ENCYCLOPEDIA
on Early Childhood
Development

Long-Term Effects of Prenatal and Early Postnatal Nutrition on Adult Psychosocial Outcomes

Lambert H. Lumey, MD, MPH, PhD, Ezra S. Susser, MD, DrPH

Columbia University, USA

May 2003

Introduction

The existence of acute and chronic malnutrition in populations across the world is of concern both because of the immediate effects on morbidity and mortality and because of the possible long-term implications. These effects could be especially pronounced after exposure to malnutrition during fetal growth or in early infancy, because of potentially irreversible structural and biochemical changes to the growing brain. Nutritional deprivation during these critical periods might thereby have long-term effects on psychosocial development and behaviour.

Problems

For obvious reasons, the effects of impaired nutrition cannot be established in experimental studies that offer investigator control of the degree of nutrition. Estimates are therefore usually based on observations of malnourished infants and well-nourished controls. As the social,

economic, and family conditions associated with malnutrition are also related to impaired development, it is difficult to separate the effects of nutrition from the effects of the concomitant conditions. Such a separation of attributes may only be feasible under special circumstances. Statistical control provides a partial solution to the confounding problem by examining various attributes of social background, but these are often incompletely measured and residual confounding cannot be excluded. Comparison with sibling controls offers tighter control of the confounding effects of family background, however few studies have available siblings. These and other issues have been well reviewed by Pollitt and Thomson,[1] Rush,[2] and Grantham-McGregor.[3] Researchers can evaluate with greater accuracy the effects of nutrition supplementation efforts initiated in infancy.

Research Context

The role of early nutrition in human development has been clarified using observational, quasi-experimental, and intervention studies.

Observational studies of early postnatal malnutrition often show developmental delays in infants hospitalized with protein energy malnutrition (marasmus and kwashiorkor) and severe growth retardation in infants between 0 and 2 years, followed until ages 8 to 10. Intellectual performance has been compared to controls selected from non-hospital settings (creche, school) or to healthy siblings. Some typical studies were carried out in the South Africa[4,5] and Jamaica (mid-to-late 1950s),[6,7] Barbados (late 1960s),[8-10] and the Philippines[11] and Peru (late 1980s).[12] The magnitude of these studies varied between 40 and 250 subjects. In some studies, malnourished infants showed a 10- to 15-point deficit in intelligence scores around ages 8 to 10 compared to controls,[5,12] but they also came from markedly underprivileged backgrounds and living conditions[5] or had parents who were less educated[12] compared to controls. These attributes complicate the interpretation of the results. In studies with better controls for social background at the time of illness or in studies with sibling controls, recorded differences were smaller or non-existent.[4,6,7]

In an early observational study of the combined effects of prenatal and postnatal nutrition across a wide range of nutritional intakes among the women, children, and infants enrolled in the WIC (Women Infants Children) supplemental food program in the United States, supplemented children showed better intellectual performance at age 6 compared to non-supplemented older siblings.[13] These findings could not be confirmed in a subsequent national WIC evaluation of program participation of over 2,300 children aged 4 to 5 on outcomes of simple tests of behaviour,

vocabulary, and memory since the control families tended to be more privileged, and the WIC recipients only did better on selected cognitive development tests after an adjustment for socio-demographic indicators. It was therefore not possible to definitively establish that WIC supplementation was related *per se* to child cognition and behaviour.[14]

During the Dutch Hunger (the winter of 1944–1945), urban populations in the Western Netherlands were exposed to acute starvation because of wartime occupation conditions. These conditions represented a quasi-experiment in that the famine was imposed by an occupying army upon a civilian population solely defined by time and place. Comparing exposed and non-exposed infants, there was no relation between prenatal or early postnatal famine exposure and subsequent intellectual performance in over 300,000 military recruits aged 18.[15]

Elsewhere, the impact of nutritional interventions during pregnancy and early childhood on mental behaviour and function through the 7th year of life were assessed in over 1,000 children between 1969 and 1977 in four rural villages in Guatemala.[16,17] In the first two villages, ad libitum feeding of a high-protein maize (atole) was provided and in the other two, a protein-free sweet fruit (fresco) drink was provided. Both supplements contained vitamins and minerals, but the fruit drink contained only one-third of the calories in the atole. Although protein supplementation was linked to improved child development in some reports of this study, the effects of supplementation were inconsistent in other reports.[2] Other problems in interpreting the study results arise because the women who took the supplements for themselves and their infants lived under better social conditions than those who did not. The duration of pregnancy could also confound the observed associations as gestation time limited the quantity of calories a mother could add to her regular diet.[2]

The association between prenatal nutrition and postnatal development was further explored in a randomized two-level trial of calorie and protein supplementation given to pregnant women in a poor black New York City population. Little if any association was seen between prenatal supplementation and measures of development at age 1.[18] In a smaller cognitive intervention study of children hospitalized for protein energy malnutrition in Jamaica, outcomes were compared between the 18 children who received extra daily play visits in the hospital and after discharge, and the 21 children who did not receive play visits. Near normal performance on a mental development scale was seen in starved children if cognitive stimulation was given in addition to nutritional rehabilitation. This effect was sustained for at least one year after discharge.[19]

Key Research Questions

The problems of confounding by self-selection and by unmeasured socio-economic attributes in investigations of prenatal or early postnatal nutrition and psychosocial performance in childhood are now well recognized. There is also an understanding that the role of nutrition per se is likely to be limited. These insights have stimulated more comprehensive approaches that view interactions between nutrition and the social environment as important determinants in a psychosocial development. This rationale is the basis for an evaluation of the benefits of behavioural interventions at an early age. In special study populations with a limited risk of confounding, the follow-up for psychosocial changes over the life course continues.

Recent Research Results

In Jamaica, interventions with nutrition rehabilitation and cognitive stimulation among 129 growth-retarded infants aged 9 to 24 months showed continued benefits after two years of follow-up. Four study groups were compared: controls, supplemented infants, stimulated infants, and infants with both supplementation and stimulation. A group of matched non-shunted controls was also available for comparison. Benefits from supplementation alone were no longer apparent at 11 years of age, although the benefits from stimulation remained.[20] In the Netherlands, the prenatal famine exposure in utero of 18-year old military recruits was associated with an increased risk of anti-social personality disorder (ASPD).[21] Admissions to psychiatric hospitals in the Netherlands of men and women born in 1944–1945 suggest an increased risk of schizophrenia and of affective psychosis after prenatal famine exposure in mid-pregnancy.[22,23] An overview of these follow-up studies is given elsewhere.[24] Analyses from the British 1946 national birth cohort and the United States Collaborative Perinatal Project show an association between birthweight and school age IQ, even within the normal range of birthweight.[25,26] It is not clear whether these outcomes are driven by differences in prenatal nutrition that affect infant size at birth or whether there are other explanations.

Conclusions

Many studies to date have shown associations between prenatal and early postnatal malnutrition and growth retardation on the one hand and delayed cognitive and psychosocial development on the other. It is also clear that most of these differences in outcome cannot be attributed exclusively to the effects of poor nutrition or growth. Observational studies in particular are likely

to be confounded by self-selection and by unmeasured socio-economic attributes of early nutrition. These problems were already well recognized several decades ago[1,15,18] and can only be avoided through improved research designs that use sibling comparisons or include interventions beyond the control of the study subjects. Recent follow-up studies of infants born during the Dutch famine suggest that prenatal nutrition may play a role in the origin of some cases of schizophrenia or other neuropsychiatric outcomes.

Implications for Services and Policy Perspectives

Optimal psychosocial development requires adequate nutrition and social and emotional stimulation. In nearly all circumstances, these elements are intimately intertwined and not easily separated. Therefore, nutritional supplementation alone is no easy fix.

References

1. Pollitt E, Thomson C. Protein-calorie malnutrition and behavior: a view from psychology. In: Wurtman RJ, Wurtman JJ, eds. *Control of feeding behavior and biology of the brain in protein-calorie malnutrition*. New York, NY: Raven Press; 1977:261-306. *Nutrition and the brain*; vol 2.
2. Rush D. The behavioral consequences of protein-energy deprivation and supplementation in early life: an epidemiological perspective. In: Galler JR, ed. *Nutrition and behavior*. New York, NY: Plenum Press; 1984:119-157.
3. Grantham-McGregor S. A review of studies of the effect of severe malnutrition on mental development. *Journal of Nutrition* 1995;125(8 Suppl.S):S2233-S2238.
4. Evans DE, Moodie AD, Hansen JD. Kwashiorkor and intellectual development. *South African Medical Journal* 1971;45(49):1413-1426.
5. Stoch MB, Smythe PM, Moodie AD, Bradshaw D. Psychosocial outcome and CT findings after gross undernourishment during infancy: a 20-year developmental study. *Developmental Medicine and Child Neurology* 1982;24(4):419-436.
6. Richardson SA, Birch HG. School performance of children who were severely malnourished in infancy. *American journal of Mental Deficiency* 1973;77(5):623-632.
7. Richardson SA, Koller H, Katz M, Albert K. The contributions of differing degrees of acute and chronic malnutrition to the intellectual development of Jamaican boys. *Early Human Development* 1978;2(2):163-170.
8. Galler JR, Ramsey F, Solimano G, Lowell WE, Mason E. The influence of early malnutrition on subsequent behavioral development I. Degree of impairment in intellectual performance. *Journal of the American Academy of Child Psychiatry* 1983;22(1):8-15.
9. Galler JR, Ramsey F, Solimano G. The influence of early malnutrition on subsequent behavioral development III. Learning disabilities as a sequel to malnutrition. *Pediatric Research* 1984;18(4):309-313.
10. Galler JR, Ramsey FC, Forde V, Salt P, Archer E. Long-term effects of early kwashiorkor compared with marasmus. II. Intellectual performance. *Journal of Pediatric Gastroenterology and Nutrition* 1987;6(6):847-854.
11. Mendez MA, Adair LS. Severity and timing of stunting in the first two years of life affect performance on cognitive tests in late childhood. *Journal of Nutrition* 1999;129(8):1555-1562.
12. Berkman DS, Lescano AG, Gilman RH, Lopez SL, Black MM. Effects of stunting, diarrhoeal disease, and parasitic infection during infancy on cognition in late childhood: a follow-up study. *Lancet* 2002;359(9306):564-571.

13. Hicks LE, Langham RA, Takenaka J. Cognitive and health measures following early nutritional supplementation: a sibling study. *American Journal of Public Health* 1982;72(10):1110-1118.

14. Rush D, Leighton J, Sloan NL, Alvir JM, Horvitz DG, Seaver WB, Garbowski GC, Johnson SS, Kulka RA, Devore JW, Holt M, Lynch JT, Virag TG, Woodside MB, Shanklin DS. The national WIC Evaluation: evaluation of the special supplemental Food Program for Women, Infants, and Children. VI Study of infants and children. *American Journal of Clinical Nutrition* 1988;48(2 Suppl):484-511.

15. Stein Z, Susser M, Saenger G, Marolla F. Nutrition and mental performance. *Science* 1972;178(62):708-713.

16. Klein RE, Arenales P, Delgado H, Engle PL, Guzman G, Irwin M, Lasky R, Lechtig A, Martorell R, Mejia Pivaral V, Russell P, Yarbrough C. Effects of maternal nutrition on fetal growth and infant development. *Bulletin of the Pan American Health Organization* 1976;10(4):301-306.

17. Freeman HE, Klein RE, Townsend JW, Lechtig A. Nutrition and cognitive development among rural Guatemalan children. *American Journal of Public Health* 1980;70(12):1277-1285.

18. Rush D, Stein Z, Susser M. A randomized controlled trial of prenatal nutritional supplementation in New York City. *Pediatrics* 1980;65(4):683-697.

19. Grantham-McGregor S, Stewart ME, Schofield WN. Effect of long-term psychosocial stimulation on mental development of severely malnourished children. *Lancet* 1980;2(8198):785-789.

20. Grantham-McGregor SM, Powell CA, Walker SP, Himes JH. Nutritional supplementation, psychosocial stimulation, and mental development of stunted children: The Jamaican study. *Lancet* 1991;338(8758):1-5.

21. Neugebauer R, Hoek HW, Susser E. Prenatal exposure to wartime famine and development of antisocial personality disorder in early adulthood. *Journal of the American Medical Association* 1999;282(5):455-462.

22. Brown AS, Susser ES, Lin SP, Neugebauer R, Gorman JM. Increased risk of affective disorders in males after second trimester prenatal exposure to the Dutch Hunger winter of 1944-45. *British Journal of Psychiatry* 1995;166(5):601-606.

23. Susser E, Neugebauer R, Hoek HW, Brown AS, Lin S, Labovitz D, Gorman JM. Schizophrenia after prenatal famine: Further evidence. *Archives of General Psychiatry* 1996;53(1):25-31.

24. Susser E, Hoek HW, Brown A. Neurodevelopmental disorders after prenatal famine: The story of the Dutch Famine Study. *American Journal of Epidemiology* 1998;47(3):213-216.

25. Richards M, Hardy R, Kuh, D, Wadsworth MEJ. Birth weight and cognitive function in the British 1946 birth cohort: longitudinal population based study. *British Medical Journal* 2001;322(7280):199-203.

26. Matte TD, Bresnahan M, Begg MD, Susser E. Influence of variation in birth weight within normal range and within sibships on IQ at age 7 years: cohort study. *British Medical Journal* 2001;323(7308):310-314.