The origins of health and disease susceptibility for many of the complex, common disorders that confer the major, global burden of disease in developed societies as well as societies in rapid transition can be traced back to the intrauterine period of life (i.e. the concept of fetal or developmental programming of health and disease risk [1]. A large number of studies of fetal programming of obesity and metabolic dysfunction have focused on the critical role of maternal nutrition prior to or during gestation and have produced important findings and insights [reviewed in 2]. Questions currently under investigation include those related to mechanisms or pathways by which nutritional programming can exert lifelong effects on the developing organism. Some major nutrition-related pathways relate to the effects of nutritional insults on maternal-placental-fetal glucose/insulin physiology and downstream effects on the developing fetal brain and peripheral systems. We propose that in addition to maternal nutrition-related processes it may be important to concurrently consider the potential role of intrauterine stress and stress biology for the following reasons: (a) From an evolutionary-developmental perspective, energy availability (i.e. nutrition) and challenges that have the potential to impact the structural or functional integrity and survival of the organism (i.e. stress) represent the most important environmental conditions underlying natural selection and developmental plasticity along all times scales. It is therefore likely and plausible that stress represents an important aspect of the intrauterine environment that would be expected to influence many, if not all, developmental outcomes. (b) Stress-related biological factors may exert direct effects on fetal targets of programming of body composition and metabolic function. (c) Many of the effects of nutritional insults (both undernutrition and overnutrition) may be mediated by common stress-related pathways involving the hypothalamic-pituitary-adrenal axis...
and inflammation. Hence, stress biology may represent a common underlying mechanism. (d) Stress and stress biology are known to alter nutrition at several levels, including caloric intake, selection of food types, and metabolic fate of energy. Conversely, nutritional status is also known to alter stress at multiple levels in the brain and periphery, including appraisals of potentially stressful circumstances, psychological and physiological stress responses, and feedback regulation. Hence, in natural settings it is likely that the effects of either nutrition or stress are modified by or conditioned upon the state of the other. This issue is particularly important in the human context since nutritional insults and stress tend to co-occur in populations across the world. We therefore propose and review evidence that supports the concept that maternal-placental-fetal endocrine and immune/inflammatory stress biology represents a candidate mechanism that may underlie the long-term effects of many different kinds of adverse intrauterine exposures on subsequent risk of child and adult obesity and metabolic dysfunction [3].

References