Introduction to the workshop1–3

Stephanie A Atkinson

ABSTRACT
The workshop entitled “Early Risk Determinants and Later Health Outcomes: Implications for Research Prioritization and the Food Supply,” reported in this issue, was borne of a quest to consolidate current knowledge on the early determinants of maternal and child health outcomes related to obesity, cardiovascular disease risk, and neurodevelopment. The primary goal was to delineate the relative influence of genetics and environmental factors, particularly in relation to specific nutrients and food components, on determinants of risk within the developmental stages of pregnancy, infancy (0–12 mo), and early childhood up to 5 y of age. A panel of experts was charged with critiquing the evidence presented and with identifying research gaps and challenges for future research, such as when and how the food industry might translate knowledge of the determinants of disease into improvements in human health through food product development. Am J Clin Nutr 2009;89(suppl):1S–3S.

Emerging evidence from epidemiologic and animal studies supports the hypothesis of an interaction effect of genes and environmental exposures during embryonic, fetal, neonatal, and even childhood life on the growth and body composition of progeny. In many cases, detrimental exposures in early life have been linked to susceptibility to various chronic diseases developing in later life. Risk of adiposity, cardiovascular disease, type 2 diabetes, metabolic syndrome, and osteoporosis in adult life have all been associated with small size at birth (reviewed in references 1, 2). Critical windows of effect range from pre-implantation to late pregnancy, and proposed mechanisms include disturbances in the size and phenotype of organ systems, changes in biochemical thresholds for activity, and changes in angiogenesis (3). Such changes in the offspring have been linked to alterations in placental physiology during pregnancy (4, 5). Epigenetic processes such as DNA methylation and histone modification are thought to occur in response to environmental exposures, thus modulating gene expression during development or what has been termed “developmental plasticity” (6). These phenomena, often referred to as programming or imprinting effects, may occur during embryonic, fetal, or early childhood development when the human genome is especially vulnerable to even minor adverse influences.

The original observations underpinning the “early origins” hypotheses, such as the one linking small size at birth to ischemic heart disease (7), were based on epidemiologic studies in historical cohorts growing up before the current obesogenic environment. For the most part, little information was provided about these cohorts between their birth and adulthood years, and no account was taken of a myriad of confounding factors known to influence the ultimate disease outcome identified. Such confounders include maternal smoking, maternal health (eg, pre-eclampsia), and maternal socioeconomic status, conditions that independently result in lower birth weight and are associated with coronary vascular disease risk. The earlier retrospective epidemiologic studies provided important insights that generated hypotheses now being explored in contemporary prospective investigations and animal studies. The concept of the early origins of disease is being substantiated through prospective longitudinal studies now in progress that begin before or during pregnancy to control for the relative contribution of the determinants of maternal health, birth events, postnatal nutrition, physical activity, growth trajectory, and environmental exposures through early childhood. Birth cohort studies now exist or are being established in both developed [Australia (8), United Kingdom (9, 10), Denmark (11), Netherlands (12), United States (13), Canada (14), and Germany (15)] and developing countries (16). Gene-environment interactions are a recent focus in some studies. Any examination of the determinants of disease risk must take into account the contribution of heritability by maternal, paternal, and fetal genes (17) because the relative contribution of genetic inheritance and external exposures remains unclear even for outcomes such as body weight and adiposity (18).

Contemporary prospective, longitudinal birth cohort studies provide opportunities to explore gene-environment interactions within the context of maternal influences on fetal programming. Evidence is accumulating that maternal health status and lifestyle practices affect not only pregnancy and birth outcomes but also the future health of the offspring. For example, maternal prepregnancy weight and gestational weight change have been identified as significant predictors for the development of diabetes, heart disease, hypertension, and dyslipidemia in the mother (19). However, there is also a link between maternal nutrition, lifestyle, and metabolic status during pregnancy and adiposity in childhood. On the basis of a systematic review (20),

1 From the Department of Pediatrics, Faculty of Health Sciences, McMaster University, Hamilton, Canada.
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3 Reprints not available. Address correspondence to SA Atkinson, the Department of Pediatrics, Faculty of Health Sciences, McMaster University, HSC 3A42, 1200 Main Street West, Hamilton, ON L8N 3Z5, Canada. E-mail: satkins@mcmaster.ca. doi: 10.3945/ajcn.2009.27113A.

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the risk of developing childhood obesity increased by 40% if maternal diabetes was present, by 90% if maternal undernutrition occurred in early pregnancy, and by 50–100% if the mother smoked during pregnancy. With respect to maternal diet, consumption of omega-3 fatty acids through fish consumption during pregnancy and lactation has been associated with benefits to mental and visual development in infants and young children (21). Advantages to maternal health status, pregnancy outcome, and mental development of the offspring have also been attributed to iron intake and status in infancy (22).

Postnatal factors of interest in the programming of adult disease include nutrition, which may operate through modulating growth trajectory in infancy. Growth velocity has been identified as an important risk factor for later obesity (9, 23) and cardiovascular disease risk (24) in children born either small or an appropriate size for gestational age. If rapid infancy weight gain is a reflection of variable nutritional exposures during early infancy, then early nutrition may contribute to programming of metabolic health and obesity, but more research is required (25).

The workshop reported in this issue was borne of a quest to consolidate the current knowledge on early determinants of maternal and child health outcomes related to obesity, cardiovascular disease risk, and neurodevelopment. A primary objective was to focus on the relative influence of genetics and environmental factors, particularly in relation to specific nutrients and food components on determinants of risk within the developmental stages of pregnancy, infancy (0–12 mo), and early childhood up to 5 y of age. On the basis of the key presentations of the workshop, an expert panel was charged with discussing targets for research prioritization in this field that could guide researchers in the next steps of investigation. The panel was also charged with deliberating about whether the current state of knowledge can be translated into practice and, in particular, whether it can lead to the development of food products that would improve the availability of dietary choices for pregnant women and their offspring during the vulnerable critical windows of development. The idea of targeting such populations is not novel. In a recent review of the developmental programming of obesity (26), it was concluded that the perinatal environment should be a potential therapeutic target for interventional strategies for preventing obesity in childhood. If the genetic determinants and key exposures that cause such permanent changes in growth and health outcomes can be identified, prospective intervention studies can be designed to prevent the exposures that underpin such risk factors that occur in the perinatal and childhood periods. On the basis of such intervention studies, guidelines for optimizing diet and lifestyle during pregnancy and the early childhood years should be easily formulated.

Through the contemporary birth cohort studies, the complexity of the “early origins” hypothesis is unraveling, with more questions to be addressed. The timing and specificity of the critical windows of exposure remain unclear. Are the critical windows the same for all disease endpoints? Are the changes invoked during one developmental period amplified, minimized, or reversible by subsequent exposures? What, if any, are the transgenerational effects that may be expressed in subsequent offspring? The workshop speakers and panelists brought illumination to these questions and on how to approach definitive answers. (Other articles in this supplement to the Journal include references 27–34.)

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REFERENCES
INTRODUCTION