Iodine

https://open-global.kcl.ac.uk/iodine/

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Related nutrients/biomarkers: selenium, iron, vitamin A

Importance of iodine for health

Iodine is an essential micronutrient required for the synthesis of thyroid hormone. The effects of iodine deficiency are known as the Iodine Deficiency Disorders and include hypothyroidism, goitre, loss of IQ and cretinism (1-3). However, iodine excess can also be harmful; optimal iodine intakes require a careful balance between deficiency and excess, and there is a U-shaped relationship between iodine intake and thyroid function (4-7).

Thyroid hormone maintains vital cellular functions and controls many metabolic processes in the body, and is crucial for optimal growth and development from conception onwards. The developing

foetus relies on adequate iodine and thyroid hormone from the mother to accelerate myelination of the nerves in the brain and central nervous system, and a deficiency in iodine during this critical period can lead to a loss of up to 10 IQ points (8). The foetus and infants are vulnerable to effects of iodine deficiency, and pregnant and lactating women are high-risk groups for iodine deficiency due to increased requirements (9-13). During lactation, women must consume enough iodine to provide for their infants as well as themselves, until lactation is complete (14, 15).

Universal Salt Iodisation (USI) is the primary public health strategy to ensure adequate population iodine intakes (16, 17). Monitoring and surveillance of iodine fortification policy is critical for its success.

Human biomarkers of population iodine intake and status

Traditionally, iodine status was assessed by population goitre rate (16), however goitre is not sensitive to recent changes in iodine intakes and can be challenging to assess manually, particularly when small. Thyroid volume, measured by ultrasound, is often used clinically and can be an adjunct in research studies. **Urinary iodine concentration (UIC) is the recommended biomarker of population iodine status (16).** Thyroglobulin (Tg) measured in serum or whole blood on dried blood spots (DBS) has proved to be a sensitive and complementary biomarker of iodine status (4, 6, 7, 18, 19). Neonatal TSH may be used to assess iodine sufficiency in the population (16). Measurement of serum TSH and one or both thyroid hormones is routine in clinical settings to diagnose thyroid disorders, but thyroid function markers are usually within normal ranges in mild iodine deficiency and not recommended for monitoring iodine nutrition.

Table: Summary of biomarkers of iodine intake and status (adapted from (22)

Table legend:

BMIC: breast milk iodine concentration; DBS: dried blood spot; NA: not applicable; Tg: thyroglobulin; TgAb: thyroglobulin autoantibodies; TSH: thyroid stimulating hormone (thyrotropin); Tvol, Thyroid volume; UIC: urinary iodine concentration; mUIC: median UIC.

Biomarker	Population assessment	Threshold for sufficiency	Thresholds for excess	Notes	Reference
UIC	Iodine status	In schoolchildren: mUIC 100–299 μg/L <20 % of sample population should have UIC<50 μg/L In non-pregnant, adult women: mUIC >100 μg/L In pregnant women: mUIC 150–249 μg/L	Population median: ≥300 μg/L in school children ≥500 μg/L in pregnant women ≥200 μg/L in populations with longstanding iodine deficiency with rapid increases in iodine intake	Reflects recent iodine intake	(16, 17)
Tg	Iodine status Iodine intakes during preceding ~month Thyroid activity	Serum: Iodine-sufficient adults: 3-40 μg/L (a) DBS: Schoolchildren: 4-40 μg/L (b) Pregnant women: 0.3-43.5 μg/L (c)	Schoolchildren: >3% of values >40 μg/L	Reference range may vary by specimen type, assay or population. Some reports of confounding due to TgAb	(a) (20) (b) (7, 19, 21) (c) (6)
Tvol	Iodine sufficiency	Schoolchildren: <5% TGR in sample population	Not established	Undertaken by palpation or ultrasound. Inter-observer variation high.	(16)
TSH	Population risk of iodine deficiency (using neonatal TSH screening data)	In neonatal TSH screening programs: <3% of values >5 mIU/L	NA	Reference range may vary by specimen type, assay or population. Neonatal TSH data may reflect population risk of moderate to severe iodine deficiency during pregnancy. May be confounded by use of iodine-containing antiseptics at birth.	(16)
BMIC	Iodine status of lactating women	NA	NA	Recommended as adjunct to UIC in lactating women	(15)

Urinary iodine concentration

Urinary iodine concentration is the recommended biomarker of population iodine status (16, 17).

Excretion of iodine in the urine reflects recent iodine intake and UIC is the primary biomarker for population iodine nutrition (9, 16, 23). UIC reflects the risk of inadequate/excessive iodine intakes in a population, and in turn, the risk of developing thyroid disorders (9).

In healthy, iodine-replete adults >90% of dietary iodine is absorbed from the small intestine and >90% is excreted within 24-48 hours (23). UIC is conventionally measured in spot urine samples and expressed as a population median in μg/L (9, 16). WHO thresholds for the median UIC reflect insufficient, adequate and excessive iodine intakes. Assessment of individual iodine status using spot UIC is not recommended due to intra-diurnal variations in intake (24-26). At population level, variations are considered to even out with adequate sample size (16, 23), and correction for hydration (e.g. with creatinine) is typically not applied (16).

UIC surveys have mainly been collected in school-age children, since they are assumed to represent much of the population, except for pregnant and lactating women, and infants. However, assessment of iodine status in women of reproductive age, pregnant women and at risk groups is encouraged as resources allow (16, 17). Note: assessment of the iodine status of lactating women using UIC alone may be inadequate since iodine is also present in breast milk; breast milk iodine concentration has been proposed as a more reliable biomarker of iodine status in lactating women (15). See Other Methods, below.

Methods

The gold standard for the assessment of iodine in urine is with inductively-coupled plasma mass spectrometry (ICP-MS), however this method requires expensive equipment and trained laboratory staff, which may not be available in all laboratories. Instead, the Sandell-Kolthoff method is an accurate and widely-used alternative.

Note: Urine is a potential biohazard, and safety precautions should be employed at all times whilst handling or manipulating urine samples.

Inductively-Coupled Plasma Mass Spectrometry

Inductively-Coupled Plasma Mass Spectrometry (ICP-MS) is a robust technique useful for analysis of multiple elements in a single sample. The ICP generates a high temperature (10,000°C) plasma source, through which the pre-treated, nebulized sample is passed. At such high temperatures, the elements in the sample are iodized. These ions then are directed into the MS, which sorts the ions according to their mass/charge ratio, which identifies individual isotopes of each element present. These are then detected by an electron multiplier tube detector, which identifies and quantifies each ion, giving the concentration of the element present.

The US CDC provides the method from their NHANES surveys: https://wwwn.cdc.gov/nchs/data/nhanes/2003-2004/labmethods/l06uio_c_met_urine_iodine_icpms.pdf

Sandell-Kolthoff Method

The Sandell-Kolthoff method is a relatively simple colorimetric method using less technical equipment, which generally has a satisfactory agreement with ICP-MS measurements (27, 28). This method uses iodine to catalyse the reduction of the yellow ceric ion to the colourless cerous form in the presence of arsenious acid, in a modification of the Sandell-Kolthoff reaction. The rate of the colour disappearance is directly proportional to the iodide concentration. The reaction must be timed precisely.

This method is simple and inexpensive to install in most laboratories, and produces little toxic waste. However, it is important to avoid all sources of contamination. Trained staff are required for the assay manipulation, and a relatively large sample size (>300) is required to obtain population iodine intake estimates with a reasonable power and precision. Sample sizes should be estimated using previous data on urinary iodine status where possible (25, 29).

Click the following link to download the method: Sandell-Kolthoff UIC method. *Kindly provided by the Human Nutrition Laboratory, ETH Zurich, Zurich, Switzerland.* Download method from https://open-global.kcl.ac.uk/iodine/

Quality control

1. For iodine analysis, all subject and laboratory consumables (plastic cups, syringes, infant nappies/diapers, collection bags, Eppendorf tubes, pipette tips etc.) should be certified trace-element free, or pre-tested for iodine contamination before use.

2. Urine should be collected without using preservatives, and urine that has been previously used for dipstick analysis e.g. for glycosuria, should not be used due to risk of contamination.

3. Pooled in-house urine quality controls need to be prepared. Ideally, persons (e.g. laboratory colleagues) with a low and high intake should provide a urine sample, which is aliquoted for use as internal quality control standards. After urine collection, the intended quality controls should be analysed at least 10 times across three different plates and compared with existing standards and controls. If the UIC obtained from volunteers is lower than that needed for adequate low and high quality controls for assay purposes, the urine can be spiked with iodine standard to obtain the desired UIC concentration. If needed, control samples can also be obtained from the CDC EQUIP scheme - see below.

4. Laboratories conducting urinary iodine analysis by ICP-MS or the Sandell-Kolthoff method are strongly encouraged to participate in the EQUIP accreditation scheme run by CDC to ensure the quality of urinary iodine analyses. See below for more information.

Further resources on the Sandell-Kolthoff method and urinary iodine assessment can be found via the WHO Guide for Programme Managers (2007)(15) and the CDC EQUIP scheme, or contact OpeN-Global directly.

Stability and storage:

Spot urine samples obtained in the clinic or at the study site should be transferred to the laboratory for processing. Transport does not have to be cold or frozen as the iodine in urine samples is stable. However, for the comfort of the laboratory operator, urine samples are best kept refrigerated.

Once samples have been aliquoted into the required number of aliquots, they should be frozen at -20°C or colder until analysis.

Iodine is stable in urine when frozen at -22°C or colder for 15 years (30). Iodine is stable in urine for repeated freeze-thaw cycles, however freeze-thaw cycles beyond requirement should be avoided to prevent unnecessary evaporation.

Thyroglobulin

Thyroglobulin (Tg) is a large (660kDa molecular weight) glycoprotein that is synthesized in the thyrocyte and secreted into the thyroid colloid. It is the framework for thyroid hormone synthesis and has an important role in intracellular regulation (31-33). Healthy euthyroid glands release Tg into the circulation in small amounts (34-36). Upon hyperstimulation of the thyroid by TSH or thyroid stimulating antibodies, production and release of Tg is elevated. Tg is a sensitive indicator of both low and excess iodine intake, following a U-shaped curve in response to iodine excretion (7), as shown in school-age children (7, 19), pregnant women (5, 6) and infants (4). Research has demonstrated the utility of Tg to confirm improved thyroid function after iodine repletion (19, 21, 37). Due to a high day-to-day variability, however, the utility of Tg as an individual biomarker of iodine status is uncertain (38).

Methods

There are numerous different ways to measure Tg, including immunoassay (including ELISA), radioimmunoassay, dedicated kits, and by mass spectrometry (6, 18, 39).

Note: Blood, as whole blood, plasma, serum or on dried blood spots, is a potential biohazard, and safety precautions should be employed at all times whilst handling or manipulating samples.

LC-MS: For an example of methods measuring Tg by liquid chromatography-tandem mass spectrometry (LC-MS), see (39) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4524993/

***Serum-ELISA*:** Click the following link to download the Serum-ELISA method: Serum Tg ELISA. *Kindly provided by the Human Nutrition Laboratory, ETH Zurich, Zurich, Switzerland.* Download method from https://open-global.kcl.ac.uk/iodine/

An ELISA technique has been developed using dried blood spots (18), which facilitates the collection, processing, storage and transport of blood samples, and is a field-friendly method of Tg assessment, suitable for use in LMIC settings. This method has validated reference ranges for iodine sufficiency in school-age children and pregnant women (6, 7, 19, 21) (see table above).

Dried Blood Spot (DBS)-ELISA Click the following link to download the DBS-ELISA method: DBS-Tg ELISA. *Kindly provided by the Human Nutrition Laboratory, ETH Zurich, Zurich, Switzerland.* Download method from https://open-global.kcl.ac.uk/iodine/

Notes: Orders from HyTest need to be made by email. See https://www.hytest.fi/home

When ordering the Anti-Tg HRP-conjugated antibody (antibody 2), ensure to quote "in agreement with ETH Zurich", since Hytest only manufacture this antibody for laboratories wishing to undertake this assay: "2TG12ccC 5E6cc Anti-Thyroglobulin HRP-conjugated, **in agreement with ETH Zurich**"

Quality control

For all methods, in-house quality controls should be prepared from volunteers with low and high Tg concentrations, respectively.

Venous blood samples can be drawn from volunteers and spotted onto filter paper cards using a pipette set to 50 µL. Note: blood should be drawn into the appropriate tube: **blood tubes with EDTA as an anticoagulant should not be used to handle blood for Tg analysis,** since the EDTA can interfere with sample assessment (40).

Standards should be produced using washed red blood cells and the Biorad Liquicheck Tumor Marker Controls # 547, 548 and 549. Haematocrit and blood spot volume should be carefully controlled when these reference materials are produced. For an example method, please contact OpeN-Global.

Venous blood samples

Venous blood samples should be drawn by appropriately-trained personnel. Blood should be drawn into the appropriate tube: **blood tubes with EDTA as an anticoagulant should not be used to handle blood for Tg analysis**, since the EDTA can interfere with sample assessment (40). (This recommendation also applies when collecting blood from volunteers to prepare in-house DBS control cards.)

Serum or plasma should be separated using a centrifuge according to manufacturers' instructions, within 60 minutes or less. After centrifuging, check that the serum has properly separated. Discard any haemolysed samples. Transfer into the designated labelled storage vials, and transfer to the freezer without delay.

Plasma/serum samples should be frozen at -20°C or colder until analysis.

Stability: Results from stability testing of Tg in serum and on DBS is inconsistent. Some reports state that serum Tg is stable when frozen at -20°C and there is no influence of freeze thaw cycles (41) whereas other reports have suggested that serum Tg is vulnerable to freeze thaw cycles (small decrease in Tg with 3 cycles, large decrease after subsequent cycles (40). Repeated freeze-thaw cycles should therefore be minimised to only those necessary.

Dried blood spot (DBS) sample

It is important to collect dried blood spots correctly. See https://open-global.kcl.ac.uk/common-methods/ for advice on taking DBS sample cards.

DBS card samples should be frozen at -20°C or colder in airtight bags containing a desiccant, until analysis.

Thyroglobulin is stable on DBS when frozen at -20°C or colder for 15 weeks, and there is minimal effect of freeze-thaw on samples (18, 19, 40), however these should be minimised and care should be taken to ensure the card stays dry by regularly replacing the desiccant in the storage bag and ensuring dry conditions during defrosting.

Data interpretation

Assay specific thresholds (serum, DBS) should be applied, and age- and population-specific cut offs should be used. See the table above.

Influence of Thyroglobulin Antibodies

Thyroglobulin antibody (TgAb) positivity may confound Tg assay measurement (42), however, the relationship is unclear since the association between TgAb and Tg concentration in assays is poor (43), and data to date are inconclusive (39, 44-46). No apparent interference of TgAb with population Tg results measured on DBS from pregnant women was found in data from eleven countries (6), though other studies suggest an interference of TgAb in the metabolic clearance of Tg, and therefore its measurement (47). The influence of TgAb can also method-dependent.

Eventual screening is only indicated in adults as TgAb are generally rare in children (48). It is currently not considered necessary to measure DBS-Tg and DBS-TgAb in parallel for assessment of iodine status in population studies.

Other methods

Thyroid Volume

The size of the thyroid gland changes inversely in response to iodine intake, and due to a relatively long lag time, it can give an indication of historical iodine intakes, though it is not suitable to assess response to recent changed in iodine intakes. Goitre means a thyroid gland that is enlarged, with a volume greater than the terminal phalanx of the thumbs of the subject being examined (16). This non-invasive, empirical technique has been used in many epidemiological surveys of iodine nutrition and endemic goitre, and population total goitre rate was one of the first measurements undertaken to assess the iodine status of a population. A more precise assessment of thyroid volume (Tvol) by ultrasound has been widely used to assess iodine deficiency. Tvol tends to decrease with time following initiation of iodine supplementation in previously endemic countries, though because Tvol can also increase with excessive iodine intakes, Tvol is not a sensitive stand-alone biomarker to distinguish between deficient and excessive population iodine intakes.

Palpation

The assessment of Tvol by palpation requires careful training by medical personnel.

The basic method is given in the WHO Guide for Programme Managers (2007) (15).

Ultrasound

Measuring thyroid size by ultrasound is a safe and non-invasive technique that can be done in 2-3 minutes per subject in the field. It requires specialist training to be undertaken correctly because results may be biased by inter-observer variation (i.e. between different technicians). It is more accurate than palpation.

Reference values have been proposed by a WHO/Nutrition for Health and Development Iodine Deficiency Study Group Report (49), available here: https://academic.oup.com/ajcn/article/79/2/231/4690086

Method for determining thyroid size by ultrasonography (http://www.ign.org/p142003263.html?from=0142002801 courtesy of IGN, linked to the WHO Guide for Programme Managers (2007)).

Method for determining thyroid size by ultrasonography (courtesy of EUthyroid http://euthyroid.eu)

Thyroid stimulating hormone

TSH, also known as thyrotropin, is secreted from the pituitary gland in response to changes in circulating thyroid hormone, in an intricate negative feedback mechanism involving the hypothalamus-pituitary-thyroid (HPT) axis. Serum TSH rises when T4 levels are low, to stimulate the thyroid gland to produce more T4. When T4 levels are high, TSH falls. Moderate to severe iodine

deficiency may lower circulating T4 levels, therefore moderately-to-severe iodine deficient populations may have a higher serum TSH level than iodine-sufficient populations (16).

TSH is routinely measured in many countries as part of neonatal congenital hypothyroidism screening programs, usually by heel prick. It is not recommended to monitor TSH as a biomarker of iodine surveillance, though secondary analysis of neonatal data can help establish population iodine status (16). The prevalence of neonates with elevated TSH levels is therefore a good indication of moderate-to-severe iodine deficiency during pregnancy, but its value in mild iodine deficiency is uncertain (50, 51).

In addition to newborn screening, TSH is routinely used in clinical practice as a sensitive marker for hypo- and hyperthyroidism, and can be used as a diagnostic tool (alone or in conjunction with other tests) for thyrotoxicosis (52). Paired with T4 data, population-level TSH values are valuable in estimating population prevalence of thyroid dysfunction. Age-specific reference values should always be used (48).

Data interpretation

When a sensitive TSH assay is used on samples collected 3-4 days after birth a <3% frequency of TSH values >5 mIU/L indicates population iodine sufficiency (16).

Note: interpretation can be confounded by use of iodine-containing antiseptics at birth (16).

Breast milk iodine concentration

During lactation, breast milk iodine concentration is a more accurate biomarker of iodine status than urinary iodine concentration in exclusively breastfeeding women (15). It is recommended as an adjunct to urinary iodine concentration measurement in lactating women.

Analysis of breast milk iodine concentration (BMIC) can be performed using ICP-MS.

Method

Examples of ICP-MS methods in published literature (53, 54) are found via the following open-access links:

https://www.ncbi.nlm.nih.gov/pubmed/26563466

https://www.ncbi.nlm.nih.gov/pubmed/25153367/

Quality control and technical assistance

Quality Control

Please see the relevant methods for specific instructions on quality control.

Technical assistance

For technical assistance and questions on methods of population iodine assessment, please contact OpeN-Global at https://www.open-global.kcl.ac.uk/contact or, for urinary iodine procedures, write to the CDC EQUIP programme: https://www.cdc.gov/labstandards/equip.html

Laboratory accreditation

Urinary iodine procedures

US Center for Disease Control and Prevention: EQUIP Accreditation Scheme

Ensuring the Quality of Iodine Procedures (EQUIP) is a standardization program that addresses laboratory quality-assurance issues related to testing for iodine deficiency. The US Center for Disease Control and Prevention(CDC)'s EQUIP program currently assists more than 126 iodine laboratories in more than 60 countries. CDC provides each laboratory with quality-control materials, analytical guidelines, and technical training and consultation so that these laboratories can accurately measure iodine levels in their national surveys. Three times a year, CDC sends participating laboratories EQUIP samples for analysis. Participation is free.

For more information and details of how to become and EQUIP-accredited laboratory, visit the EQUIP website: https://www.cdc.gov/labstandards/equip.html

Thyroid ultrasound (EU only)

OpeN-Global users based in the European Union and wishing to undertake thyroid ultrasound measurements are invited to participate in ARCUS (Advanced Reader Certification for Unified Studies), an online training and certification tool with the aim of standardizing the training of ultrasound observers as well as thyroid ultrasound measurements in population-based studies. ARCUS consists of a comprehensive thyroid image data repository for the training and certification of ultrasound observers. Successful completion of the three thyroid modules leads to a certification according to the Study of Health in Pomerania (SHIP) standards. This certification has no clinical application; it is uniquely for the purpose of standardizing thyroid ultrasound measurements in population-based studies.

ARCUS is a EUthyroid initiative developed by a Euthyroid partner, and is available here: http://euthyroid.eu/training/

For further details on other laboratory accreditation, validation or proficiency testing schemes, please see the OpeN-Global page on Laboratory accreditation: https://open-global.kcl.ac.uk/accreditation/

Useful links and further reading on human biomarkers of iodine status

Iodine Global Network

The Iodine Global Network (formerly the International Council for the Control of Iodine Deficiency Disorders, ICCIDD), is a non-profit non-governmental organisation that was established in 1986. It has the strategic goal to attain optimal iodine nutrition worldwide. The IGN core role is to advise on scientific and policy issues to achieve optimal iodine nutrition, in partnership with over 100 regional and national coordinators and partner agencies including UNICEF, the Global Alliance for Improved Nutrition and Nutrition International. The IGN provides numerous resources for program managers and researchers working on iodine nutrition. IGN have created a resource of information for programme managers on iodine, and offer a regularly-updated global scorecard of worldwide iodine status.

Website: http://www.ign.org

World Health Organization

The World Health Organisation (WHO) provides guidance on the assessment of population iodine status: Assessment of Iodine Deficiency Disorders and Monitoring their Elimination. A Programme Manager's Guide; available here. Further, the WHO *Vitamin and Mineral Nutrition Information Service (VMNIS)* have several resources on iodine: Micronutrient deficiencies: iodine, Urinary iodine concentrations for determining iodine status in populations (2013), Database on iodine deficiency.

Website: http://www.who.int/vmnis/indicators/urinaryiodine/en/

Biomarkers of Nutrition for Development

For a comprehensive review of iodine biology and biomarkers, including the interpretation of biomarker results and constraints around using them, consult the Biomarkers of Nutrition for Development (BOND) review for iodine, available as an open-access resource: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4093988/

UNICEF

UNICEF Nutrition (https://www.unicef.org/nutrition/) features a wealth of information on iodine, including:

Guidance on monitoring of salt iodisation (2018):
https://www.unicef.org/nutrition/files/Monitoring-of-Salt-Iodization.pdf

Sustainable Elimination of Iodine Deficiency (2008):
https://www.unicef.org/publications/index_44271.html

Data on worldwide prevalence of iodine deficiency: https://data.unicef.org/topic/nutrition/iodine-deficiency/

US Centers for Disease Control and Prevention(CDC)

Along with running the EQUIP scheme to ensure the quality of urinary iodine assessment (see page 4), CDC have several resources on iodine: Iodine and breastfeeding, and International Micronutrient Malnutrition Prevention and Control (IMMPaCt) Program, which works with global partners to contribute CDC skills and resources to eliminate micronutrient malnutrition among vulnerable populations throughout the world. IMMPaCt focuses primarily on helping eliminate deficiencies in iron, vitamin A, iodine, folate, and zinc.

EQUIP: https://www.cdc.gov/labstandards/equip.html

IMMPaCT: https://www.cdc.gov/nutrition/micronutrient-malnutrition/about/index.html

Iodine and breastfeeding: https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/diet-and-micronutrients/iodine.html

EUthyroid

The EUthyroid Project is a pan-European initiative with the aim of investigating and optimizing the iodine intake of the European population, in cooperation with national European authorities. One of its primary goals is to optimize and harmonize population iodine biomarker assessment methods across Europe. Euthyroid has created guidelines for researchers conducting population studies, with a focus on the monitoring of iodine deficiency disorders. It includes general recommendations and issues related to study planning; detailed instructions and recommendations for specimen collection and sample handling, and an overview of laboratory analysis related to urinary iodine concentration and thyroid function parameters.

Website: http://euthyroid.eu

The American Thyroid Association

The American Thyroid Association (ATA) is the leading worldwide organization dedicated to the advancement, understanding, prevention, diagnosis and treatment of thyroid disorders and thyroid cancer. The ATA produces numerous guidelines and manuals on thyroid health.

Website: https://www.thyroid.org

The European Thyroid Association

The aims of the European Thyroid Association are to promote knowledge in the thyroid field (fundamental and clinical) and improve knowledge of the thyroid gland and its diseases. Similar to the ATA, the ETA produce many useful guidelines and publications.

Website: https://www.eurothyroid.com

Further reading

Dried Blood Spot thyroglobulin as a biomarker for iodine status:

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Breast Milk Iodine Concentration as biomarker for iodine status in lactating women:

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