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COMMENT

Appropriate maternal thyroid hormone levels: a crucial factor in protecting offspring's vascular health

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The maternal environment plays a pivotal role in shaping the cardiovascular health of offspring, as proposed by the "fetal origins of adult disease" (FOAD) hypothesis [1]. Adverse maternal conditions, such as malnutrition, hypertension, or thyroid dysfunction during gestation, can induce developmental reprogramming that predisposes offspring to chronic diseases, including cardiovascular disease (CVD) such as hypertension. Previous studies have demonstrated that maternal hypothyroidism is associated with an increased risk of hypertension and impaired vascular function in offspring, mediated by oxidative stress and impaired endothelial mechanisms [2, 3]. Thyroid hormones, critical regulators of growth and metabolism, play an essential role during fetal development. Maternal thyroid hormone deficiency can disrupt vascular development in utero, potentially leading to long-term cardiovascular dysfunction in offspring [4, 5].

The study by Guo et al. investigates the long-term effects of maternal hypothyroidism on the vascular health of adult male offspring [6]. Using a rat model of maternal hypothyroidism induced by propylthiouracil (PTU), the authors assessed vascular function in mesenteric arteries of the offspring. Their findings revealed increased blood pressure, reduced nitric oxide (NO)-mediated vasodilation, and elevated oxidative stress in the offspring of hypothyroid mothers. Mechanistically, the study identified downregulation of the TRα1/PGC-1α/SIRT3 signaling axis—a critical pathway involved in mitochondrial function and oxidative stress regulation—as a key contributor to these vascular changes. Furthermore, triiodothyronine (T3) supplementation mitigated oxidative damage in smooth muscle cells by enhancing PGC-1α and SIRT3 expression, highlighting the protective role of thyroid hormones (Fig. 1) [6].

Maternal hypothyroidism-induced vascular dysfunction in offspring is closely linked to oxidative stress and impaired mitochondrial signaling. The findings provide further evidence that thyroid hormone receptor α1 (TRα1) plays a central role in mediating the protective effects of thyroid hormones [6]. Reduced TRα1 expression in vascular smooth muscle cells diminishes the downstream activation of PGC-1α and SIRT3, leading to heightened reactive oxygen species (ROS) production and impaired vasodilation. This aligns with earlier studies highlighting the antioxidant properties of thyroid hormones and their role in maintaining vascular homeostasis. Importantly, this study elucidates how mitochondrial dysfunction contributes to hypertension in offspring, offering new insights into the impact of intrauterine hypothyroid conditions [6].

There is ongoing debate regarding universal screening for thyroid dysfunction in pregnancy. While it is widely accepted that overt hypothyroidism is associated with adverse pregnancy outcomes, including pregnancy loss, intrauterine growth retardation, preterm birth, and preeclampsia [7], the implications of subclinical hypothyroidism (SCH) are less clear. SCH is found in approximately 3.2% of pregnant women [8]. Importantly, even mild thyroid dysfunction is associated with a higher risk of preeclampsia. Studies have also shown that offspring of subclinical hypothyroid mothers have higher systolic blood pressure compared to those of euthyroid mothers [9].

Some guidelines advocate for targeted screening based on risk factors, such as a personal or family history of thyroid disease, presence of goiter, or autoimmune disorders like type 1 diabetes. However, targeted screening may miss a significant number of cases, leading some experts to recommend universal screening to ensure early detection and treatment. Future research should explore the extent to which thyroid function screening during pregnancy should be expanded and identify

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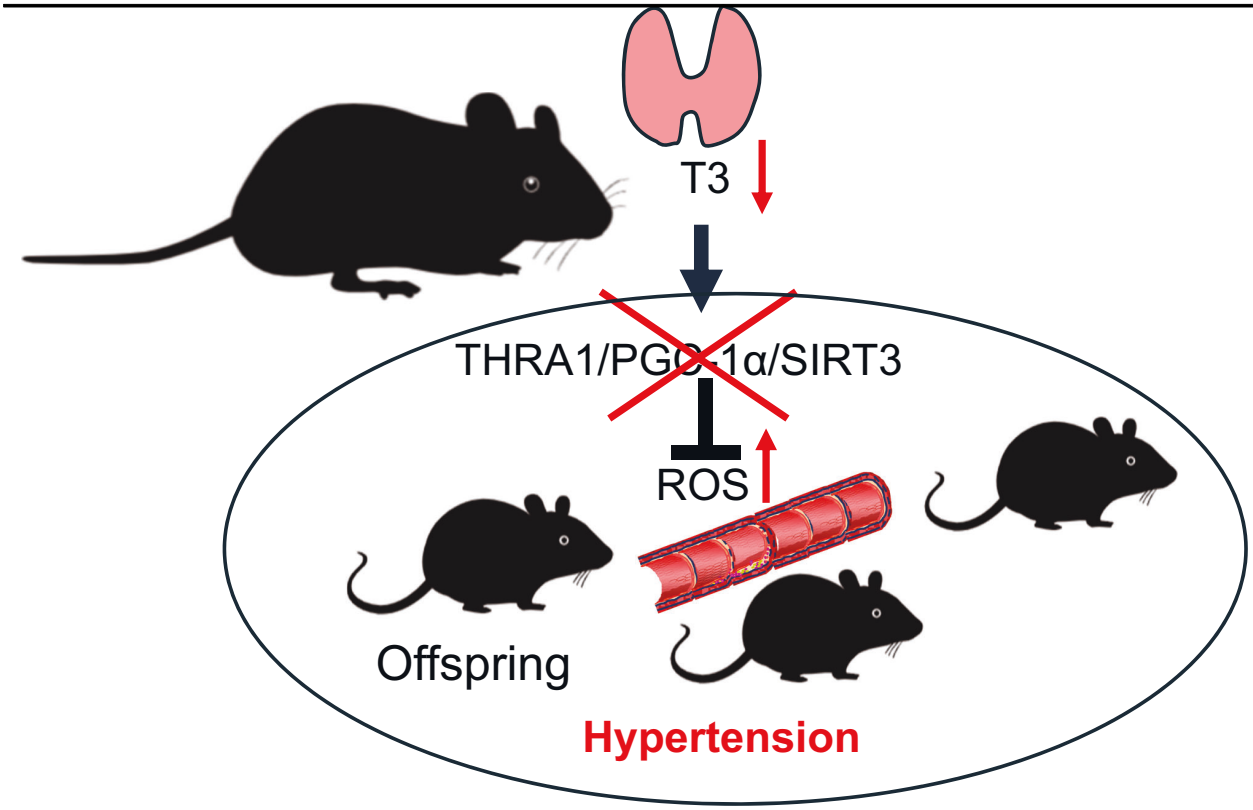

Fig. 1 Maternal thyroid function and offspring hypertension

which levels of dysfunction warrant treatment to prevent CVD, including hypertension, in offspring.

Compliance with ethical standards

Conflict of interest The author declares no competing interests.

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