ELEMENTS AND THE THYROID

Thyroid Hormone: Essential for Regulating Metabolism

Few would dispute that our planet is awash in environmental pollutants that adversely affect our health and quality of life and significantly increase our risk of developing diseases of modern society such as diabetes, heart disease, senile dementia, and cancer. Environmental pollutants are in the air we breathe, water we drink and bathe in, and food we eat. In excess, and when persistent, they can have profound negative effects on the basic mechanisms of our body chemistry and affect the synthesis and actions of hormones essential for maintaining our body's health. One such endocrine gland profoundly affected by natural and environmental pollutants is the thyroid, which is primarily responsible for regulating metabolism at many different levels.

Thyroid Hormone Synthesis is Iodine and Selenium Dependent

Thyroid hormone is manufactured in the thyroid gland from a simple amino acid, tyrosine, and the essential element iodine. The chemical process of attaching iodine molecules to tyrosine-rich thyroglobulin, which occurs exclusively in the lumen of the thyroid gland, requires the enzymes thyroid peroxidase (TPO) and hydrogen peroxide (H_2O_2) to convert iodide to the highly reactive iodine (I_2). If this highly reactive process is not buffered by antioxidant enzymes, it can progressively damage the thyroid gland. The primary protective enzymes in the thyroid gland that prevent this oxidative destruction are the antioxidant enzymes glutathione peroxidase and thioredoxin reductase. The activity of both of these enzymes is dependent on selenium, which is incorporated into the active site of both enzymes in the form of a unique selenium containing amino acid, selenocysteine. About 25 selenocysteine containing proteins have been identified to date, each of them playing a role in shuttling electrons from molecules like glutathione, vitamins C and E to electron-hungry (deficient) reactive oxygen species (ROS) such as H_2O_2 and other oxidized (electron deficient) molecules formed during thyroid hormone synthesis and normal oxidative metabolism.

Conversion of T4 to T3 and rT3 is Dependent on Selenium-Dependent Deiodinases

Selenium also plays a secondary role in the conversion (deiodination) of the relatively inert thyroid hormone thyroxine (T4) to the active thyroid hormone, triiodothyronine (T3). Most of the thyroid hormone manufactured by and released from the thyroid gland is in the form of T4 (about 80%), which must be converted to the active T3 in peripheral organs (mostly liver and kidney) or target cells. T3 has a much shorter half-life in the bloodstream than T4, and many tissues are dependent on local intracellular conversion of T4 to T3. All cells of the body require T3 and nuclear T3 receptors to regulate metabolism and energy production. T3 synthesis from T4 is regulated by one of three thyroid deiodinases, all three of which are selenium-dependent enzymes. Deoiodinase I (D1) is present mostly in the thyroid, kidney, and liver, and T3 formed in these organs is released into the bloodstream for availability to tissues that require direct uptake of T3, such as the heart. Deiodinase II (D2) is present in peripheral tissues, and responsible for cellular conversion of T4 to T3. The majority of T3 utilized by peripheral tissues is derived from direct intracellular conversion of T4 to T3 by D2. Every cell in the body has thyroid receptors and requires either direct uptake of circulating T3, or intracellular conversion of T4 to T3, prior to binding the thyroid receptor. D2 is responsible for most of the T3 that is produced in the body. A third deiodinase

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(D3) is responsible for deactivating T4 by converting it to reverse T3 (rT3). D2 is present in the interior (cytoplasm) of cells allowing for intracellular conversion of T4 to T3 and direct interaction with thyroid receptors. D3, on the other hand, is present on the outer surface of cells, which allows it to interact directly with T4, converting it to rT3 before T4 enters the cell and is converted to active T3. D3 is activated when conversion of T4 to T3 would be detrimental to cellular function, such as during times of excessive stressors. High cortisol, which occurs during times of excessive stress, activates D3.

Thus, selenium present in antioxidant enzymes in the thyroid gland, and in thyroid deiodinases, is essential not only for thyroid hormone synthesis, but also for activation/deactivation of T4 to T3/rT3 at the individual cell level. Without selenium and the enzymes containing it, the process of thyroid hormone synthesis would be too damaging for the thyroid due to free radical attack. Also, without selenium, T4 would not convert to the more active T3 for binding and activation of the nuclear thyroid receptor, which turns on specific gene sites regulating synthesis of key proteins and enzymes.

Iodine and Selenium Deficiencies Affect Thyroid Hormone Synthesis and Function

Since iodine and selenium are supplied in the food, water and nutrients we consume, low levels in these sources can result in deficiencies and directly impact thyroid hormone synthesis and action. This can have profound effects on many metabolic processes and directly impact proper cell differentiation and growth, tissues' and glands' ability to produce other hormones, physical development, weight maintenance, and heat production. This results in the myriad of symptoms associated with low thyroid production (thyroid) and function (peripheral cellular conversion of T4 to T3).

In some parts of the world deficiencies in these essential nutrients are severe, as is their clinical manifestation (goiter, mental retardation, cretinism). Moderate deficiencies in these essential nutrients cause more subtle effects associated with low thyroid synthesis and function. Surprisingly, even in more developed regions of the world, including the United States, iodine and selenium deficiencies persist. Part of the problem with iodine arose when iodized salt was replaced with regular salt in most restaurants, and the iodine commonly used in baking breads was replaced with bromine. Dietary shifts away from iodine-rich foods (eggs and milk) to reduce fat intake, and iodine-deplete vegan diets, have also resulted in lower overall iodine consumption.

Iodine and Selenium Antagonists Can Exacerbate Low Iodine and Selenium Conditions

Mild deficiencies in iodine and selenium can be exacerbated when natural and environmental pollutants are present that compete with and inhibit iodine incorporation into thyroid hormone and selenium incorporation into selenoproteins. Various types of competitors and inhibitors are present naturally in the food and water we consume, while some are by-products of industrial pollution. Foods such as cruciferous vegetables and soy contain goitrogens that can block iodine uptake and synthesis of thyroid hormone; however, these goitrogens generally only have significant impact when iodine intake is very low, as occurs in certain geographical regions.

More insidious are the thyrotoxic environmental pollutants bromine, arsenic, and mercury. Bromine, at high concentrations, and in the presence of iodine deficiency, competes with iodine uptake into the thyroid gland, and can replace iodine in thyroid hormone synthesis. In the presence of adequate iodine, bromine has little effect on iodine uptake and thyroid hormone synthesis; however, when iodine is low and bromine

levels are elevated this can lower both iodine uptake and thyroid hormone synthesis. Bromine is present in many different commercial products that we drink (e.g., colas), eat (e.g., bread), and expose our bodies to daily (e.g., fire-retardants).

Arsenic and mercury form extremely tight bonds with selenium, effectively removing it from gut absorption, preventing its incorporation into selenocysteine and selenoproteins (i.e., glutathione peroxidase, thioredoxin reductase, and thyroid deiodinases). Arsenic is present in high concentrations in well-water in many geographical regions of the world, including the United States. Arsenic is colorless, odorless and tasteless; therefore excessive exposure from drinking water or food grown in water contaminated by arsenic (e.g., rice) gives no warning other than the symptoms and diseases associated with overexposure.

Mercury is released into the atmosphere from industrial sources, accumulates in fish we eat, is used as a preservative for immunizations, and is released from mercury-silver amalgams. The highest exposure to mercury is from dental amalgams and fish consumption. Fish higher in the food chain contain the greatest amounts of mercury due to bioaccumulation. Mercury in fish is not thought to be as harmful as mercury released from amalgams because the former is tightly complexed with equal amounts of selenium, which essentially inactivates the mercury and prevents its bioaccumulation.

Needless to say, we are awash in toxic pollutants that can potentially affect our ability to utilize iodine and selenium to create thyroid hormone and convert the inactive form (T4) to the active form (T3) in the liver, kidneys, and peripheral tissues. Thus, low levels of iodine and/or selenium, coupled with high levels of thyroid antagonists, both natural and man-made, can have significant effects on thyroid hormone synthesis in the thyroid gland as well as on conversion of T4 to T3 within tissues.

A Simple Urine Collection Method for Detecting Levels of Iodine, Selenium, Bromine, Arsenic, and Mercury

Since these five elements (iodine, selenium, bromine, arsenic, and mercury) are excreted mainly in urine, the degree of exposure to them can be determined by urine testing. To better appreciate how thyroid agonists (iodine and selenium) and antagonists (bromine, arsenic, and mercury) might be affecting thyroid hormone synthesis and cellular conversion of T4 to T3, ZRT Laboratory has developed a urine test to monitor the levels of these five elements. Until now, collection of urine for this type of testing was cumbersome and inconvenient as it involved capturing all urine in a jug over a 24 hour period. ZRT has simplified this collection process, requiring collection of only a small amount of urine on a filter card at two convenient times during the day—first morning and last night voids. Collection is simple, and is done by either urinating directly on the filter, or urinating in a cup and dipping the filter into the urine. The saturated urine filter card is allowed to dry and then shipped to ZRT Laboratory for element testing. Elements present in the urine dried on the strip are extracted and tested by ICP-Mass Spectrometry or run directly on a mercury analyzer.

Importance of Knowing Your Thyroid-Element Status

Why is this important? Knowing your exposure to these elements will help provide insight into why you may not be synthesizing adequate amounts of thyroid hormones, or why your thyroid hormone levels in blood may be normal, but you suffer from thyroid deficiency symptoms caused by poor intracellular conversion of T4 to T3.

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