

Newcastle University e-prints

Date deposited: 7th April 2010

Version of file: Author final

Peer Review Status: Peer Reviewed

Citation for published item:

Pearce MS, Relton CL, Unwin NC, Adamson AJ, Smith GD. [The relation between diarrhoeal episodes in infancy and both blood pressure and sodium intake in later life: The Newcastle Thousand Families Study](#). *Journal of Human Hypertension* 2008,**22** 8 582-584.

Further information on publisher website:

<http://www.nature.com/>

Publishers copyright statement:

This article was originally published by Nature Publishing, 2009 and is available (with permissions) from the site below:

<http://www.nature.com/jhh/journal/v22/n8/pdf/jhh200845a.pdf>

Always use the definitive version when citing.

Use Policy:

The full-text may be used and/or reproduced and given to third parties in any format or medium, without prior permission or charge, for personal research or study, educational, or not for profit purposes provided that:

- A full bibliographic reference is made to the original source
- A link is made to the metadata record in Newcastle E-prints
- The full text is not changed in any way.

The full-text must not be sold in any format or medium without the formal permission of the copyright holders.

<p>Robinson Library, University of Newcastle upon Tyne, Newcastle upon Tyne. NE1 7RU. Tel. 0191 222 6000</p>

The relation between diarrhoeal episodes in infancy and both blood pressure and sodium intake in later life: The Newcastle Thousand Families Study

Mark S. Pearce¹, Caroline L. Relton¹, Nigel C. Unwin¹, Ashley J. Adamson¹, George Davey Smith²

¹Institute of Health and Society and School of Clinical Medical Sciences, Newcastle University, Newcastle upon Tyne, UK

²Department of Social Medicine, University of Bristol, Bristol, UK

Corresponding author:

Dr Mark Pearce, Sir James Spence Institute, Newcastle University, Royal Victoria Infirmary, Newcastle upon Tyne, NE1 4LP, UK.

Tel: +44 191 2023082

Fax: +44 191 2023060

Email: m.s.pearce@ncl.ac.uk

Keywords: Blood pressure, dehydration, growth, infant, sodium

Running title: Diarrhoeal episodes in infancy and both blood pressure in later life

It has been suggested that episodes of diarrhoea in infancy are associated with increased blood pressure in later life. Using data on 408 individuals from the Newcastle Thousand Families Study we found no robust differences in systolic or diastolic blood pressure or carotid artery intima-media thickness at age 50 between those with and without recorded episodes of diarrhoea in infancy. However, mean daily dietary sodium intake was higher in those with an episode of diarrhoea in infancy

Two recent studies have suggested that dehydration in infancy, through acute infant diarrhoea, could lead to high blood pressure in later life [1,2]. Severe dehydration in infancy may result in both greater sodium retention and a greater taste for salty foods throughout life [3]. The central hypothesis tested in these studies was that developmental plasticity occurs [4], in this case that dehydrated infants adapt to retain sodium, and hence water, which would be protective in case of future severe dehydration [3].

High sodium intake during pregnancy has been associated with elevated blood pressure in adult offspring [5]. Evidence is emerging that these changes may be mediated by epigenetic modification of genes in the renin-angiotensin system and resultant alteration of gene expression leading ultimately to the development of hypertension [6].

Of the two recent human studies, one was in seven year-old children with dehydration in the first six months of life severe enough to require hospital admission as the exposure [1]. The second study used climatic conditions in the first years of life as an indicator of

the risk of severe dehydration [2]. Neither was able to also consider whether increased salt intake in later life may be influenced by dehydration in early life and could lie on the causal pathway between early life dehydration and future risk of hypertension and stroke.

Episodes of illness such as diarrhoea may lead to faltering of growth [7]. Thus associations of growth trajectories and adult stature with blood pressure may reflect early-life experiences.

We investigated the potential association of recorded diarrhoeal illness in infancy with salt intake, childhood growth and blood pressure, anthropometric measures in adulthood and carotid artery intima-media thickness (CAIMT) using data from the Newcastle Thousand Families cohort study.

The Thousand Families study began in 1947 when all 1142 children born in May and June that year to mothers resident within the city of Newcastle upon Tyne were recruited. Episodes of diarrhoea in infancy were recorded prospectively by health visitors, who visited the families regularly, or by the participants' general practitioner. Childhood heights and weights at 9 and 13 years, also recorded prospectively by health visitors, were expressed as standard deviation scores relative to growth standards to adjust for sex and age at measurement.

Between October 1996 and December 1998, questionnaires on health and lifestyle were completed and study members attended for clinical examination. Height, weight and blood pressure were measured using standard guidelines [8]. CAIMT was measured bilaterally by ultrasonography at three locations in the common and internal carotid

arteries [9]. Cross-sectional data on total daily sodium intake, excluding that from salt added during preparation or eating, was estimated from responses to the EPIC food frequency questionnaire [10]. Additional questions on the frequency (always, usually, sometimes, rarely, never) of addition of salt during preparation and at the table and the use of medications were also asked.

Differences in outcomes between those with and without a recorded episode of diarrhoea in infancy were assessed using t-tests. Adjusted differences were assessed using multivariable linear regression. Frequency of addition of salt was categorised as 'always' or 'usually' versus the other categories and analysed in relation to diarrhoea in infancy using Pearson chi-squared tests.

Of the original study members, 574 completed the questionnaire and 412 attended for clinical examination [11]. Complete data in infancy and on clinical measurements were available for 408, of whom 27 (19 female) had at least one episode of diarrhoea recorded in infancy. Dietary sodium intake at age 50 was available for 398, including all of those with an episode of diarrhoea recorded in infancy.

No significant differences in BMI, systolic or diastolic blood pressure or CAIMT at age 50 were seen between those with and without recorded episodes of diarrhoea in infancy (table 1). Those with at least one episode tended to be slightly shorter at age 50. Standardised heights and weights at ages 9 and 13 years were similar for those with and without a recorded diarrhoeal disease episode.

Those with at least one episode of diarrhoea in infancy had a higher daily intake of sodium from food (excluding discretionary salt) than those without. Sodium intake was

higher in males. Adjusting for sex, mean daily sodium intake remained higher, equivalent to approximately 1g of salt, in those with an episode of diarrhoea in infancy. Diarrhoea in infancy and the frequency of adding salt to food, either while cooking or while eating, were unrelated ($p=0.33$ and 0.54 respectively).

While our results provide limited support for the hypothesis that dehydration in infancy influences sodium intake in later life, they do not support the suggestion that dehydration may in turn influence blood pressure in middle age.

Sodium consumption usually exceeds physiological need, and has increased in developed countries, primarily due to the increased consumption of processed foods which have been reported to account for 75% of salt consumed [12]. The World Health Organisation recommend that salt intake be limited to less than 5g per day. Mean self-reported daily sodium consumption in this study was 2821mg (equivalent to approximately 7g of salt) plus an unspecified amount from salt added during food preparation and at the table.

Our findings for dietary sodium intake from foods are consistent with the hypothesis that dehydration in very early life results in an increased appetite for salt throughout life [3]. Our measure of dietary sodium intake is likely an underestimate of total daily intake as it does not include discretionary salt added during food preparation or at the table. However, frequency of use of salt during food preparation or at the table was similar between those with and without an episode of diarrhoea recorded in infancy.

There are a number of limitations that should be taken into consideration when interpreting these results. The first is that the relatively small sample available to us may

have led to the analyses being underpowered. We have no measure of the severity of dehydration that diarrhoea in infancy may have caused and the cases considered in this study may not have been severe enough to cause sufficient dehydration to influence childhood growth and later blood pressure. It is also possible that children without diarrhoeal illness may have had other illness related to severe dehydration, such as severe vomiting.

It is possible that individuals with high blood pressure may have reduced their salt intake for health reasons. Given the cross-sectional nature of the dietary assessment in this study, it was not possible to assess this. Of the 37 study members who reported using medication to lower their blood pressure, none had a recorded episode of diarrhoea in infancy. However, we have no data on whether an individual not on medication for blood pressure decreased their salt intake for health reasons.

In conclusion, despite the inconsistent findings of this and previous studies, the potential for an association between severe dehydration in infancy and later blood pressure requires further investigation. Future studies are also needed to ascertain how salt preferences may be influenced by events in very early life.

References

1. Davey Smith G, Leary S, Ness A, The ALSPAC study team. Could dehydration in infancy lead to high blood pressure? *J Epidemiol Community Health* 2006; 60: 142-143.
2. Lawlor DA, Davey Smith G, Mitchell R, Ebrahim S. Adult blood pressure and climate conditions in infancy: a test of the hypothesis that dehydration in infancy is associated with higher adult blood pressure. *Am J Epidemiol* 2006; 163: 608-614.
3. Fessler DM. An Evolutionary explanation of the plasticity of salt preferences: prophylaxis against sudden dehydration. *Med Hypotheses* 2003; 61: 412-415.
4. Leon DA. Biological theories, evidence and epidemiology. *Int J Epidemiol* 2004; 33: 1167-1171.
5. Vindonho AFJr, da Sliva AA, Catanozi S, Rocha JC, Beutel A, Carillo BA et al. Perinatal salt restriction: a new pathway to programming insulin resistance and dyslipidemia in adult wistar rats. *Pediatr Res* 2004; 56: 842-848.
6. Bogdarina I, Welham S, King PJ, Burns SP, Clark AJ. Epigenetic modification of the rennin-angiotensin system in the fetal programming of hypertension. *Circ Res* 2007; [Epub ahead of print]
7. Assis AM, Barreto ML, Santos LM, Fiaccone R, da Silva Gomes GS. Growth faltering in childhood related to diarrhoea: a longitudinal community based study. *Eur J Clin Nutr* 2005; 59: 1317-1323.

8. World Health Organisation. *Monitoring trends and determinants in cardiovascular disease project. MONICA manual, part III*. Geneva: World Health Organisation, 1990
9. Howard G, Sharrett AR, Heiss G, Evans GW, Chambles LE, Riley WA, et al. Carotid artery intimal-media thickness in general population as evaluated by B-mode ultrasound. *Stroke* 1993; 24: 1297-1304.
10. Bingham SA, Gill C, Welch A, Cassidy A, Runswick SA, Oakes S, et al. Validation of dietary assessment methods in the UK arm of EPIC using weighed records, and 24-hour urinary nitrogen and potassium and serum vitamin C and carotenoids as biomarkers. *Int J Epidemiol* 1997; 26:S137-S151.
11. Pearce MS, Unwin NC, Parker L, Alberti KGMM. Life course determinants of insulin secretion and sensitivity at age 50 years: the Newcastle thousand families study. *Diabetes Metab Res Rev* 2006; 22: 118-125.
12. Scientific Advisory Council on Nutrition. *Salt and Health*. Norwich: The Stationery Office, 2003.

Table 1. Outcome data according to whether an episode of diarrhoea was recorded in infancy.

Outcome	Diarrhoea recorded in infancy		Diarrhoea not recorded in infancy		P	Unadjusted difference (95% CI)	Sex-adjusted difference (95% CI)
	N	Mean (sd)	N	Mean (sd)			
Adulthood							
Systolic blood pressure (mm HG)	27	123.7 (14.1)	381	126.0 (17.0)	0.51	-2.2 (-8.83, 4.38)	-1.45 (-8.01, 5.10)
Diastolic blood pressure (mm HG)	27	76.7 (11.0)	381	78.7 (10.0)	0.31	-2.02 (-5.96, 1.92)	-1.13 (-4.91, 2.65)
Carotid intima-media thickness	25	0.78 (0.17)	333	0.77 (0.16)	0.75	0.01 (-0.05, 0.08)	0.02 (-0.05, 0.08)

(mm)

Height (cm)	28	164 (8.5)	381	167 (8.5)	0.11	-2.69 (-5.97, 0.59)	-1.21 (-3.58, 1.17)
BMI	28	25.9 (3.9)	381	26.7 (4.6)	0.39	-0.78 (-2.55, 0.99)	0.72 (-2.50, 1.05)
Sodium intake (mg)	27	3243 (922)	371	2861 (1034)	0.06	380 (-21.9, 783)	412 (12.4, 813)

Childhood

Standardised height at age 9 years	26	-0.91 (1.15)	287	-0.76 (1.08)	0.50	-0.15 (-0.59, 0.29)	-0.16 (-0.60, 0.28)
Standardised weight at age 9 years	26	-0.46 (0.94)	287	-0.52 (0.93)	0.76	0.06 (-0.32, 0.44)	0.05 (-0.32, 0.43)
Standardised height at age 13 years	24	-1.03 (1.12)	265	-0.96 (1.06)	0.77	-0.07 (-0.51, 0.38)	-0.13 (-0.57, 0.31)
Standardised weight at age 13 years	24	-0.58 (1.15)	264	-0.68 (1.11)	0.67	0.10 (-0.37, 0.57)	0.06 (-0.05, 0.08)

What is known about topic

- Risk of adverse health in middle age has been suggested to be influenced by factors in early life, including during the fetal period
- Two recent studies have suggested that dehydration in infancy, for instance that consequent on acute infant diarrhoea, could lead to elevated blood pressure in later life.
- Animal studies suggest that severe dehydration in early life results in both greater sodium retention and a greater taste for salty foods throughout life

What this paper adds

- Mean daily dietary sodium intake was higher in those with an episode of diarrhoea in infancy.
- No meaningful differences in systolic or diastolic blood pressure or carotid artery intima-media thickness were seen between those with and without recorded episodes of diarrhoea in infancy.
- Our findings suggest that salt preferences may be influenced by events in very early life.