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Invited Commentary

Measuring iodine status in diverse populations

Measurement of iodine status is one of those things that can seem simple until you get into the details. The recent paper by Andersen *et al.*[1] in the *British Journal of Nutrition* provides some important new insights into, and an opportunity to reflect on, some fundamental considerations.

Iodine is an essential nutrient through its role in thyroid hormones, and must be obtained from the diet in sufficient, but not excessive, amounts[2]. Iodine deficiency is a global public health issue[3] and although progress has been made, there is continuing concern[4] so that it remains necessary to monitor iodine status in diverse populations. Excessive iodine consumption may be a more localised than widespread phenomenon, as relatively few food groups are rich in iodine[5], although some areas with high iodine content of drinking water, for example, also cause concern about high iodine exposures[6]. Some subpopulations, such as those with autoimmune thyroiditis, may be more sensitive to excess iodine[7].

Urinary iodine excretion (UIE) is commonly used as a population biomarker to assess recent iodine exposure or iodine status across the spectrum from deficiency to excess[2], as typically more than 90 % of ingested iodine appears in urine within 24–48 h[8]. The concentration of iodine is ideally measured on a 24-h urine sample, though practicalities (including concerns of compliance with 24-h sampling) or study logistics (such as large field surveys) may dictate the use of a timed interval other than 24 h or, more often, a convenient 'spot' urine sample.

A single measurement of a spot or 24-h urine sample cannot provide reliable information about the iodine status of an individual, due to high intra-individual variation[9]. The population median of measurements on spot or 24-h samples from a sufficiently large group, say 50–100 or more[10–12] can be used as an index of the overall iodine status of the group; this is what is suitable for comparison with established population thresholds[3]. Newer methodologies involve two independent urine iodine measurements per participant for a sufficient subsample of the study population. When followed by appropriate statistical procedures to eliminate intra-individual variation, population distribution curves of usual iodine intake or excretion can be obtained; these are suitable for evaluation of the proportion of the population with deficient or excessive intakes[2,10]. In contrast, traditional methodologies require as many as ten or twelve independent measures per individual in order to determine an individual's iodine status even within 20 % precision[13,14].

The result of urinary iodine excretion measurement is commonly expressed as 24-h UIE (μg/24 h or μg/d) in the case of 24-h collection. In the case of analysis of spot urine samples the result is expressed in terms of urinary iodine concentration (UIC, μg/l). In some instances, the UIC is adjusted for measured urinary creatinine concentration (creatinine-adjusted UIC, or UICC, μg/g creatinine). Creatinine-adjusted values can further be extrapolated to an estimate of 24-h UIE (eUIE, μg/24 h) based on the expected level of creatinine excretion for a 24-h period, since creatinine production from body creatine pools is relatively constant[15]. These different ways of expressing urine iodine are sometimes treated interchangeably, as reflected by the statement in the present Andersen *et al.*[1] paper: 'The different measures of iodine in urine were compared as they are all used to portray the iodine nutrition by the same unit (μg)'; but the units are indeed different. This generalisation may be more reasonable when the study focuses on school-aged children, whose daily urine volume approximates 1 litre. But it does not apply well to adults whose daily urine volume is usually larger. Andersen *et al.*[1] go on to demonstrate clearly that the population median iodine values can also be quite different, when the four measures UIE, UIC, UICC and eUIE are all determined within one study.

Creatinine adjustment has fallen out of favour for global comparisons, although it is intended to account for differences in hydration level of the participants of research studies. This because the expected creatinine excretion can be much lower in cases of protein malnutrition[10]. In a population sample large enough, differences in hydration are considered to cancel out, so that the population median UIC is adequately representative of the group. Excluding severe malnutrition, other factors such as age, sex (or more specifically muscle mass) and even diets high in red meat are known to influence creatinine excretion[15]. Creatinine adjustment of UIC, referred to previously, can involve the use of age- and sex-specific estimates of 24-h urine creatinine excretion to yield eUIE (μg/24 h)[16]. Andersen *et al.*[1] in their present paper have extended this principle to include age-, sex-, and ethnic-specific creatinine adjustment, having recently established that Inuit *v.* non-Inuit study participants in Greenland differed significantly in their creatinine excretion[17]. Thus, in the context of a specific study such as their investigations on Greenland populations[1], creatinine adjustment can provide advantages that outweigh the burden of additional analyses.

Andersen *et al.*[1] identified differences in iodine excretion between Inuit and non-Inuit in the present study, and noted that the ethnicity influence was accounted for by differences

in diet. This differs somewhat from the conclusions of their recent work on vitamin D status in this population, where they documented a diet–ethnicity interaction[18], but still speak of an important effect of dietary changes on nutritional status in a society in transition, which they had first documented for iodine a decade ago[19].

The key conclusion of the present work by Andersen *et al.*[1] is that the relationship between spot *v.* 24-h urine sampling as biomarkers for iodine status is not necessarily the same across the spectrum from deficiency to excess. They highlight this as a risk for misinterpretation of iodine status, depending upon the biomarker being used, particularly at higher levels of iodine excretion. This is a useful concept, as it expands on the considerations for selection and interpretation of appropriate biomarkers; it reinforces the need for validation of a biomarker for the specific purpose to which it is being applied in investigational or surveillance contexts. The Biomarkers of Nutrition for Development project is set to document these kinds of considerations for nutrients of high public health importance, including iodine[2]. Careful and appropriate selection of biomarkers will better address the questions asked in research and in population monitoring.

Kevin A. Cockell

Nutrition Research Division, Food Directorate, Health Canada, 2203E Banting Research Centre, 251 Sir Frederick Banting Driveway, Ottawa, ON, Canada K1A 0K9
email: kevin.cockell@hc-sc.gc.ca

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