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Ovarian iodide uptake and triiodothyronine generation in follicular fluid The enigma of the thyroid ovary interaction

A.B. Ślebodziński *

Professor emeritus, Polish Academy of Sciences, ul. Promienista 166A/34, 60-157 Poznań, Poland

Abstract

Since 1928, the iodine concentration in the ovary has been known to be higher than in every other organs except the thyroid. The ovarian iodide uptake varies with sexual activities, is enhanced by estrogens and a hypothyroid state and blocked by goitrogens. The recent discovery of a sodium iodide symporter (NIS) in ovaries has offered a possible mechanism for ovarian iodide uptake and other functional similarities to its thyroid counterpart. Nevertheless, the physiological significance of ovarian iodine uptake and accumulation remains unknown. The presence of thyroid hormones (TH) in follicular fluid (FF) has been established recently. Our preliminary studies on TH in FF (1996–1998) in rabbits, pigs, horses showed that the concentration of T_4 is generally lower than that in serum and that for T_3 is within the normal range or higher. A positive correlation exists between the T_4 levels in FF and serum but not between the corresponding T_3 levels. These studies revealed, for the first time, the presence of the ovarian 5′-monodeiodinase system in FF capable of generating T_3 (ovary-born T_3) by outer ring deiodination of T_4. In mares, seasonal polyestrus, ovarian 5′-monodeiodinase (MD) activity and FF T_3 levels have been found to be higher during the ovulatory period than in the anovulatory one. The exact physiological significance of this system generating T_3 and coexisting with isoforms of TH receptors in granulosa cells has not been elucidated. A direct role of T_3 for the early follicular development, differentiation and for the steroidogenic capability of granulosa cells, although strongly suggested by data obtained from in vitro studies, has to be elucidated.

Keywords: Iodide; Follicular fluid; Ovarian deiodinase; Ovary-born T_3; Thyroxine

* Tel.: +48 61 868 5328; fax: +48 61 868 5328.
E-mail address: endocrin@rose.man.poznan.pl.

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1. Introduction

From the wide field of thyroid–ovary interaction this retrospective and current research concentrates on two aspects of the interaction in normal mature, non-pregnant females—the involvement of the ovaries in iodide uptake and the presence and origin of thyroid hormones in follicular fluid.

2. The ovaries and body iodide economy

2.1. Ovarian iodine uptake

The concentration of iodine in mammalian ovaries depends largely on sexual activity: lower in the pre-puberal and in post-menopausal periods, higher during the stage of follicular growth [1,2] and reduced during pregnancy. As shown by Elmer in his review [2] the amount of iodine found in ovarian tissue varies greatly across species, reflecting both species variability and differences in sexual activity at the time of ovarian dissection. Expressed as the concentration of iodine (μg iodine /100 mg wet tissue) the following values (mean or range) were found: in man 741, in pig 600–648, in rabbit 60–2150, in guinea pig 340 and in dog 104–161.

The accumulation of radioiodide in ovarian follicles occurs first in the walls of large Graafian follicles. It reaches a maximum 4 h later and shows a higher concentration in the central parts than in others. After 4 days, the accumulation disappears from the follicular walls and is then higher in the follicular fluid (FF) than in surrounding tissues and the blood [1]. The accumulation rate constant (K_m) is higher for small oocytes and can be within the range for K_m in the thyroid, as found in Japanese quail [3]. Although ovarian tissue does not synthesize hormonal iodo-proteins, the ovary's ability to take up and accumulate iodine is inhibited by thiocyanate, perchlorate and excessive doses of iodide (the Wolff–Chaikoff effect), as in thyroidal tissue.

2.2. The effects of hypothyroidism

There is an increase in ovarian iodide uptake during hypothyroidism induced by thiouracil. The hypothyroid state is characterized by an absolute or relative depletion of thyroid hormones (TH), altered sensitivity and ovarian response to gonadotropins leading to a rise in the content of mucopolysaccharides, followed by a tendency in some species towards the development of polycystic ovaries [4,5]. In fact, ovarian cyst formation is greatly intensified in women with primary hypothyroidism and in experimentally hypothyroid animals exposed to hyperstimulation with gonadotropins [6,7].

2.3. Exogenous estrogens

Estrogens administered to euthyroid intact female guinea pigs alter their iodine economy. Small quantities of stilboestrol increase the bodily retention of iodine in a dose-dependent manner [8]. During 24 h post-injection the highest accumulation of radioiodine, amongst the