




Repercussion of thyroid dysfunctions in thyroidology on the reproductive system: *Conditio sine qua non?*

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Thyroid hormones, i.e., L-thyroxine (3,5,3',5'-tetraiodothyronine, T₄) and L-triiodothyronine (3,5,3'-triiodothyronine, T₃), are vital for the normal reproductive function of *Homo sapiens* and animals by affecting directly ovarian, uterine, and placental tissues through specific nuclear receptors, modulating their development and metabolism¹, thus, alteration of the hormonal status of endocrine gland, such as hypothyroidism and hyperthyroidism, may give rise to subfertility or infertility in both humans and animals². Deiodination of T₄ via deiodinases (D1, D2, and D3) in the peripheral tissues results in the output of T₃ and reverse T₃ (rT₃). D3 possesses high expression in the uterus, amniotic membrane, and placenta in order not to transfer excessive maternal thyroid hormones toward the growing fetus, while fetal T₃ is principally produced by D1 and D2^{1,3}. Moreover, the placenta, unlike thyroid-stimulating hormone (TSH), is easily permeable to thyrotropin-releasing hormone (TRH). Maternal TRH, transported to the fetus, has been estimated to play a crucial role in controlling fetal hormonal status prior to the full maturation of the fetal hypothalamic–hypophysal–thyroid axis, 16th–18th week, 17th day, and 5th–6th week of gestations in human, rat, and sheep, respectively^{3,4}. Thyroid hormones are transpired to affect estrous cycle control, maternal ability, ovulation, sexual maturation, maintenance of pregnancy, postnatal maturation, and even lactation via molecular mechanisms. Some authors expressed hypothyroid state as attenuating proliferation of granulosa cells from preantral follicles in rats associated with diminishing the number of nucleolar organizing regions, while some propounded that the granulosa of antral follicles did not exhibit any alteration. The stage of follicular development is substantial for the causal link of hypothyroidism-to-granulosa cell proliferation¹. *A posteriori*, repercussion of thyroid dysfunctions on the ovaries of *Homo sapiens* and animals have been revealed, *inter alia*, it affects the ovarian activity in rats, *per se*, not only in prepubertal and peripubertal

period but also during pregnancy. Furthermore, maternal hormonal dysfunction of this endocrine gland may also influence the offsprings' postnatal ovarian development in rats. Maternal hypothyroidism and hyperthyroidism were asserted to attenuate postnatal follicular progression in the neonatal and prepubertal ovarian activities with a reduction in the numerical data of primordial, primary, secondary, and antral follicles in rats⁵. It has also been reported that thyroid dysfunctions affect luteal vascularization and luteolysis in cyclic and pregnant rats. Although the exact mechanism is unknown, severe hypothyroidism may lead to ovarian cysts in humans and animals through alteration in luteinizing hormone (LH), and preovulatory LH and follicle-stimulating hormone (FSH) levels. Hypothyroidism was demonstrated as attenuating endometrial thickness, the numerical value of endometrial glands, and volume and height of the epithelial layer of the uterus, while hyperthyroidism, in contrast, was reported when the numerical values of secondary and tertiary follicles and corpora lutea were greater, with a reduction of follicular atresia^{1,6}. Despite severe hypothyroidism leading to ovarian cysts, the debate is still ongoing in terms of its true causative mechanism^{7,8}. Thyroid dysfunctions act on fetal-placental development. However, it depends on the time of onset, associated conception, and severity of the condition. Clinical hypothyroidism and hyperthyroidism necessitate treatment. In addition, it was propounded that the treatment for subclinical hypothyroidism in gestation is useful as it is on the occasion of autoimmune thyroid disease^{9,10}. Herewith, hormones of this delicate¹¹⁻¹³ endocrine gland are crucial and vital, *sine qua non*, in terms of miscellaneous physiological processes of humans and animals. Furthermore, their alterations in serum concentrations do jeopardize the direct functioning of the living organisms, particularly in the reproductive system. *In fine*, the hormones of *papillon glande thyroïde* are also vital for reproductive purposes. All roads lead to the thyroid.

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