

# Supplementation of Sufficient Iodine Nutrition Intake during Pregnancy and Lactation

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## INTRODUCTION

Iodine is an essential nutrient that humans need in very small quantities. A small gland in the neck, known as the thyroid, uses iodine to produce thyroid hormones.<sup>1</sup> These hormones are vital to ensure normal development of the brain and nervous system before birth, in babies and young children. For this reason, it is very important that pregnant and breastfeeding women get enough iodine. Humans store iodine in the thyroid. As only small amounts can be stored, any excess is excreted.

Pregnancy is associated with profound changes in thyroid function and the requirement for iodine. Under the influence of a rise in the concentration of oestrogen, there is a marked increase in the concentration of serum thyroxine-binding globulin, which begins during early gestation, reaches a plateau at mid-gestation and is maintained thereafter. Also, starting in early gestation, there is an increase in renal blood flow and glomerular filtration, which leads to an increased iodide clearance from the plasma and thus to an obligatory loss of iodine. Occurring transiently near the end of the first trimester, there is direct stimulation of the thyroid gland by an increase in the concentration of human chorionic gonadotrophin that may lead temporarily to a slightly increased concentration of free thyroxine. Finally, significant changes occur in the peripheral metabolism of maternal thyroid hormones during the second half of gestation, mainly under the influence of placental type 3 iodothyronine deiodinase.

Together, these events represent profound metabolic changes associated with the first half of gestation that constitutes a transition from a preconception steady-state thyroid gland to a pregnancy steady-state thyroid gland. In order for such metabolic changes to happen, this needs an increase in hormone production by the maternal thyroid gland of about 50%. Once the new equilibrium has been reached, the increased demand for hormones during pregnancy is sustained until full term. For a healthy pregnant woman with a sufficient iodine intake before conception of about 150 µg day<sup>-1</sup>, the challenge for the thyroid gland is to adjust its hormonal output to achieve a new equilibrium and then maintain it until pregnancy is completed: this corresponds to the physiological adaptation of the thyroid economy to the pregnant state. However, when pregnancy takes place in healthy women who live in areas with an inadequate iodine intake of approximately 50–75 µg day<sup>-1</sup>, physiological

adaptation is progressively replaced by pathological alterations. Pregnancy typically acts therefore to reveal the underlying lack of iodine: the more severe the iodine deficiency, the more pronounced are the consequences for the maternal and foetal thyroid glands.

Healthy pregnant women with a sufficient iodine intake before conception and consequently adequate store of iodine in the thyroid, are able to adjust their thyroid economy for the pregnant situation. In contrast, pregnant women from iodine-deficient areas may have pathologic changes in maternal thyroid function. The main consequences are a relative decrease of maternal free thyroxine levels and an increased concentration of serum thyroid-stimulating hormone (TSH).

## **IODINE INTAKE IN THE WORLD DURING PREGNANCY**

Several countries in recent years have analyzed the iodine nutritional status during pregnancy. On one hand, it has been shown that countries without a program of universal salt iodization have less than optimal iodine nutrition during pregnancy (for example Bosnia and Herzegovina, India and Thailand). On the other hand, countries like Australia and Iran, with programs of universal salt iodization, show that this type of program may not be sufficient to reach the optimal iodine intake.

A study in Tasmania showed that the addition of iodine to salt and bread effectively corrected the deficiency of this halogen in the general population; however this strategy was not effective in correcting the insufficient iodine intake during pregnancy. In contrast, countries like Switzerland and the United States of America without programs of universal salt iodization reach an adequate iodine consumption. These developed countries, however, have permanent monitoring systems that allow the implementation of corrective actions on its population in case of deficiency. In the United States of America there has been detected a significant reduction in UIC in the last 40 years. It is noteworthy that the current UIC values are close to the minimum value of iodine sufficiency. In fact, the American Thyroid Association recommends to people of the United States of America and Canada that pregnant women should receive 150 µg of iodine in vitamin supplements.

In Latin America, countries like Argentina, Brazil, Mexico and Venezuela have recent data about iodine nutrition during pregnancy in some regions. In Argentina (Buenos Aires) the median of UIC was <150 µg/L whereas in Brazil (Porto Alegre), Mexico (Queretaro) and Venezuela (Trujillo) there was a median UIC >150 µg/L. In all these Latin American countries the universal salt iodization is mandatory. In addition, there is a considerable decline in UIC at the end of pregnancy; several countries like Bosnia and Herzegovina, Iran and Thailand have exhibited this type of behavior. The reduction in median UIC at the end of pregnancy is most evident in places where there is a clear iodine deficiency. A study in Tasmania showed that at the beginning of pregnancy a 22% of samples

had UIC levels  $< 50 \mu\text{g/L}$  and 40% at the end. This decline could suggest a depletion of iodine storage due to its consumption by the maternal-fetal binomial, its renal elimination and/or by inadequate dietary compensation.

## **IMPORTANCE OF ADEQUATE IODINE NUTRITION**

Consequences of iodine deficiency include endemic goiter, cretinism, intellectual impairments, growth retardation, neonatal hypothyroidism, and increased pregnancy loss and infant mortality, many of which were recognized beginning in the 1970s by Pharoah and colleagues in Papua New Guinea. Research since then has shown that thyroid hormone plays a particularly vital role in fetal and infant neurodevelopment in utero and in early life because it is required for oligodendrocyte differentiation and myelin distribution. Animal studies have demonstrated that low levels of thyroid hormone in early pregnancy up to midgestation, when the developing fetus is completely reliant on maternal thyroid hormone stores, impair radial migration of neurons to the cortex and hippocampus and result in behavior changes.

Insufficient iodine levels during pregnancy and the immediate postpartum period result in neurologic and psychological deficits in children. The prevalence of attention deficit and hyperactivity disorders is higher in the offspring of women living in iodine-deficient areas than those in iodine-replete regions. Intelligence quotient (IQ) levels of children living in severely iodine-deficient areas are an average of 12.45 points lower than those living in iodine-sufficient areas and are improved with iodine supplementation. In Spain, a region of mild iodine deficiency, children with urinary iodine levels more than  $100 \mu\text{g/L}$  have significantly higher IQ levels than those with urinary iodine levels less than this threshold. Although public health efforts have improved iodine nutrition over the past few decades, iodine deficiency affects more than 2.2 billion individuals (38% of the world's population) and remains the leading cause of preventable mental retardation worldwide.

## **IODINE SUPPLEMENTATION DURING PREGNANCY**

Many studies have established the benefits of iodine supplementation during pregnancy in areas of severe iodine deficiency. One of the earliest studies was a randomized controlled trial during the early 1970s in Papua New Guinea, in which pregnant women living in the remote highlands were administered injections of Lipiodol, a solution of iodinated poppy seed oil, and found to have decreased rates of fetal death and endemic cretinism for up to 5 years compared with untreated women.

In a mildly iodine-deficient, consumption of iodized salt in the 24 months preceding pregnancy,

compared with initiation of iodized salt ingestion on becoming pregnant, decreased the risk of maternal thyroid dysfunction in women with negative thyroid antibody titers. In the only 2 studies of iodine supplementation in mildly and moderately iodine-deficient women evaluating neurobehavioral outcomes, infants born to mothers who received iodine during pregnancy had improved psychological and neurocognitive measures compared with those born to nonsupplemented mothers. Berbel and colleagues reported that children of women who were both mildly hypothyroxinemic from a mildly iodine-deficient region and supplemented with 200 µg potassium iodide per day beginning at 12 to 14 gestational weeks compared with women who received no supplementation had delayed neurocognitive performance at 18 months of age compared with children of women who received supplementation at 4 to 6 gestational weeks. Similarly, Velasco and colleagues found that infants aged 3 to 18 months of mildly iodine-deficient mothers who received 300 µg potassium iodide per day during the first trimester had higher neuropsychological assessment scores than those of mothers who received no iodine supplementation.

## **IODINE NUTRITION IN LACTATION**

Because breastfed infants are reliant on maternal dietary iodine intake, recommendations for dietary iodine intake during lactation range from 250 to 290 µg/d, higher than the 150 µg/d recommended for nonpregnant and nonlactating adolescents and adults. These thresholds were determined based on a mean breast milk iodine concentration of 146 µg/L, as was measured in 37 women, and the assumption that infants ingest an average of 0.78 L/d of breast milk during 0 to 6 months and 0.60 L/d during 6 to 12 months. Data regarding breast milk iodine levels in lactating women are extremely limited. Small studies (57 women in the largest sample) have demonstrated that median breast milk iodine levels in women range from 35 to 155 µg/L.<sup>52,54-57</sup> Furthermore, breast milk iodine levels vary temporally, as was reported by Kirk and colleagues in a study of 10 lactating women in the United States. Among 108 total samples, there was considerable variation of breast milk iodide levels within and between individuals over a 3-day period. Larger studies are needed to determine the iodine sufficiency of lactating women in India. In nutshell, adequate iodine intake during pregnancy is essential to ensure proper brain development and its deficiency in critical periods generates irreversible damage. Iodine metabolism during pregnancy is different from the non-pregnant woman, and this physiological scenario should be taken in account for an adequate nutritional assessment. The UIC determination in the general population for the monitoring of iodine consumption is essential for the design and application of policies directed to ensure an adequate iodine intake. The use of iodine supplementation (multivitamins) in pregnancy should be considered especially when the consumption of table salt is reduced.

