INVITED COMMENTARY

What do we call a goiter?

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The prevalence of goiter and the median urinary iodine concentration are the most important indicators for assessing iodine deficiency disorders (IDD) and for defining criteria of the severity of any associated public health problem (1). For years, palpation has been the single method available for defining thyroid volume. A slight modification (2) of the method of Perez et al. (3) has been most commonly used: by definition, ‘a thyroid gland whose lateral lobes have a volume greater than the terminal phalanges of the thumbs of the person examined will be considered as goitrous’. When this criterion is met, overall thyroid volume is at least four to five times greater than normal (3).

However, as technology progressed, ultrasonography became to be considered the most reliable method for the estimation of thyroid volume (4–7). School-age children are the most useful target group for IDD surveillance (1); consequently, normative values for thyroid volume measured by ultrasonography in iodine-replete schoolchildren were needed. After a few preliminary studies (Table 1), the normative values proposed by Gutekunst & Martin-Teichert (8) were those most commonly used. A major change as compared with palpation was that the criterion for goiter was now a thyroid volume above the 97 percentile of the reference population.

The criteria of Gutekunst & Martin-Teichert (8) were also used during the early phase of a collaborative study on thyroid volume and urinary iodine conducted by Delange et al. (9) at 57 locations in 12 European countries and including 7599 schoolchildren aged 6–17 years. In this population as a whole there was, as could be expected, a highly significant inverse correlation between urinary iodine and the prevalence of goiter. However, an unexpected observation was that, when these criteria were used, the prevalence of goiter was systematically largely above the cut-off point of 5% considered as the upper limit of normal (1) at all the locations of investigation, even when the median urinary iodine concentration was above the cut-off point of 100 μg/l. Therefore, the suitability of the criteria of Gutekunst & Martin-Teichert (8) was questioned, and updated normative values were derived from a cluster made of 3265 European schoolchildren from 23 different locations in The Netherlands, the Slovak Republic, Austria and France who had a median urinary iodine of at least 100 μg/l. When these new normative values were used, the inverse relationship between urinary iodine and the prevalence of goiter persisted, but the prevalence of goiter was almost systematically below 5% as long as the urinary iodine concentration was greater than 100 μg/l (Fig. 1), further justifying the cut-off points of 5% for the prevalence of goiter and 100 μg/l for the median urinary concentration of iodine proposed by WHO, UNICEF and ICCIDD (1). These new normative values were endorsed by WHO (10).

The origin of the discrepancy between the two sets of normative values was unknown. The characteristics of the reference population studied by Gutekunst & Martin-Teichert (8) (number of children, geographical and racial origin, general nutritional status, sex) were not reported, and the possible role of genetic and environmental factors could not be evaluated, although these authors indicated that ‘mean thyroid volume was found to be similar in all ethnic and racial groups with sufficient iodine intake’ (8). The possible role of the long-term sequelae of a past history of iodine deficiency in Europe (11) was, of course, considered as one of the possible explanations for the higher values obtained during the European study (9). The results reported by Bürgi et al. (12) are therefore particularly important: in two cities in Switzerland, the authors measured thyroid volume in 408 schoolchildren aged 6–16 years with median urinary iodine concentrations of 150 μg/l. The children were born more than half a century after correction of iodine deficiency was implemented in Switzerland and, in particular, at least 1 year after the iodine content of salt had been increased from 7.5 to 15 mg/kg and the iodine intake maintained at the optimal level of 150 μg/day. The results reported by Bürgi et al. (12) were similar to those reported in the European study (Table 1). Twelve of the 408 Swiss children (3%) had thyroid volumes above the 97 percentile of the European reference population, ‘exactly what would be expected if the reference and the Swiss population were the same’ (12). It should be emphasized that, in the Swiss study, thyroid ultrasonography and urinary iodine were determined by the same investigators using exactly the same methods and equipment as in the global European study (9). This work clearly shows that the past history of iodine deficiency in Europe does not account for the difference between the two sets of normative values currently available. Another contribution to the problem is provided by the very careful and elegant study by Foo et al. (13), reported in this issue of European Journal of
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Figure 1 Relationship between the median urinary iodine concentrations and the prevalence of goiter estimated on the basis of ultrasonographic criteria at 57 locations in 12 European countries. Comparison of the results obtained using the criteria for goiter proposed by Gutekunst & Martin-Teichert (8) (left) with those based on the criteria of WHO & ICCIDD (10) (right). ULN, upper limit of normal. Adapted from Delange et al. (9), with permission.

Table 1 Average (median 50 percentile (P50) or mean) and upper limit of normal (97 percentile (P97) or mean + 2.6 s.d.) reported for thyroid volume measured by ultrasonography in iodine-replete school-age boys as a function of age. Review of the literature (references given in parentheses).

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a Derived from the graph of ref. (17).
c Delange, F, Benker G, Caron P, Eber O, Ott W, Peter F et al. (see (9)) (unpublished observations).
Endocrinology. These authors reported that, in Malaysia, thyroid volume measured by ultrasonography in 7410 schoolchildren aged 7–10 years and with a median urinary iodine concentration of 138 μg/l were much smaller (by 30–36%) than the normative values proposed by WHO and ICCIDD (10), even when adjusted for body surface area (BSA) (6–25% smaller). They were closer to the normative values reported by Gutekunst & Martin-Teichert (8) (Table 1). The authors suggested the need for population-specific references, even for BSA-adjusted thyroid volumes. This point is certainly valid, because body mass and growth velocity are markedly different in different parts of the world. However, this concept implies the elaboration of multiple regional normative value scales, and the loss of the universal criteria that were available when the volume of the terminal phalange of the thumb of the person examined was the criterion for consideration.

A further contribution to the problem, also reported in this volume, comes from the study by Xu et al. (14). These authors studied 303 schoolchildren from the Atlanta Metropolitan area, Georgia, USA, aged 7–12 years and with a median urinary iodine concentration of 282 μg/l. Their thyroid volumes were in a range between the normative values reported by Gutekunst & Martin-Teichert (8) and those reported by Delange et al. (9). If the long-term consequences of mild iodine deficiency in Europe (11) and mild iodine excess in the USA (15) can be excluded as possible explanations for the differences between Europe and the USA, the question arises of the possible role of the investigators and of the equipment used in the evaluation of thyroid volume by ultrasonography in schoolchildren.

In conclusion, the suitability of the concept of universal normative values for thyroid volume measured by ultrasonography in iodine-replete schoolchildren can be questioned. The possible need for regional evaluative scales remains open and intercalibration for the methods used for ultrasonography remains an important issue. It is interesting that, 1 year before the deadline of the year 2000 for the sustainable elimination of the disorders induced by iodine deficiency, the question ‘what do we call a goiter?’ is still current.

References

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