

Early Psychosocial Exposures, Hair Cortisol Levels, and Disease Risk

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abstract

BACKGROUND: Early psychosocial exposures are increasingly recognized as being crucial to health throughout life. A possible mechanism could be physiologic dysregulation due to stress. Cortisol in hair is a new biomarker assessing long-term hypothalamic-pituitary-adrenal axis activity. The objective was to investigate whether early-life adverse psychosocial circumstances influence infant cortisol levels in hair and health outcomes in children prospectively until age 10.

METHODS: A cohort study in the general community using a questionnaire covering 11 psychosocial items in the family during pregnancy and the cumulative incidence of diagnoses until age 10 years in 1876 children. Cortisol levels in hair were measured by using a radioimmunoassay in those with sufficient hair samples at age 1, yielding a subsample of $n = 209$.

RESULTS: Children with added psychosocial exposures had higher infant cortisol levels in hair ($B = 0.40$, $P < .0001$, adjusted for gender and size for gestational age) in a cumulative manner and were significantly more often affected by 12 of the 14 most common childhood diseases, with a general pattern of increasing odds ratios.

CONCLUSIONS: The findings support the model of physiologic dysregulation as a plausible mechanism by which the duration and number of early detrimental psychosocial exposures determine health outcomes. The model indicates that the multiplicity of adversities should be targeted in future interventions and could help to identify children who are at high risk of poor health. Furthermore, given the prolonged nature of exposure to a stressful social environment, the novel biomarker of cortisol in hair could be of major importance.

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Dr Karlén conceptualized and designed the study, managed the literature searches, undertook the statistical analysis and interpretation of data, and wrote the first draft of the manuscript; Dr Ludvigsson is founder and project leader of All Babies in Southeast Sweden (ABIS) and organized collection of material (biological samples and questionnaires), conceptualized and designed the study, undertook analysis and interpretation of data, and reviewed and revised the manuscript; Dr Hedmark participated in the concept and design, managed literature searches, undertook the statistical analysis and interpretation of data, and reviewed and revised the manuscript; Drs A. Faresjö and Theodorsson participated in the concept and design and analysis and interpretation of data, undertook and developed the method for hair cortisol analyses, and reviewed and revised the manuscript; Dr T. Faresjö conceptualized and designed the study, undertook the statistical analysis and interpretation of data, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2014-2561

DOI: 10.1542/peds.2014-2561

Accepted for publication Mar 3, 2015

WHAT'S KNOWN ON THIS SUBJECT: Early psychosocial exposures are increasingly recognized as crucial to health throughout life. A possible mechanism is physiologic dysregulation due to stress. Cortisol in hair is a new biomarker assessing long-term hypothalamic-pituitary-adrenal axis activity.

WHAT THIS STUDY ADDS: Added early psychosocial exposures seem to increase infant long-term hypothalamic-pituitary-adrenal axis activity and risk of common childhood diseases in a cumulative manner, supporting the model of physiologic dysregulation as a plausible mechanism through which early detrimental exposures determine health outcomes.

Early life is increasingly recognized as crucial to health throughout life.^{1,2} Psychosocial circumstances impact health as early as in childhood, being associated with, eg, obesity, mental problems, drug abuse, suicide, and chronic illness.^{3,4} They also act as a disadvantageous trajectory of adult health.^{5,6} Epidemiologic evidence that even conditions during fetal development affect health in adulthood is particularly compelling.^{7,8} Common childhood complaints, although not as thoroughly explored, suggest an association with, eg, otitis media, respiratory infections, and asthma.⁹⁻¹¹

The actual biological pathways linking psychosocial environmental exposures to health disparities are difficult to uncover, but 1 plausible mechanism is physiologic dysregulation due to stress.¹² This dysregulation, in turn, affects other physiologic functions, such as the immune system.¹³ Some evidence suggests that even prenatal stress could shape the development of the hypothalamic-pituitary-adrenal (HPA) axis, often measured through short-term output of the stress hormone cortisol in saliva,^{14,15} as well as increasing susceptibility to later psychopathology.¹⁶

Cortisol in hair is a new method that measures cortisol output over longer periods of time, because hair grows ~1 cm/month and is suggested to be an assessment of frequent or prolonged activation of the HPA axis.¹⁷ There is some evidence for an association between higher hair cortisol levels and psychosocial factors in adults,^{18,19} but there have been only a few studies on child hair cortisol, although the results point in the same direction with a correlation to, eg, parental education and residence type.^{20,21}

The aim of this study was to investigate whether adverse psychosocial circumstances in the family during early life alter

long-term HPA axis activity, assessed through cortisol concentrations in the hair, and to explore a possible relation with health outcomes in children followed prospectively until the age of 10 years.

METHODS

Participants

All Babies in Southeast Sweden (ABIS) is a prospective study of a birth cohort of every child born in southeastern Sweden between October 1, 1997, and October 1, 1999 ($N = 21\,700$), for which 17\,055 parents (78.6%) gave their informed consent. We selected a subsample of $N = 2447$ children, consisting of every participant living in the 2 cities of Linköping and Norrköping: these 2 cities are within the same county council responsible for practically all health care, operating under the same clinical practice guidelines, and with an extensive regional health care register. We excluded 571 children due to a lack of complete data on the independent variable, which left 1876 children ($n = 926$ girls and $n = 950$ boys). Cortisol in hair was analyzed in those with sufficient hair samples collected at age 1, yielding a subsample of $n = 209$ ($n = 103$ boys and $n = 106$ girls). This sample was stratified according to the distribution of the vulnerability score (see below) and gave an oversampled ≥ 3 category ($n = 90$). The Research Ethics Committee at the Faculty of Health Sciences, Linköping University, Sweden, approved the study.

Psychosocial Vulnerability: A Score of Risk Factors

The children's mothers answered a questionnaire shortly after birth that contained a broad range of psychosocial factors. We used the novel concept of "vulnerability" to analyze the complex interplay between these factors.²² This concept is a convergence of multiple health-affecting risk factors that uses a "deficit accumulation approach,"

which could help identify high-risk populations and uncover connections not evident when considering single risk factors. We included variables in the existing database associated with a detrimental impact on health as suggested in previous research. Some answers were dichotomized: for example, schooling was simplified into having an education above elementary school or not.

Eleven psychosocial items resulted in the final composite independent variable: the psychosocial vulnerability score. The items were as follows: father's highest level of education elementary school; mother's highest level of education elementary school; father unemployed or on sick leave the year before pregnancy; mother unemployed or on sick leave during pregnancy; living in an apartment, as opposed to own house; single mother; parents born abroad; maternal experienced serious life event during pregnancy ("Have you been exposed to something which you perceive as a serious life event during your pregnancy?"); maternal lack of support ("Do you feel your surroundings give you the support you and your newborn child need?"); mother not feeling safe ("Do you feel safe and in the circumstances needed to give you and your newborn child a good start?"); mother worried over the possibility of child falling ill with serious disease ("How do you usually feel when you consider the possibility that your child could fall ill with a chronic or serious disease in the future?"). For these, a stepwise 6-grade Likert-type scale was applied between not worried and very worried, with 4 to 6 being classified as worried.

Cortisol in Hair: Long-term HPA Axis Activity

Nurses at the well-baby clinics cut the children's hair from the posterior vertex area of the head at age 1 year, and the first 3 cm of outgrowth was analyzed for cortisol concentrations

by using a competitive radioimmunoassay in methanol extracts.¹⁸ Hair samples >3 mg were required to maintain a total interassay coefficient of variation <8%.

Health Outcome: Cumulative Incidence of Diagnoses

International Classification of Diseases diagnoses (ICD-10) were derived from the regional health care register containing data on all health care visits within the publicly financed health care provision, which represents practically all health care. There is no evidence of systematic misclassification in this health care register.²³ Diagnoses from birth to February 2008 were recorded on a case per case basis. Children were aged 8 to 10 years at follow-up, hence describing the cumulative incidence of diagnoses. This follow-up was almost 100% because dropouts due to death or moving out of the region were negligible. In some cases, we merged closely related diagnoses, eg, codes J00 through J06 were all registered in the category "J00–J06: acute upper respiratory infections."

Statistical Analyses

We used an independent-samples *t* test when testing the psychosocial vulnerability score against both hair cortisol and health outcome. The score was transformed into a categorical variable (participants with ≥ 3 psychosocial items were treated as 1 group due to the small number of cases, yielding 4 groups: 0 (reference), 1, 2, and ≥ 3) when testing against binary diagnoses. Regression analysis was used when adjusting for gender and small for gestational age (SGA; calculated according to the National Swedish Board of Health and Welfare criteria, 2 SDs from the mean depending on gestational age) against both cortisol levels and health outcome. The measured cortisol concentrations included 2 outliers defined with the Grubbs test, which were kept in the analyses. Before the statistical

analysis, all cortisol values were logarithm transformed due to positive skewness in the distribution.

RESULTS

Mothers' and fathers' mean ages (95% confidence intervals [CI]) at the birth of the child were 30.17 (29.97–30.96) and 32.24 (31.99–32.48) years, respectively. There was no difference in cortisol levels with respect to gender (boys = 2.45 pg/mg and girls = 2.79 pg/mg) or weight. We found an association between vulnerability score and lower birth weight and birth height for girls. The reference group had a mean weight of 3570 g, those with 2 items had a mean weight of 3459 g ($P = .023$), and those with ≥ 3 items had a mean weight of 3413 g ($P = .027$). Children with ≥ 3 items were also shorter at birth than the reference group (49.8 vs 50.4 cm; $P = .035$). No association between cortisol levels and individual diagnoses was found. All single vulnerability items correlated significantly with the composite vulnerability score, and regression analysis could not distinguish a single item driving the associations to the different outcomes.

Psychosocial Vulnerability Score and Cortisol in Hair

An association was found ($r = 0.22$, $P = .002$) between the vulnerability score and logarithmized cortisol concentrations in the hair, as shown in Fig 1. When adjusting for gender and SGA, vulnerability was still significant. ($B = 0.40$, $P < .0001$). There was also a dose-response-like increase in cortisol concentrations; 0 items ($n = 33$) gave a mean of 1.90 pg/mg (95% CI: 0.91–2.89); 1 item ($n = 46$) gave a mean of 2.18 pg/mg (95% CI: 2.17–4.16); 2 items ($n = 27$) gave a mean of 3.17 pg/mg (95% CI: 2.18–4.16); 3 items ($n = 49$) gave a mean of 2.76 pg/mg (95% CI: 2.12–3.41); 4 items ($n = 24$) gave a mean of 2.82 pg/mg (95% CI:

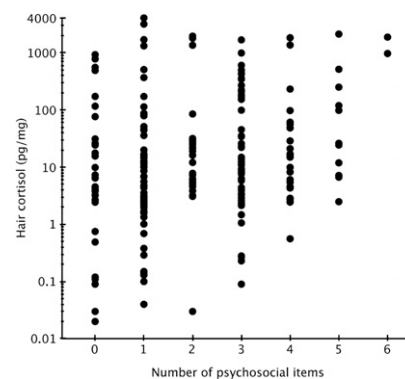


FIGURE 1 Psychosocial vulnerability score and hair cortisol concentration at age 1 year ($n = 209$).

1.99–3.65); 5 items ($n = 10$) gave a mean of 3.86 pg/mg (95% CI: 2.46–5.26); and 6 items ($n = 2$) gave a mean of 7.21 pg/mg (95% CI: 6.88–7.54). Of the 11 single dichotomous items, a significant difference in mean cortisol values was found for 2 variables (Table 1). Also, all but 1 of the items (father's occupation), exhibited higher mean cortisol levels in the exposed group, although this finding was nonsignificant.

Psychosocial Vulnerability Score and Health Outcome

Cumulative incidence was analyzed for the 14 most common diagnoses, ranging from 0.81 (acute upper respiratory infections) to 0.09 (urticaria). Rates below this level were too low for reliable statistical analyses. Comparing the mean vulnerability score in diagnosed versus undiagnosed groups, it was significantly higher for diagnosed children in 12 out of the 14 International Classification of Diseases, 10th Revision, groupings. After adjusting for gender and SGA, 10 diagnoses were still significant ($B = 1.92$, $P < .0001$) (Table 2). Gender was also independently significant in some cases. Among boys, acute upper respiratory infections ($P = .002$); injury, poisoning, and certain other consequences of external causes ($P < .0001$); and asthma ($P = .018$) were significant. Among girls, urinary

TABLE 1 Psychosocial Vulnerability Score, Single Items, and Hair Cortisol Concentration at Age 1 Year

Psychosocial Exposure	<i>n</i>	Cortisol, Mean (95% CI), log pg/mg	<i>P</i> ^a
Vulnerability score (number of single items)	209	2.62 (2.28–2.96)	.002 ^b
Single items			
Mother's marital status			
In a relationship	191	2.43 (2.28–3.00)	.733
Single	18	2.64 (1.43–3.43)	
Mother's occupation			
Employed	162	2.43 (2.05–2.82)	.041
Unemployed/sick leave	47	3.27 (2.54–4.00)	
Father's occupation			
Employed	193	2.62 (2.27–3.98)	.941
Unemployed/sick leave	16	2.57 (1.39–3.77)	
Residence type			
House	73	2.12 (1.50–2.73)	.031
Apartment	136	2.89 (2.49–3.29)	
Father's educational level			
College or university	170	2.47 (2.08–2.86)	.067
High school/9 years	39	3.28 (2.57–3.99)	
Mother's educational level			
College or university	182	2.55 (2.17–2.92)	.257
High school/9 years	27	3.13 (2.39–3.87)	
Foreign origin			
Neither or 1 parent	191	2.54 (2.19–2.88)	.096
Both parents	18	3.55(2.19–4.91)	
Maternal serious life event			
No	174	2.57 (2.20–2.95)	.523
Yes	35	2.88 (2.01–3.66)	
Maternal lack of support			
No	208	2.60 (2.25–2.93)	—
Yes	1	6.88 (—)	
Mother feeling safe ^c			
Yes	204	2.59 (2.25–2.93)	—
No	5	4.01 (2.08–6.93)	
Mother worried about child falling ill with serious disease			
No	116	2.37 (2.92–2.82)	.099
Yes	93	2.94 (2.43–3.45)	

—, not applicable.

^a Mean cortisol in exposed group versus nonexposed group (independent-samples *t* test).

^b Pearson correlation, *r* = 0.22, *P* = .002.

^c Question was phrased, "Do you feel safe and in the circumstances needed to give you and your newborn child a good start?"

tract infections were significant (*P* < .0001). Moreover, there was a correlation with the number of different diagnoses (*r* = 0.15, *P* < .0001). An increase in vulnerability score was associated with and graded to a corresponding increase in odds ratio (OR) for most diagnoses, although this finding was mostly significant among those in the highest category. One exception was urinary tract infections, where having some degree of vulnerability increased all of the ORs approximately twofold. The largest increases in ORs, with a more than twofold increase in the ≥3 category, were seen among viral

infections of unspecified site, intestinal infectious disease, and urticaria.

DISCUSSION

The objective of this study was to investigate whether early-life adverse psychosocial circumstances influence infant hair cortisol levels and affect health outcomes in children. A general pattern was seen throughout the results: added detrimental exposures resulted in a corresponding increase in levels of cortisol in hair and the risk of being diagnosed with almost all diseases common in childhood. This pattern

has, to our knowledge, never been shown before and there are few, if any, risk indicators that have such a wide impact on disease risk, which supports the model of physiologic dysregulation as a plausible pathway through which early-life psychosocial environmental exposures affect health outcomes.^{7,24,25}

Furthermore, infant cortisol levels were significantly positively associated with 2 of the 11 single psychosocial items. In 8 of the remaining 9 items, mean cortisol levels were higher in the exposed group, although not significantly so. This finding is in line with the few studies undertaken on cortisol in hair in children, in whom higher hair cortisol levels seem to be linked to different psychosocial factors.^{17,21}

The actual pathways linking psychosocial exposures to altered the HPA axis activity of the child are not fully known. A possible mechanism in the prenatal period could be, eg, epigenetic modification of DNA,²⁶ and early postnatal experiences are thought to alter the developing brain circuits controlling the stress response.²⁵ Thus, it is not far-fetched to think that the novel biomarker of cortisol in hair, which assesses HPA axis activity over longer periods of time, could reflect the continuous stress load in the daily social environment. These findings fit the accumulation of risk model (allostatic load) well, stating that health damage increases with the duration and number of detrimental exposures,^{1,2,24} as well as suggesting that these are extra toxic due to "the wear and tear of the body."^{12,25}

However, no association between cortisol levels and individual diagnoses was found, which could be due to the pathogenesis most often being multifactorial and probably dependent on several mechanisms but also because cortisol in hair is a novel biomarker that needs to be developed further, and in this case was measured in a smaller

TABLE 2 Psychosocial Vulnerability Score and Risk of the 14 Most Common Childhood Diagnoses Prospectively Until Age 10 Years

Diagnosis (ICD-10)	Number of Psychosocial Items	n (%)	Diagnosis Risk		P ^a	P ^b
			OR	95% CI		
Acute upper respiratory infections (J00–J06)	0	346 (78)	Ref	—	.003	.004
	1	603 (79)	1.06	0.80–1.41		
	2	368 (83)	1.34	0.96–1.87		
	≥3	196 (87)	1.83	1.17–2.86		
Otitis media (H65–H67)	0	288 (65)	Ref	—	.009	.007
	1	496 (65)	1.00	0.79–1.28		
	2	298 (67)	1.09	0.83–1.44		
	≥3	172 (76)	1.71	1.19–2.46		
Injury (S00–T98)	0	247 (56)	Ref	—	.048	.053
	1	418 (55)	0.96	0.76–1.22		
	2	271 (61)	1.24	0.95–1.61		
	≥3	138 (62)	1.24	0.90–1.76		
Viral infections of unspecified site (B34)	0	99 (22)	Ref	—	<.0001	<.0001
	1	210 (28)	1.32	1.01–1.74		
	2	138 (31)	1.56	1.16–2.11		
	≥3	85 (38)	2.10	1.48–2.97		
Infections of the skin (L00–L08)	0	123 (28)	Ref	—	.618	—
	1	205 (27)	0.96	0.74–1.26		
	2	126 (28)	1.03	0.77–1.38		
	≥3	66 (29)	1.07	0.75–1.53		
Other acute lower respiratory infections (J20–J22)	0	81 (18)	Ref	—	.038	.029
	1	133 (18)	0.95	0.70–1.28		
	2	92 (21)	1.17	0.84–1.62		
	≥3	55 (24)	1.44	0.98–2.12		
Conjunctivitis (H10)	0	69 (16)	Ref	—	.012	.020
	1	137 (18)	1.19	0.87–1.63		
	2	89 (20)	1.36	0.96–1.92		
	≥3	52 (23)	1.62	0.98–2.12		
Dermatitis and eczema (L20–L30)	0	65 (15)	Ref	—	.001	.032
	1	123 (16)	1.12	0.81–1.55		
	2	82 (18)	1.31	0.92–1.88		
	≥3	57 (25)	1.96	1.32–2.92		
Intestinal infectious diseases (A00–A09)	0	52 (12)	Ref	—	<.0001	.002
	1	102 (13)	1.16	1.18–2.92		
	2	74 (17)	1.50	1.34–3.51		
	≥3	54 (24)	2.36	1.03–3.25		
Urinary tract infections (N30, N34, N39.0)	0	27 (6)	Ref	—	.013	.003
	1	82 (11)	1.86	1.18–2.92		
	2	55 (12)	2.17	1.34–3.51		
	≥3	24 (11)	1.83	1.03–3.25		
Viral infections characterized by skin and mucous lesion (B00–B09)	0	36 (8)	Ref	—	.021	.061
	1	66 (9)	1.07	0.70–1.64		
	2	52 (12)	1.50	0.96–2.34		
	≥3	28 (12)	1.60	0.95–2.70		
Asthma (J45)	0	32 (7)	Ref	—	.006	.004
	1	63 (8)	1.16	0.77–1.80		
	2	48 (11)	1.55	0.97–2.48		
	≥3	29 (13)	1.89	1.11–3.21		
Pneumonia (J12–J18)	0	40 (9)	Ref	—	.160	—
	1	66 (9)	0.96	0.63–1.44		
	2	46 (10)	1.16	0.74–1.81		
	≥3	27 (12)	1.37	0.82–2.29		
Urticaria (L50)	0	29 (7)	Ref	—	.002	.016
	1	64 (8)	1.31	0.83–2.06		
	2	47 (11)	1.69	1.04–2.73		
	≥3	30 (13)	2.19	1.27–3.74		

N = 1876. ICD-10, International Classification of Diseases, 10th Revision; Ref, reference; —, not applicable.

^a Mean vulnerability score in diagnosed versus undiagnosed groups (independent-samples *t* test).

^b Adjusted for gender and SGA (binary regression).

subsample. There is also emerging evidence that exposure to intense stimuli could actually dampen HPA axis reactivity in some cases, which could affect all of the cortisol-related outcomes in this study, although this has been shown among adults and again using methods measuring short-term activity.²⁷ There were 2 potential outliers regarding cortisol levels that were included in the analyses even though the correlation coefficient for vulnerability increased to $r = 0.24$ when excluded. The reason for this is that the biological variance of cortisol seems to be greater at an early age,²⁰ so these outliers could not be considered measurement errors and excluded due to the risk of introducing selection bias. Other possible limitations were related to the novelty of the biomarker cortisol in hair: for example, its incorporation in hair is not fully known and the effect of the use of cortisone-containing creams as well as the influence of age and gender need further investigation.¹⁹ However, in this study, responses to the question "During pregnancy, did you take any medicine? Cortisone (yes/no)" did not alter the results.

In 12 of the 14 most common childhood diseases, children diagnosed with diseases had a higher vulnerability score than did children in the undiagnosed groups. There was also a general pattern of increasing ORs for every added vulnerability item, which was statistically significant for the most vulnerable category of children. These results are in line with earlier findings suggesting a relationship between early psychosocial risk factors and ill health in childhood,^{9–11} as well as suggesting a relationship between the multiplicity of early detrimental psychosocial factors and disease risk. Diagnoses are not a measure of actual disease; however, in Sweden, children with parents of low socioeconomic status (SES) are less likely to see a physician,²⁸ and thus in our study, such bias could have made the

association between vulnerability and disease weaker than it actually is. Most of the diagnoses that showed a significant association were common infections. There could be an inference consisting of differences in, eg, hygiene, siblings, and day care use that might expose the children in highly vulnerable families to pathogens to a greater extent than was controlled for in this study. Although, in Sweden, there are only small differences in type of child care (which includes free meals) with respect to, eg, SES, children in families of low social status attend day care less often, which is known to be associated with common infectious diseases.²⁸ Families also receive free or heavily subsidized maternity and child health care as well as medicines. Earlier research in adults showed susceptibility to the common cold among adults suffering from psychosocial stress and that the cells of the immune system are unable to respond to hormonal control.²⁹

The concept that the family situation during pregnancy predicts future health outcomes for the child due in part to an alteration in the maturing HPA axis is intriguing. However, an obvious weakness in this kind of research is that the association found may not equal causal effects. Although this study had a true prospective framework, it is not proof of causality and thus "neuroendocrine programming" could represent the quality of maternal care that supposedly remains the same throughout childhood.³⁰ It is probable that family vulnerability during pregnancy predicts future vulnerability and that the effects on health are exerted throughout life. However, it seems that childhood SES also acts independently of adult SES.²⁴ Another weakness is that the psychosocial vulnerability score is a theoretical and multifaceted latent trait, which makes it difficult to discern what was actually measured. It could therefore be argued that variables that are associated with

diagnoses should be treated as confounders; however, this possibility does not take interactions or potentiating effects into account.²² Even though the items used were crude, our hypothesis was articulated a priori and the general direction of the outcome suggests that the results cannot be explained by chance. Regression analysis could not distinguish a single item driving the associations with the different outcomes, which supports the theory behind the vulnerability construct, stating that the accumulation of adversities also matters. Furthermore, we only included participants who had complete answers for each 1 of the 11 items in the composite vulnerability variable. There is possibly an underrepresentation of individuals in the higher categories of vulnerability and the observed associations might have been even more pronounced if these children could have been included.

A general strength is the prospective design of this study, although some psychosocial factors studied could be seen as retrospectively collected because the mothers recalled them soon after delivery. Thus, we cannot rule out possible recall bias from the mothers. However, the recall accuracy of the mothers might also be quite sound, something that has been found for mothers' recall of the duration of their breastfeeding dating back over 20 years.³¹ Furthermore, another strength is that the actual number of diagnoses studied was quite high, a feature lacking in many former studies.²⁴

Although there is a natural uncertainty that derives from the novelty of the measures used, the widespread effect of vulnerability on the outcomes suggests that the results are not an effect of chance. As such, there is a possibility that the further development of cortisol in hair and the psychosocial vulnerability score could make the

associations observed even more pronounced. The cumulative nature of psychosocial disparities, not only single risk factors, seems to increase HPA axis activity as well as risk of disease. This finding indicates that interventions should also target the multiplicity of adversities, as well as emphasizing the importance of preventive measures at an early age of the life course, to decrease both illness and future cost.

CONCLUSIONS

Children born into families fraught with multiple adverse psychosocial

exposures seem to have increased long-term HPA axis activity and are more likely to be affected by common childhood diseases in a dose-response-like manner. This finding supports the model of physiologic dysregulation as a plausible mechanism by which the duration and number of early detrimental psychosocial exposures act as a trajectory to poor health outcomes. It also indicates that the multiplicity of psychosocial disparities is of importance and should be targeted in future interventions, because it could help to identify vulnerable children

who are at high risk of poor health. Moreover, given the prolonged nature of the exposure to a stressful social environment, the novel biomarker of cortisol in hair could be of major importance in this area of research.

ACKNOWLEDGMENTS

We thank all of the children, mothers, and family members participating in the ABIS (All Babies in Southeast of Sweden) study, as well as the staff and nurses working at the well-baby clinics.

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: This study was supported in part by The Swedish Child Diabetes Foundation (Barndiabetesfonden), the Research Council of Southeast Sweden (FORSS-87771, FORSS-36321), the Swedish Medical Research Council (K99-72X-11242-05A), the Wallenberg Foundation (K 98-99D-12813-01A), and the County Council of Östergötland project grant, Linköping, Sweden.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

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Pediatrics; originally published online May 4, 2015;
DOI: 10.1542/peds.2014-2561

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OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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