

A Small Early Imbalance, a Great Late Disorder: Intrauterine Nutritional Imbalance and Adult Hypertension

MANUEL RODRÍGUEZ¹

Several basic and clinical research studies encourage the idea that an unfavorable intrauterine environment is determinant for various pathologies that develop in adult life. This phenomenon is known as “fetal programming” and is linked to higher risk for heart defects, insulin resistance, and immune disorders. (1, 2) The mechanisms involved in fetal programming of adult diseases include long term changes in the blood pressure regulatory systems, as it is suggested by the inverse relationship between weight at birth and blood pressure in adulthood. Thus, certain heart and kidney diseases may develop as a result of changes during fetal life caused by adverse conditions.

Different etiologies may cause a suboptimal fetal environment that contributes to the development of diseases in adulthood. Today, special attention is paid to nutritional imbalance during pregnancy, breastfeeding, and childhood, since many studies have demonstrated that a nutritional deficiency in fetal and postnatal life predispose to the development of diseases in adults. Among the various agents analyzed, the zinc stands out as an essential micronutrient for growth, although the exact mechanisms of such participation have not been completely elucidated. Zinc is necessary for the normal progression of the cell cycle, and it is essential for the DNA synthesis, since it is a cofactor of several enzymes involved in the formation and regulation of the nucleic acids, as well as a cofactor of many other zinc-dependant enzymes. It is an essential element in the proteins synthesis, many of them necessary for growth. Indeed, severe zinc deficiency has been recognized for many years as the cause for growth delay.

The most common growth delay caused by nutrition worldwide is the malnutrition due to poverty. Growth delay is also an infraestimated entity in pediatric patients, because these patients do not have significant clinical evidences of malnutrition, or nutrient-deficiency symptoms. In this context, the suboptimal intake of zinc is particularly relevant, since it has been recently demonstrated that a mild or moderate deficiency during pregnancy and childhood results in growth delay.

In this issue, Ploder et al. (3) expand and go deeper into previous studies of their work group, regarding the changes in heart and kidney that occur in adulthood, when there is a moderate zinc restriction in

the diet during growth periods. (4, 5) Those studies had already stated that a diet low in zinc during childhood would increase the risk of having hypertension during adulthood. Ploder et al.'s work was awarded the *Premio al Mejor Trabajo de Investigación Básica en Cardiología 2008* (Best basic research in cardiology award for 2008). This work shows experimental evidence that insufficient zinc during fetal development and postnatal growth results in changes in the blood pressure regulating system and in the kidney function during adult life, what cause hypertension and decrease of the glomerular filtration volume. Moreover, lower levels of this mineral during fetal life induced lower weight at birth, and a negative correlation with blood pressure in adult life. The study is not only observational; it also tries to explain how these changes are produced, pointing out that they are associated to a decrease of the renal and vascular nitric oxide system.

Their findings are interesting, since they lend weight to the hypothesis posed by different studies, according to which an inadequate zinc intake during prenatal and postnatal growth constitutes a heart and kidney risk factor in adult life; they join the recent works that add new etiopathogenic factors to hypertension. This research becomes even more relevant because it includes the high proportion of Argentine children under the age of three under a diet poor in zinc, and a similar situation occurs during pregnancy, when the needs for the micronutrient are higher. The work is a warning call that shows how nutritional imbalances not clearly evident during pregnancy, breastfeeding, and growth may result in fetal and neonatal hypertension programming; these imbalances have a possibly irreversible impact on the individual's health in adulthood, and are difficult to solve.

BIBLIOGRAPHY

1. Ojeda NB, Grigore D, Alexander BT. *Developmental programming of hypertension: insight from animal models of nutritional manipulation*. *Hypertension* 2008; 52:44-50.
2. Alexander BT. *Developmental programming of hypertension*. *Am J Physiol Regul Integr Comp Physiol* 2006; 290:R1-R10.
3. Ploder MM, Tomat AL, Elesgaray R, Fellet AL, Balaszczuk AM, Costa MA et al. *Programación temprana de alteraciones en el sistema*

¹ Cardiovascular Physiopathology Institute, Department of Pathology, Faculty of Medicine, University of Buenos Aires.

del óxido nítrico renal y vascular inducidas por la deficiencia de cinc (Early programming of changes in renal and vascular nitric oxide system, induced by zinc deficiency). *Rev Argent Cardiol* 2008; 76:459-64.

4. Tomat AL, Costa MA, Girgulsky LC, Veiras L, Weisstaub AR, Inserra F, Balaszczuk AM, Arranz CT. *Zinc deficiency during*

growth: influence on renal function and morphology. *Life Sci* 2007; 80:1292-302.

5. Tomat AL, Weisstaub AR, Jauregui A, Piñeiro A, Balaszczuk AM, Costa MA, Arranz CT. *Moderate zinc deficiency influences arterial blood pressure and vascular nitric oxide pathway in growing rats*. *Pediatr Res* 2005; 58:672-6.