Combined nephroprotective effect and low nephron endowment as a consequence of postnatal growth restriction in the rat?

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TO THE EDITOR: In a very interesting recent paper, Tarry-Adkins et al. (6) describe the beneficial effects of slow growth during lactation in the rat. With increasing age, rats nurtured by dams that were fed a low-protein diet during lactation showed, among other favorable effects, no proteinuria in contrast with control male rats that showed progressive urinary protein loss. These results are similar to a previous study from the same group (2), which additionally showed no difference in the development of proteinuria between control rats and rats born from dams subjected to protein restriction during pregnancy [a widely used model for intrauterine growth restriction (IUGR)]. However, as IUGR has been shown to lead to a low nephron endowment in both humans and many animal models (3), an increase in proteinuria in both groups of growth restriction could be expected on the basis of the hyperfiltration hypothesis (1). Indeed, rats born after IUGR have been shown to have both a lower nephron number and an increase in proteinuria (3, 4).

We have also shown that growth restriction during postnatal nephrogenesis, which continues until days 7–10 after birth in rats, leads to a 25% reduction in nephron number (5). Growth of the pups in the models of Tarry-Adkins et al. (6) seems to be even more restricted than in our model [weight of the growth-restricted pups at day 21 on average was 46% of controls and 66% of controls in the study of Tarry-Adkins et al. and Schreuder et al. (5), respectively]. The postnatal period is highly important in determining final nephron number, as a recent study showed that a normal lactational environment could even restore the effect of IUGR on nephron endowment (7). Together with the significant association between body weight during the growth restriction and glomerular number (5), an even greater reduction in nephron number can be expected.

However, to my surprise, the results from the study of Tarry-Adkins et al. point in the exact opposite direction, i.e., toward a nephroprotective effect. As the methods of growth restriction are different [protein restriction (6) vs. a restriction in total intake (5)], it would be very interesting to know the number of nephrons in the model of Tarry-Adkins, especially as the kidneys were found to be smaller (6). If this number would be lower as expected, additional research is needed to shed light on the intriguing and seemingly incompatible combination of low nephron endowment with subsequent glomerular hyperfiltration and renal protection in the long run.

REFERENCES