Invited Commentary
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Small for Gestational Age Infants: Reading Their Future[1]

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In a recent edition of Central European Journal of Paediatrics, Fister et al. look at the difference in infants born small for gestational age (SGA) versus those who are appropriate for gestational age (AGA) in an attempt to characterise the risk factors for or the biomarkers of future metabolic syndrome (1). Over the last three decades, there has been a great deal of interest in this area. Barker first described origins of health and disease as beginning in utero and the importance of antenatal care to minimise risks of future disease has become a priority (2). In particular there is much focus on the provision of adequate antenatal care to prevent SGA as an outcome, though there is much we don't understand about the pathogenesis. In this study venous blood samples taken day 3 of life were compared between 45 infants who were born SGA and 24 infants who were AGA. Infants who were otherwise unwell were excluded leaving well infants who had a birth weight, length or head circumference <10th centile to define the SGA group.

Blood biomarkers were compared between groups finding that adiponectin was significantly lower and triglycerides significantly higher in the SGA group. These findings mirror other studies in a similar cohort of children. Lower adiponectin measures are strongly associated with metabolic syndrome in general and hyperlipidaemia is, of course, a defining feature of the syndrome.

Goto et al. reported lower adiponectin levels in the cord blood infants when compared with AGA infants. Interestingly this effect was not mirrored in maternal blood (3). A metanalysis performed by the same authors, compiled data from 5 studies of SGA infants and came to the same conclusion (4). Work done in pre-pubertal children who were SGA again shows lower adiponectin levels, even compared to age matched children who were obese but had not been SGA. Catch up growth was associated with lower concentrations of adiponectin in this group, though triglyceride levels were higher in the obese AGA group (5). Abnormality persists into young adulthood with lower adiponectin levels in former AGA infants with higher levels of insulin resistance in this group compared to controls. A linear relationship between adiponectin levels and insulin resistance was not found however (6).

It is not entirely clear, whether these abnormalities found shortly after birth and which presumably persist into adult life are cause or effect. Are triglyceride levels raised in the blood of newborn infants who are SGA in a response to lipid storage attempting to compensate for size or are these individuals pre-programmed genetically to inefficient

[1]A commentary on: Fister et al. Potential Biomarkers of Metabolic Syndrome in a Group of Small for Gestational Age Neonates.

substrate processing leading to both SGA and lipid abnormalities? The major question raised by Fister et al. is what prognostic value that these findings will have on the future lives of infants born SGA. As blood for makers was drawn day 3 of life, early post-natal exposures such as breast feeding, the microbiome and catch up growth will presumably have little to no effect on the expression of the markers of interest. It will be especially important to attempt to follow up this cohort to evaluate the true incidence of metabolic syndrome in those in both the SGA and AGA groups and the cumulative effect of post-natal exposures on improvement or exacerbation of outcomes.

In addition, although it has been shown that maternal adiponectin levels are not predictive of a pregnancy leading to an infant which is SGA, it would be useful to know the influence if any of the potentially modifiable maternal risk factors in the cohort including smoking, gestational diabetes etc. on biomarkers in neonatal blood. How much do these antenatal and postnatal exposures affect the development of metabolic syndrome in later life in those who are genetically destined to be small versus those more 'epigenetically' small? Fister et al. contribute to a field in helping to untangle the complex interactions in both in utero and ex utero life. We await the follow-up of these infants with great interest.

Conflict of Interest: The author declares that she has no conflict of interest.

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