ENCYCLOPEDIA on Early Childhood Development

CHILD OBESITY

The Prenatal Origins of Obesity: Evidence and Opportunities for Prevention

Véronique Gingras, RD, PhD, Emily Oken, MD, MPH

Harvard Medical School and Harvard Pilgrim Health Care Institute, USA

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Introduction

The obesity epidemic has spared no segment of the population, even infants and young children.[1] In 2015-16, almost 14% of U.S. toddlers aged 2 to 5 years and over 18% of children between 6 and 11 years had obesity.[2] Over the past decades, researchers have looked to events that occur in very early life, even before birth, to understand the causes of childhood obesity and identify factors that may be targeted for prevention.[3] In this section, we outline parameters for normal growth in infancy, review prenatal factors that have been found to be associated with later obesity, and identify areas for intervention.

Subject

During well-child visits, pediatric clinicians use growth charts to document serial measures of weight and length, and screen for abnormalities in weight status.[4] In the U.S., among children over the age of two years, obesity is defined as a body mass index (BMI, weight in kg divided by height in m squared)[2] at or above the 95th percentile for age and sex, compared with a reference population – typically the Centers for Disease Control and Prevention (CDC) 2000 growth charts.[5] Overweight is a BMI between the 85th and 94th percentile.[5]

In infants below 24 months, excess weight has traditionally been defined using weight for length percentiles based on the CDC reference data. However, weight for length percentiles do not reflect age-dependent variations in weight or length. The World Health Organization (WHO) 2006 Growth Standard, which includes BMI percentiles for infants under age 2 years, has therefore been recommended by the American Academy of Pediatrics and other groups as a better reference for healthy growth in infancy.[6] Another advantage of this standard is that WHO included only healthy term infants who were breastfed for at least 12 months, followed them longitudinally, and excluded data for children with excess adiposity and growth failure. Using the WHO Growth Standard, fewer children are diagnosed with poor weight gain, and more with excess adiposity, than when using the CDC Growth Reference.[7,8] A BMI above the 97th percentile for sex and age indicates excess adiposity.[9] Since BMI reflects both lean and fat mass, however, BMI screening may result in misdiagnosis of individuals with higher or lower lean body mass than expected. In a recent study using two large prospective birth cohorts in the United States (Project Viva) and Belarus (Promotion of Breastfeeding Intervention Trial), Aris et al. showed that using either weight for length or BMI to define overweight during the first 2 years of life both strongly predict adiposity and cardio-metabolic outcomes in early adolescence.[10]

In addition to an infant's weight at any given time, a rapid weight gain trajectory predicts later risk of obesity as well as later prevalence of several health outcomes including cardio-metabolic diseases and asthma.[11-13] Rapid weight gain in infancy, often defined as a change in weight z-score > 0.67 (equivalent to the upward crossing of at least one percentile band on growth charts), has been associated with increased odds of obesity in adulthood.[12] In a study of 44,622 children aged 1 month to 10 years with 122,214 length/height and weight measurements, Taveras et al. found that upward crossing of ≥ 2 major weight-for-length percentiles (i.e., the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentile lines on the growth chart) in the first 6 months of life was not only common but was also associated with the highest risk of obesity 5 and 10 years later.[14] Growth and weight trajectories have been increasingly studied over the past years and could provide useful indicators of risks for later obesity and associated cardio-metabolic risk.[15-18] Typically, a child's BMI will peak around one year of age, followed by a decrease through 4 to 6 years of age, called the "BMI rebound".[16] An infancy BMI peak at a later age and of greater magnitude, and an earlier adiposity rebound, each predict later risk for obesity and related cardio-metabolic disorders.[17-18]

Problems

Obesity in infancy predicts obesity and related cardio-metabolic risk in later life. Also serious morbidity associated with obesity may occur even within childhood, including asthma, orthopedic problems, psychosocial adversity, high hospital admission rates, and increasingly, type 2 diabetes.[19-24] The biggest babies are not necessarily the fattest – babies born small for gestational age have reduced lean body mass, and thus are relatively fatter compared with appropriate-for-gestational-age babies, both at birth and in later life.[25] Since the combination of low weight at birth and rapid postnatal weight gain is a strong predictor of later metabolic disease risk, it is especially important to avoid ‘fattening up’ these small babies.[26]

Research Context

Numerous animal experiments dating back decades show that perturbations before birth can have lifelong effects on health.[27,28] Whereas early studies focused on under-nutrition in early life as a risk factor for cardiovascular disease, more recently research has focused on a wider range of early life exposures that may predispose to later obesity and cardiometabolic diseases. In humans, accumulating research demonstrates that maternal prenatal obesity, excess weight gain during pregnancy, nutritional inadequacies, gestational diabetes, maternal prenatal environmental exposures, and smoking during pregnancy predict later obesity and its adverse sequelae.[29-36]

Key Research Questions

Current research into the developmental origins of obesity clusters around the following questions: 1) What factors in early life predict later obesity risk, and how much influence do these early life factors have compared to risk factors that occur later? 2) What are the pathways and mechanisms by which early life exposures influence later health? 3) How can we intervene in these early life exposures to prevent or ameliorate risks for obesity and its adverse health effects?

Recent Research Results

Mothers with obesity tend to have overweight children.[37-39] Initially these associations were mostly studied as evidence for a genetic underpinning of obesity risk.[40] Studies have now provided strong evidence that the obese intrauterine environment itself programs body weight.[41] Similarly, a number of epidemiologic studies have found that higher maternal gestational weight gain, especially in early pregnancy, is associated with higher child weight in childhood and adolescence, and consequent risk for obesity and elevated blood pressure.[32,34,42-44] Pre-conception obesity and excessive gestational weight gain are both associated with increased odds of gestational diabetes, which itself has been associated with child's obesity risk. Infants born to mothers with diabetes during pregnancy are heavier at birth, but then grow slower after birth and are often no larger during the preschool years. However, even in early life they are likely to have more body fat,[45] and beginning in mid-childhood these children are heavier than their peers who were not born to mothers with diabetes during pregnancy.[29] Finally, although infants born to mothers who smoked during pregnancy are small at birth, they grow faster and have a higher risk for obesity in childhood and adulthood.[33]

The question remains whether these intrauterine experiences actually program long-term weight regulation and disease risk, or whether they are solely markers for other, shared causes of both maternal weight and child weight. Shared genes and extra-uterine environment certainly account for some of the similarity in maternal and offspring weight.[46,47] For example, parents and children tend to have similar diet quality and physical activity habits.48 Also, mothers who smoke, are obese, had gestational diabetes, or gained excessive weight during pregnancy are less likely to breastfeed, which itself predicts later overweight.[49-52]

However, associations of these prenatal factors with child weight persist even after statistical adjustment for factors such as socioeconomic status, infant feeding, and child diet and physical activity.[42] Furthermore, studies that compare siblings with discordant prenatal exposures but presumably otherwise similar genetic and extra-uterine experiences, provide additional evidence that the prenatal is a critical period for obesity risk.[53-55] Also, these human findings are supported by abundant evidence from animal studies among rodents, sheep and primates.[56-58]

Research Gaps

An optimal approach to understanding the role of intrauterine exposures for later health would be to conduct a well-powered randomized clinical trial, in which women are randomized to usual care or to an effective weight change intervention before and/or during pregnancy, and follow children longitudinally. Evidence of the effectiveness of preconception interventions for the mother and child's health is scarce; yet, a few trials are underway and might provide new insights in the near future.[59] Trials to improve diet or other behaviours during pregnancy have been conducted, but few have followed infants after delivery.[60] To date, the limited data available suggest that dietary and lifestyle interventions during pregnancy are modestly effective at reducing weight gain and may reduce the prevalence of gestational diabetes in overweight and obese mothers, but they have not been successful in reducing rates of large for gestational age births and macrosomia.[61] Interventions before conception might be more effective compared to those beginning in pregnancy,[62-63] and ongoing studies with larger sample sizes are expected to provide additional information in the coming years. Another area of future research is the paternal contribution to his child's later risk of obesity and disease beginning in early life. Recent evidence suggests that paternal preconception obesity and diabetes could be associated with later child outcomes.[64]

Conclusions

Childhood overweight is common and an important predictor of later health. Numerous observational studies among humans and abundant experimental data from animals suggest that experiences before birth including intrauterine exposure to maternal smoking, obesity, excess gestational weight gain or diabetes can "program" trajectories of adiposity and metabolic health throughout life. Clear guidelines exist for each of these factors, including recommendations for optimal maternal BMI before pregnancy, gestational weight gain guidelines, advice against smoking during pregnancy, and recommendations for universal gestational diabetes screening.[65-66] What is less clear, however, is how to help women achieve these optimal behaviours.

Implications for Parents, Service Providers, and Policy Makers

All young women should be encouraged to maintain a healthy weight and abstain from smoking prior to pregnancy. During pregnancy, provider advice is an important predictor of healthful behaviours and of weight gain concordant with guidelines. Women should be counseled regarding the implications of their own weight and health status for their child's health.

Pediatricians should identify and document prenatal and familial factors that are likely to increase a child's obesity risk, including parental obesity and maternal smoking, excess gestational weight gain and gestational diabetes. All infants and children should be routinely screened for overweight and for rapid weight gain using standard measurement techniques and the appropriate growth charts. The postpartum period is an opportunity to promote healthful behaviors that may not only improve the mother's long-term health and provide a role model for the infant's future behaviours, but also may optimize the mother's health entering subsequent pregnancies.

References

1. Kim J, Peterson KE, Scanlon KS, et al. Trends in Overweight from 1980 through 2001 among Preschool-Aged Children Enrolled in a Health Maintenance Organization[ast]. *Obesity*. 2006;14(7):1107-1112.
2. Hales CM, Fryar CD, Carroll MD, Freedman DS, Ogden CL. Trends in Obesity and Severe Obesity Prevalence in US Youth and Adults by Sex and Age, 2007-2008 to 2015-2016. *JAMA*. 2018;319(16):1723-1725.
3. Oken E, Gillman MW. Fetal origins of obesity. *Obes Res*. 2003;11(4):496-506.
4. Story M, Holt K, Sofka D, eds. *Bright futures in practice (Nutrition)*. 2nd ed. Arlington, VA: National Center for Education in Maternal and Child Health; 2002.
5. Centers for Disease Control and Prevention, National Center for Health Statistics. CDC Growth Charts: United States. 2000.
6. World Health Organization. *WHO child growth standards: length/height-for-age, weight-for-age, weight-for-height and body mass index-for-age: Methods and development*. Geneva, Switzerland: World Health Organization; 2006.
7. Maalouf-Manasseh Z, Metallinos-Katsaras E, Dewey KG. Obesity in preschool children is more prevalent and identified at a younger age when WHO growth charts are used compared with CDC charts. *J Nutr.* 2011;141(6):1154-1158.
8. Parsons HG, George MA, Innis SM. Growth assessment in clinical practice: whose growth curve? *Curr Gastroenterol Rep*. 2011;13(3):286-292.
9. Grummer-Strawn LM, Reinold C, Krebs NF. Use of World Health Organization and CDC growth charts for children aged 0-59 months in the United States. *MMWR Recomm Rep.* 2010;59(RR-9):1-15.
10. Aris IM, Rifas-Shiman SL, Li LJ, Yang S, Belfort MB, Thompson J, Hivert MF, Patel R, Martin RM, Kramer MS, Oken E. Association of weight for length vs body mass index during the first 2 years of life with cardiometabolic risk in early adolescence. *JAMA Netw Open.* 2018;1(5):e182460.
11. Taveras EM, Camargo CA, Jr., Rifas-Shiman SL, et al. Association of birth weight with asthma-related outcomes at age 2 years. *Pediatr Pulmonol*. 2006;41(7):643-648.
12. Gillman MW. Early infancy as a critical period for development of obesity and related conditions. *Nestle Nutr Workshop Ser Pediatr Program*. 2010;65:13-20.
13. Ong KK, Loos RJ. Rapid infancy weight gain and subsequent obesity: Systematic reviews and hopeful suggestions. *Acta Paediatr.* 2006;95(8):904-8.
14. Taveras EM, Rifas-Shiman SL, Sherry B, et al. Crossing growth percentiles in infancy and risk of obesity in childhood. *Arch Pediatr Adolesc Med*. Nov 2011;165(11):993-998.
15. Marinkovic T, Toemen L, Kruithof CJ, Reiss I, van Osch-Gevers L, Hofman A et al. Early Infant Growth Velocity Patterns and Cardiovascular and Metabolic Outcomes in Childhood. *J Pediatr.* 2017;186:57-63.e4.
16. Wen X, Kleinman K, Gillman MW, Rifas-Shiman SL, Taveras EM. Childhood body mass index trajectories: modeling, characterizing, pairwise correlations and socio-demographic predictors of trajectory characteristics. *BMC Med Res Methodol.* 2012;12:38.
17. Hughes AR, Sherriff A, Ness AR, Reilly JJ. Timing of adiposity rebound and adiposity in adolescence. *Pediatrics*. 2014;134(5):e1354-61.
18. Aris IM, Bernard JY, Chen LW, Tint MT, Pang WW, Lim WY et al. Infant body mass index peak and early childhood cardio-metabolic risk markers in a multi-ethnic Asian birth cohort. Int J Epidemiol. 2017;46(2):513-525.
19. Charney E, Goodman HC, McBride M, Lyon B, Pratt R. Childhood antecedents of adult obesity. Do chubby infants become obese adults? *N Engl J Med*. 1976;295(1):6-9.
20. Franks PW, Hanson RL, Knowler WC, Sievers ML, Bennett PH, Looker HC. Childhood obesity, other cardiovascular risk factors, and premature death. *N Engl J Med.* 2010;362(6):485-493.
21. Biro FM, Wien M. Childhood obesity and adult morbidities. *Am J Clin Nutr.* 2010;91(5):1499S-1505S.

22. Sinha R, Fisch G, Teague B, et al. Prevalence of impaired glucose tolerance among children and adolescents with marked obesity. *N Engl J Med.* 2002;346(11):802-810.
23. Noal RB, Menezes AM, Macedo SE, Dumith SC. Childhood body mass index and risk of asthma in adolescence: a systematic review. *Obes Rev.* 2011;12(2):93-104.
24. Shibli R, Rubin L, Akons H, Shaoul R. Morbidity of overweight (>or=85th percentile) in the first 2 years of life. *Pediatrics*. 2008;122(2):267-272.
25. Hediger ML, Overpeck MD, Kuczmarski RJ, McGlynn A, Maurer KR, Davis WW. Muscularity and fatness of infants and young children born small- or large-for-gestational-age. *Pediatrics*. 1998;102(5):E60.
26. Barker D. Mothers, babies, and health in later life. Second ed. Edinburgh: Harcourt Brace and Company; 1998.
27. McCance RA, Widdowson EM. The determinants of growth and form. *Proc R Soc Lond.* 1974;185:1-17.
28. Plagemann A, Heidrich I, Gotz F, Rohde W, Dorner G. Obesity and enhanced diabetes and cardiovascular risk in adult rats due to early postnatal overfeeding. *Exp Clin Endocrinol.* 1992;99(3):154-158.
29. Gillman MW, Rifas-Shiman S, Berkey CS, Field AE, Colditz GA. Maternal gestational diabetes, birth weight, and adolescent obesity. *Pediatrics*. 2003;111(3):e221-226.
30. Moore TR. Fetal exposure to gestational diabetes contributes to subsequent adult metabolic syndrome. *Am J Obstet Gynecol.* 2010;202(6):643-649.
31. Oken E, Huh SY, Taveras EM, Rich-Edwards JW, Gillman MW. Associations of maternal prenatal smoking with child adiposity and blood pressure. *Obes Res.* Nov 2005;13(11):2021-2028.
32. Oken E, Kleinman KP, Belfort MB, Hammitt JK, Gillman MW. Associations of gestational weight gain with short- and longer-term maternal and child health outcomes. *Am J Epidemiol.* 2009;170(2):173-180.
33. Oken E, Levitan EB, Gillman MW. Maternal smoking during pregnancy and child overweight: systematic review and meta-analysis. *Int J Obes* (Lond). 2008;32(2):201-210.
34. Oken E, Rifas-Shiman SL, Field AE, Frazier AL, Gillman MW. Maternal gestational weight gain and offspring weight in adolescence. *Obstet Gynecol.* 2008;112(5):999-1006.
35. Wu G, Bazer FW, Cudd TA, Meininger CJ, Spencer TE. Maternal nutrition and fetal development. *J Nutr.* 2004;134(9):2169-72.
36. La Merrill M, Birnbaum LS. Childhood obesity and environmental chemicals. *Mt Sinai J Med.* 2011;78(1):22-48.
37. Guillaume M, Lapidus L, Beckers F, Lambert A, Bjorntorp P. Familial trends of obesity through three generations. *Int J Obes Relat Metab Disord*. 1995;19 Suppl 3:S5-9.
38. Lake JK, Power C, Cole TJ. Child to adult body mass index in the 1958 British birth cohort: associations with parental obesity. *Arch Dis Child.* 1997;77(5):376-381.
39. Fisch RO, Bilek MK, Ulstrom R. Obesity and leanness at birth and their relationship to body habitus in later childhood. *Pediatrics*. 1975;56(4):521-528.
40. Stunkard AJ, Sorensen TI, Hanis C, et al. An adoption study of human obesity. *N Engl J Med.* 1986;314(4):193-198.
41. Oken E. Maternal and child obesity: the causal link. *Obstet Gynecol Clin North Am.* 2009;36(2):361-377, ix-x.
42. Oken E, Taveras EM, Kleinman KP, Rich-Edwards JW, Gillman MW. Gestational weight gain and child adiposity at age 3 years. *Am J Obstet Gynecol.* Apr 2007;196(4):322 e321-328.
43. Wrotniak BH, Shults J, Butts S, Stettler N. Gestational weight gain and risk of overweight in the offspring at age 7 y in a multicenter, multiethnic cohort study. *Am J Clin Nutr.* 2008;87(6):1818-1824.

44. Mamun AA, Mannan M, Doi SA. Gestational weight gain in relation to offspring obesity over the life course: a systematic review and bias-adjusted meta-analysis. Obes Rev. 2014;15(4):338-47.

45. Wright CS, Rifas-Shiman SL, Rich-Edwards JW, Taveras EM, Gillman MW, Oken E. Intrauterine exposure to gestational diabetes, child adiposity, and blood pressure. *Am J Hypertens.* 2009;22(2):215-220.

46. Rankinen T, Zuberi A, Chagnon YC, et al. The human obesity gene map: the 2005 update. *Obesity* (Silver Spring). 2006;14(4):529-644.

47. Nelson MC, Gordon-Larsen P, North KE, Adair LS. Body mass index gain, fast food, and physical activity: effects of shared environments over time. *Obesity* (Silver Spring). 2006;14(4):701-709.

48. Oliveria SA, Ellison RC, Moore LL, Gillman MW, Garrahie EJ, Singer MR. Parent-child relationships in nutrient intake: the Framingham Children's Study. *Am J Clin Nutr.* 1992;56(3):593-598.

49. Gunderson EP. Breastfeeding after gestational diabetes pregnancy: subsequent obesity and type 2 diabetes in women and their offspring. *Diabetes Care.* 2007;30 Suppl 2:S161-168.

50. Li R, Jewell S, Grummer-Strawn L. Maternal obesity and breast-feeding practices. *Am J Clin Nutr.* 2003;77(4):931-936.

51. Hilson JA, Rasmussen KM, Kjolhede CL. Excessive weight gain during pregnancy is associated with earlier termination of breast-feeding among White women. *J Nutr.* 2006;136(1):140-146.

52. Hilson JA, Rasmussen KM, Kjolhede CL. High pre-pregnant body mass index is associated with poor lactation outcomes among white, rural women independent of psychosocial and demographic correlates. *J Hum Lac*t. 2004;20(1):18-29.

53. Dabelea D, Hanson RL, Lindsay RS, et al. Intrauterine exposure to diabetes conveys risks for type 2 diabetes and obesity: a study of discordant sibships. *Diabetes*. 2000;49(12):2208-2211.

54. Ludwig DS, Currie J. The association between pregnancy weight gain and birthweight: a within-family comparison. *Lancet*. 2010;376(9745):984-990.

55. Smith J, Cianflone K, Biron S, et al. Effects of maternal surgical weight loss in mothers on intergenerational transmission of obesity. *J Clin Endocrinol Metab*. 2009;94(11):4275-4283.

56. Howie GJ, Sloboda DM, Kamal T, Vickers MH. Maternal nutritional history predicts obesity in adult offspring independent of postnatal diet. *J Physiol*. 2009;587(Pt 4):905-915.

57. Wu Q, Suzuki M. Parental obesity and overweight affect the body-fat accumulation in the offspring: the possible effect of a high-fat diet through epigenetic inheritance. *Obes Rev.* 2006;7(2):201-208.

58. Robinson S, Marriott L, Poole J, et al. Dietary patterns in infancy: the importance of maternal and family influences on feeding practice. *Br J Nutr.* 2007;98(5):1029-1037.

59. Barker M, Dombrowski SU, Colbourn T, Fall CHD, Kriznik NM, Lawrence WT, Norris SA, Ngaiza G, Patel D, Skordis-Worrall J, Sniehotta FF, Steegers-Theunissen R, Vogel C, Woods-Townsend K, Stephenson J. Intervention strategies to improve nutrition and health behaviours before conception. *Lancet*. 2018;391(10132):1853-1864.

60. Oken E, Gillman MW. Intervention strategies to improve outcome in obese pregnancy I: Focus on Gestational Weight gain. In: Gillman MW, Poston L, eds. *Maternal Obesity.* Cambridge, UK: Cambridge University Press; 2012.

61. Oteng-Ntim E, Varma R, Croker H, Poston L, Doyle P. Lifestyle interventions for overweight and obese pregnant women to improve pregnancy outcome: systematic review and meta-analysis. *BMC Med*. 2012;10:47.

62. Stephenson J, Heslehurst N, Hall J, Schoenaker D, Hutchinson J, Cade J, Poston L, Barrett G, Crozier SR, Barker M, Kumaran K, Yajnik CS, Baird J, Mishra GD. Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. *Lancet*. 2018;391(10132):1830-41.

63. Gingras V, Hivert MF, Oken E. Early-Life Exposures and Risk of Diabetes Mellitus and Obesity. *Curr Diab Rep*. 2018;18(10):89.

64. Fleming TP, Watkins AJ, Velazquez MA, Mathers JC, Prentice AM, Stephenson J, Barker M, Saffery R, Yajnik CS, Eckert JJ, Hanson MA, Forrester T, Gluckman PD, Godfrey KM. Origins of lifetime health around the time of conception: causes and consequences. *Lancet*. 2018;391(10132):1842-1852.

65. Institute of Medicine and National Research Council of the National Academies. *Weight Gain During Pregnancy: Reexamining the Guidelines*. Washington, DC: National Academies Press; 2009.

66. American Diabetes Association. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes—2019. *Diabetes Care*. 2019;42 Suppl 1:S165-72.