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JOURNAL ARTICLE

Increased proliferation of Leydig cells induced by neonatal hypothyroidism in the rat

M. P. Hardy, R. S. Sharma, N. K. Arambepola, C. M. Sottas, L. D. Russell, D. Bunick, R. A. Hess and P. S. Cooke

Population Council, New York, New York 10021, USA.

Treatment of male rat pups with the reversible goitrogen 6-n-propyl-2-thiouracil (PTU), administered by adding 0.1% PTU to the mother's drinking water from birth through weaning, increases adult testis size, number of Sertoli cells, and daily sperm production. Adult Leydig cell numbers are also increased by 70%, despite permanent suppression of serum luteinizing hormone (LH). The present study was designed to test whether this effect results from an increase in proliferation of Leydig cells or the mesenchymal precursors. The labeling indices (LI) of six interstitial cell types were measured by tritiated thymidine autoradiography. With the exception of Leydig cells, LI declined after birth for all interstitial cell types in both control and PTU-treated rats, but mesenchymal cell proliferation was not significantly different in control and treated rats. In contrast, the LI of Leydig cells from PTU-treated rats rose by day 10, remained elevated through day 45 (highest on day 35 at 3.6-fold higher than control, $P < 0.05$), and declined to control values by day 50. The LI of Leydig cells in control rats was unchanged during the experiment. Proliferating Leydig cells were immature, as shown by their cytoplasmic lipid droplets. Adult Leydig cells, which lack lipid droplets, did not proliferate. Mesenchymal and immature Leydig cells contained thyroid hormone receptor mRNA; levels in adult Leydig cells were reduced but detectable. In conclusion, proliferation of Leydig cells, rather than increased proliferation of their mesenchymal precursors, is the principal mechanism responsible for the increase in Leydig cell number after neonatal hypothyroidism. Increased Leydig cell proliferation could result from direct effects of hypothyroidism on these cells. Alternatively, the increased Sertoli cell population that results from PTU treatment could also stimulate increased Leydig cell proliferation, or both of these mechanisms could contribute to the Leydig cell increase.

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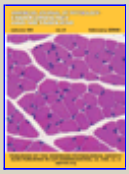

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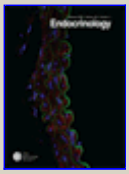

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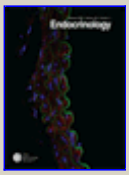

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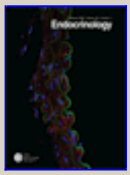

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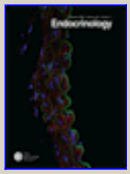

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