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Influence of iodization programmes on the epidemiology of nodular goitre

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Iodine is essential for the synthesis of thyroid hormones. Iodine deficiency can affect human health in different ways, and is commonly referred to as iodine deficiency disorders (IDD). These range from defective development of the central nervous system during the fetal–neonatal life, to goitre in the adult. Only a few countries were completely iodine sufficient before 1990. Since then, a major effort has been made to introduce salt iodization to ensure sufficient intake of iodine in deficient areas. Iodine prophylaxis has been shown to exert a pivotal role in abating goitre and other iodine-deficiency disorders, and has also been shown to modulate the pattern of thyroid diseases. An increased frequency of thyroid autoimmunity and of hypothyroidism has been observed after introducing iodization programmes. Nevertheless, available evidence clearly confirms that the benefits of correcting iodine deficiency, consisting mainly of reducing nodular goitre and non-autoimmune hyperthyroidism, far outweigh the risks of iodine supplementation.

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Introduction

Iodine is essential for the synthesis of thyroid hormones. Iodine deficiency has multiple adverse effects. Iodine intake is insufficient in more than 2 billion people, and therefore deficiency of iodine intake is high on the public health agenda worldwide. The term iodine deficiency disorders (IDD) refers to the effect of iodine deficiency in individuals. The clinical consequences of iodine deficiency include goitre, which is the most common clinical manifestation, and cerebral impairment, ranging from mild cognitive defects to cretinism. The frequency and severity of the clinical manifestations are proportional to the magnitude of iodine deficiency [1–5]. When severe iodine deficiency occurs during pregnancy, it is associated with cretinism and increased neonatal and infant mortality. Iodine deficiency remains a major global threat to health and development, and is the most common cause of preventable mental impairment worldwide [6–9].

Iodine metabolism

Alimentary iodine is absorbed by the gut and is actively concentrated by the thyroid gland. The body of an adult contains about 20 mg of iodine, and the thyroid concentrates 70–80% of the total iodine content through the sodium–iodine symporter (NIS) located on the basolateral surface of thyrocytes. A normal adult uses about 80 mg/day of iodide to produce thyroid hormones. Ninety per cent of the plasma iodine is excreted by the kidney, and only a small amount in the faeces.

Iodine requirement changes with age and in relation to various physiological conditions [7]. According to the World Health Organization/International Council for the Control of Iodine Deficiency Disorders (WHO/ICCIDD), the recommended nutrient intake of iodine is 90 mcg/day in infants and children under 6 years of age, 120 mcg/day in children 6–12 years of age, and 150 mcg/day in adults. During pregnancy, the recommended intake increases to 250 mcg/day. The recommended intake in lactating women is 250 mcg/day to compensate for the iodine loss in breast milk.

When iodine intake is slightly insufficient (i.e. <100 mcg/day), thyroid stimulating hormone (TSH) induces a higher NIS expression, with an increase of thyroid iodine uptake and preferential synthesis of T3, thus allowing a normal content of intrathyroidal iodine. In chronic iodine deficiency, the thyroid content of iodine progressively decreases, the metabolic balance of iodine becomes negative, and goitre ensues [8,10,11].

Patogenesis of goitre and iodine nutrition

Nodular goitre is probably a lifelong condition that starts in adolescence or at puberty. Minimal diffuse enlargement of the thyroid gland is found in many teenage boys and girls, and is almost a physiologic response to the complex structural and hormonal changes occurring at this time. It usually regresses but, occasionally, (much more commonly in girls) it persists and undergoes further growth during pregnancy [12,13].

Marine [14] first developed the concept, that the thyroid first goes through a period of hyperplasia in response to iodide deficiency as a consequence of the resulting TSH stimulation [15]. Eventually, the thyroid enters a resting phase characterized by colloid storage. This is possibly as a result of iodide repletion or a decreased requirement for thyroid hormone. The recurrence of these two phases would eventually result in the formation of multinodular goitre [16,17], at least in genetically predisposed individuals [18,19]. Over time, functional autonomy may occur [20], with suppression of TSH. Experimental data obtained in rats fed with an iodine-deficient diet, have clarified the natural evolution of the goitre.

Thyroid follicules are functionally heterogeneous, and cell clones differ for their replicative capacity and ability to produce thyroid hormones. The clonal development of follicles with high replication capacity will induce the onset of non-functioning (cold) or hyperfunctioning (hot) nodules, in which the uptake and thyroid hormone synthesis is independent from TSH stimulation. The increase of size and function of hot nodules induces initially a slight enhancement of thyroid hormone production, which is characterized by serum thyroid hormones within normal limits and a suppressed TSH (subclinical hyperthyroidism). With the further increase of thyroid hormone production,