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Epidemiology of nodular goitre. Influence of iodine intake

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More than one tenth of the world population is to some degree affected by goitre and most of these harbour nodules. The large differences in thyroid disease prevalence between populations may be caused by genetic and environmental factors. Among the latter, iodine deficiency seems by far to be the most important risk factor. Thus, nodular goitre is a condition predominantly seen in iodine deficient areas of the world. In the present review, we evaluated in detail autopsy and ultrasound studies of the thyroid gland. In autopsy studies, large thyroid volumes and high frequencies of goitres have been reported in countries affected by iodine deficiency. Many cross-sectional studies using thyroid ultrasound investigations have been performed world-wide and reported high thyroid volumes and goitre prevalences, and to some extent also high prevalences of thyroid nodules in iodine-deficient countries. Most of these goitres were classified as nodular goitres. On the other hand, few studies have shown that abundant iodine intake may lead to development of diffuse goitres, but world-wide this has been a minor problem compared with development of nodular goitres. In the past century we have observed a trend towards smaller thyroid glands, and hopefully less than 10% of the world population will experience goitre within a few decades.

Goitre, thyroid nodules, and iodine status

Thyroid disease affects many people worldwide. The spectrum of diseases is wide, ranging from minor structural changes not influencing the life of the patients to a variety of disorders that may

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reduce the quality of life and in some circumstances also affect life expectancy. Among the mild but frequent disorders are goitre and benign thyroid nodules. These two conditions often develop simultaneously, but many subjects harbour nodules within the thyroid gland without development of goitre, and in populations with excessive iodine intake goitres are often without nodules.

Various definitions of goitre have been used during the last hundred years depending on which study methods have been available. In the early 20th century, the definition was based on autopsy findings. Goitre was often defined as a thyroid gland exceeding 30–35 g [1]. Later, various other definitions were introduced to allow investigation of people while still alive, and studies were based on inspection and palpation of the thyroid gland [2,3]. After the introduction of thyroid ultrasound examination [4,5], the definition of goitre (or 'enlarged thyroid gland') has been based on the measurement of the total thyroid volume using various principles. Most commonly, goitre is now defined as a total thyroid volume exceeding the mean size +3 standard deviations in iodine-replete adult populations, which corresponds to a total volume larger than 18 mL in women and 25 mL in men [6]. However, the upper limit of a normal thyroid gland size has been defined differently in some studies [7–11]. Therefore, the prevalence of goitre observed in a study may depend not only on the thyroid size, but also on the upper reference limit definition. Evidently, it may be difficult to compare goitre prevalences between studies.

Nodules are discrete lesions that may be detected by palpation, autopsy/surgery, ultrasound, or other types of imaging procedures. Nodular goitre is a recognizable thyroid enlargement "characterised by excessive growth and structural and/or functional transformation of one or several areas within the normal thyroid tissue" [12].

The present review will illuminate thyroid size and enlargement in various populations and describe the presence of thyroid nodules from literature. We will focus mainly on findings from autopsy and ultrasound studies, as the palpation technique has major limitations. Only studies with reports on both thyroid architecture and iodine intake in the population will be reviewed. Thyroid disease may be a consequence of non-optimal iodine intake [13,14]. Thus, we explore the role of iodine intake level as a risk factor for goitre and nodules. It is beyond the scope to discuss the serious disorders associated with iodine deficiency such as abortions, stillbirths, and reduced intellectual capacity in the offspring (Table 1).

The prevalence of goitre and intrathyroidal nodules may depend on several factors [15]. Genes undoubtedly have some impact, but the magnitude of this is uncertain [16,17]. Among the environmental factors investigated, low iodine intake is a major cause for nodular goitre. At the other end of the iodine spectrum, a high prevalence of presumably diffuse goitre has been associated with high iodine intake from seaweed in the Japanese island of Hokkaido [18], from high iodine content of drinking water in China [19], and even in the US [20].

Table 1
Definitions of iodine status and consequences of non-optimal iodine intake in populations.

Median urinary iodine concentration (μg/L)	Iodine status	Goitre among schoolchildren (%)	Spectrum of iodine associated disorders
<20	Severe ID	>30%	Endemic cretinism, hypothyroidism, endemic nodular goitre
20–49	Moderate ID	20–29.9%	Endemic nodular goitre, low IQ, hyperthyroidism more often than hypothyroidism
50–99	Mild ID	5.9–19.9%	Hyperthyroidism more often than hypothyroidism, nodular goitre
100–199	Iodine sufficiency	<4.9%	Optimal balance between various thyroid diseases
200–299	More than adequate		Autoimmunity, iodine induced hyperthyroidism (IIH)
>300	Excessive		Iodine induced hyperthyroidism (IIH), diffuse goitre, Graves' disease, autoimmune hypothyroidism

Modified from WHO/UNICEF/ICCIDD-guide [24].