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Growth in utero and blood pressure levels in the next generation

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Epidemiological studies have consistently shown an inverse association between birth weight and systolic blood pressure in later life [1]. It is not known whether the cause of this association is intra-uterine programming in response to fetal malnutrition [2] or a genetic factor influencing both birth weight and blood pressure [3]. Family studies offer an important opportunity to distinguish between intra-uterine and genetic influences. If intra-uterine factors determine the inverse association between birth weight and blood pressure, it could be expected that offspring's systolic blood pressure is associated with maternal birth weight, but not with paternal birth weight. If, however, genetic factors do play a role, offspring's blood pressure would also be associated with paternal birth weight. Barker et al. [4] investigated these associations in 106 children of 70 fathers and 123 children of 77 mothers. Birth weight and blood pressure data in the parents were described previously [5]. In the present study, their offspring was divided in five parental birth weight strata and, according to Barker et al., the offspring's systolic blood pressures fell with increasing maternal birth weight (P for trend = 0.05), but were unrelated to paternal birth weight (P = 0.7) [4]. On the basis of these findings, the authors concluded that constrained growth of a female fetus by lack of nutrients causes persisting changes in its physiology and metabolism which lead to reduced fetal growth and raised blood pressure in the next generation. Therefore, public health policies to improve fetal growth in one generation may benefit succeeding generations. However, a closer look at their data shows that the opposite may be true. Using the three birth weight strata as defined for men and women in the original article describing the parents [5], it can be visualized that offspring's systolic blood pressure fell with increasing maternal as well as paternal birth weight (Fig. 1). This may suggest that genetic factors also play a role in the association between birth weight and blood pressure. It would be informative to test whether the association of parental birth weight with offspring's blood pressure is significantly different between mothers and fathers before and after adjustment for gestational age.

If the relationship between low birth weight and raised blood pressure is caused by genetic factors, improvement of fetal growth may neither prevent the development of raised blood pressure in the first generation, nor in succeeding generations. Low birth weight may only serve as a marker of increased risk of raised blood pressure.

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