79 mmHg (95 percent CI: −2.47, −1.11).

DISCUSSION

Consistent with our hypothesis, we found mean summer temperature in the first year of life to be positively associated with systolic blood pressure in adulthood and mean summer rainfall in the first year of life to be inversely associated with blood pressure. The basis for our hypothesis is that individuals experiencing the hottest and driest summers are more likely to have suffered dehydration, caused by diarrhea, during infancy than those experiencing cooler and wetter summers and that dehydration during infancy programs salt retention and hence higher future blood pressure. We further hypothesized that the association of summer temperature and rainfall with adult blood pressure might be greater for those born in the autumn and winter, since these infants would be older than age 6 months at the time of their first summer and perhaps more prone to diarrhea because of being weaned by that age. However, the associations were similar among those born in autumn or winter and those born in spring or summer. It is possible that our study was too small to detect a difference in the association by season of birth. We found no association between summer temperature in the first year of life and diastolic blood pressure.

Other childhood characteristics that would be associated with a greater likelihood of experiencing diarrheal illnesses (childhood home with no bathroom, childhood home with no hot water, and having four or more siblings) were also associated with higher systolic blood pressure in adulthood, although not with diastolic blood pressure. Women who experienced the hottest and driest summers were shorter, and specifically had shorter legs, in adulthood. Leg length in particular (as opposed to trunk length) may be a useful biomarker of prepubertal environmental influences on childhood linear growth; a much greater proportion of the increase in total height before puberty is due to increases in leg length (20, 21). Furthermore, the dramatic increases in height in industrialized countries over the last century appear to arise more from increases in leg length than in trunk growth (22). These trends have occurred as a result of improvements in childhood circumstances—in particular, better nutrition and reductions in serious infections.

Since severe childhood diarrhea and dehydration epidemics during the summer were associated with high rates of infant mortality at the beginning of the last century, our study results clearly pertain to those women who survived these epidemics. However, this fact is central to our hypothesis, which assumes that these women survived the epidemics because of a programmed ability to retain sodium and hence not die of dehydration. The specific association between hot and dry summers in the first year of life and leg length, but no association between these climate data and trunk length, socioeconomic position, or adult smoking, provides evidence that this is a good instrument for assessing the unconfounded association of factors that affect linear growth

in infancy and adult systolic blood pressure. Severe diarrheal illness in infancy would likely have a detrimental effect on linear growth, and our findings support our hypothesis that diarrhea and hence dehydration in infancy is associated with later blood pressure. It is unclear why this association was seen for systolic blood pressure only. Other early life exposures, for example, birth size, tend to be more robustly associated with systolic than with diastolic blood pressure (23). It may be that the physiologic processes that control systolic blood pressure are more plastic, and therefore more strongly influenced by exposures during early life development, than those that control diastolic blood pressure. Alternatively, adult exposures may have stronger influences on diastolic blood pressure, so that very little variation in adult diastolic blood pressure is explained by early life exposures. This study was of women only, and although we cannot think of a biologically plausible reason to assume that any association of infant dehydration with later blood pressure should differ between women and men, our results may not be generalizable to men.

There are clear evolutionary reasons for thinking that salt retention protects against sudden fluid loss of the kind that may occur during acute infant diarrhea that may otherwise prove fatal (1). An evolved adaptive mechanism such that experiencing dehydration leads to future salt retention could have important survival advantages (1). Our data are both intriguing and inconclusive, and they invite further studies of humans. Examining the direct association between dehydration in infancy and adult blood pressure in prospective studies conducted in places with higher rates of dehydration (e.g., sub-Saharan Africa), or long-term follow-up of randomized trials of improved hygiene practices that reduce diarrhea among infants, could provide evidence to support our hypothesis. In the past, it has been assumed that blood pressure in developing world countries—in which there are high rates of infant diarrhea and mortality from it—is low, which would tend to argue against our hypothesis. However, well-conducted surveys such as that undertaken by the World Health Organization demonstrate high rates of hypertension in developing countries (24). If established, our hypothesis would have important public health implications for the reduction of systolic blood pressure and its consequent cardiovascular disease outcomes, highlighting the importance of avoiding dehydration in infancy not just for short-term health improvement but also for benefits to long-term cardiovascular health.

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