

**Functional Medicine University's
Functional Diagnostic Medicine
Training Program**

**INSIDER'S GUIDE
INTERPRETATION AND
TREATMENT: URINARY
HALIDE TEST**

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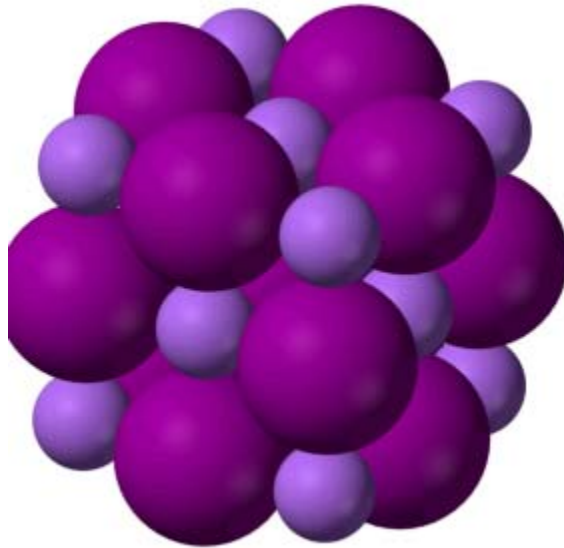
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Iodine



Iodine is an essential element required for normal function of the thyroid gland, immune system, and the integrity of thyroid and breast tissue.

Specific tissues in the body require adequate iodine and the reduced form of the element, iodide for normal metabolism and optimal health. Adequate iodide uptake and organification of iodine by the thyroid gland is required for the production, storage and release of thyroid hormones. **Triiodothyronine (T₃)** regulates metabolism in several tissues by affecting energy production and neuronal and sexual development.

Iodine insufficiency is associated with “sub-clinical” thyroid deficiency, weight gain, loss of energy, goiter and impaired mental function.

Iodine is also concentrated in breast tissue where it elicits anti-proliferative effects and protection against fibrocystic breast disease and cancer. Iodine and organic iodine compounds are also concentrated and secreted by the gastric mucosa, salivary glands and the cervix.

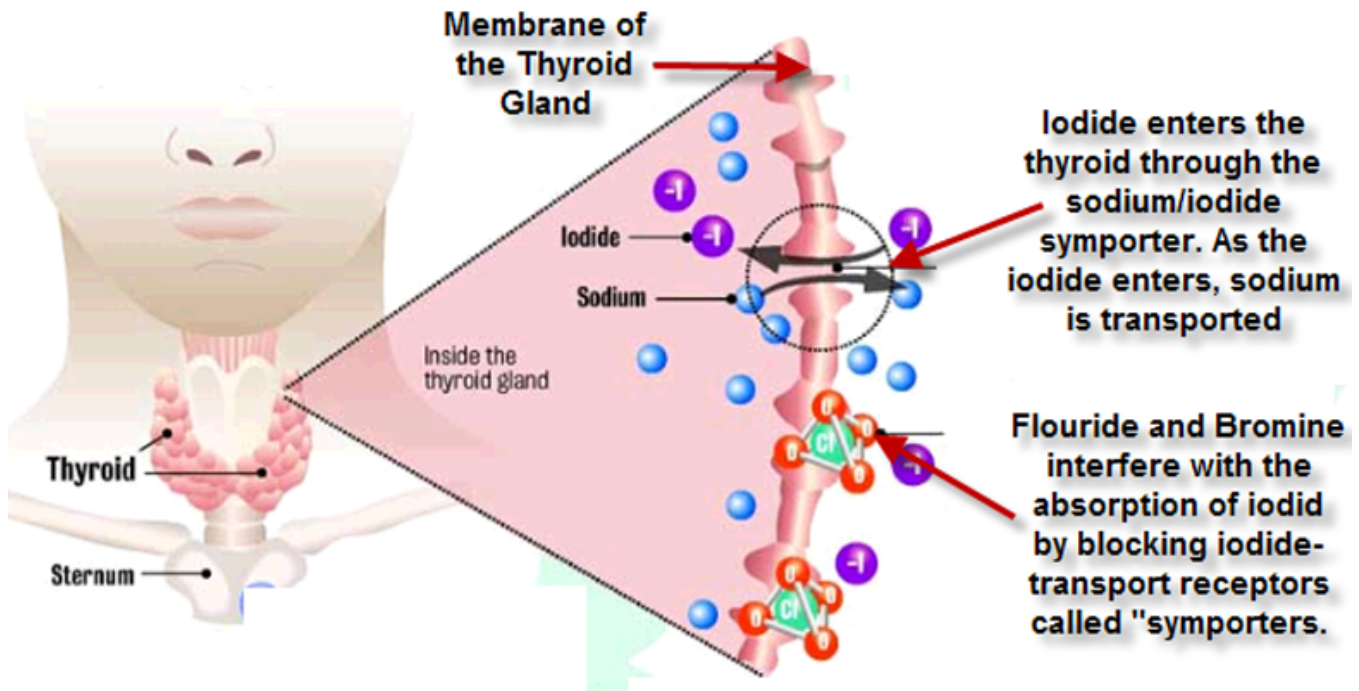
Sub-optimal total body iodine status is associated with insufficient intake of the essential element and **excessive intake of the highly antagonistic halides; bromide and fluoride.**

Iodine status and metabolism is affected not only by iodine intake but also by intake and retention of these **goitrogenic halides (bromide and fluoride).**

Iodine sufficiency and the retention of antagonistic bromide and fluoride can be readily assessed by analyses of iodine, bromine and fluoride in urine after administration of a loading dose of iodide/iodine with the functional medicine test called **urinary halide test.**

Iodide uptake by specific cells is mediated by the **energy-dependent sodium/iodide symporter (NIS)**.

Sodium-Iodide Symporter (NIS)



The **sodium-iodide symporter (NIS)** is also known as **solute carrier family 5, member 5 (SLC5A5)**

As its name indicates, the sodium-iodide symporter simultaneously transports both Na⁺ and I⁻ ions across the basolateral membrane from extracellular fluid (i.e. blood) into the thyroid epithelial cell.

Thyroid epithelial cells (also called **follicular cells** or **principal cells**) are cells in the thyroid gland that produce and secrete thyroxine (T₄) and triiodothyronine (T₃).

Thyroid epithelial cells (also called **follicular cells** or **principal cells**) are the only cells in the body which can absorb iodine. These cells combine iodine and the amino acid tyrosine to produce and secrete thyroxine (T₄) and triiodothyronine (T₃).

T₃ and T₄ are then released into the blood stream and are transported throughout the body where they control metabolism (which is the conversion of oxygen and calories to energy).

The ability of the thyroid gland to transport and concentrate iodide from blood is absolutely necessary for the synthesis of thyroid hormones. The key player in this process is the **sodium-iodide symporter**.

Active transport of iodine into the thyroid gland is an important step in the process of iodide organification and the formation of triiodothyronine (T_3) and thyroxine (T_4). The symporter is stimulated by TSH, thereby increasing iodine uptake and iodination of tyrosine.

Considering the critical role of iodine in thyroid function, it is not surprising that abnormalities in expression or function of the symporter can lead to thyroid disease.

It is well known that the toxic halides, **fluoride and bromide**, having a similar structure as iodine, can **competitively inhibit iodine absorption and binding in the body**.

Once bromide and fluoride are absorbed, they bind tightly to the iodine receptors in the body.

In addition, they can bind to the transport cells for iodine (sodium-iodide symporter--NIS) and damage the transporter cells. The oxidized form of both bromide and fluoride are stored in the fat.

Sources of Fluoride and Bromide

Bromine toxicity: Skin rashes, severe acne, appetite loss, fatigue, metallic taste. Bromine can inhibit T_4 and T_3 production. In addition, brominated tyrosine can accentuate hypothyroidism.

Fluoride toxicity: Skin rashes, acne, gastritis, migraine-like headaches, stomatitis.

Bromide Sources



- PBDE is a bromine-based fire retardant used in carpets, mattresses, upholstery, furniture and various electronic equipment.

- **Hot tubs** use bromine instead of chlorine.
- **Medications:** AtroventInhaler, Atrovent Nasal Spray, Pro-Banthine(for ulcers), anesthesia.
- All bakery products that use white flour contain bromine.
- **Brominated vegetable oils** used as an emulsifier in citrus-flavored soft drinks such as Mountain Dew, Gatorade, Sun Drop, Squirt and Frescato help fat-soluble citrus flavors stay suspended in the drink.
- Bromide can be found in medications, citrus drinks and commercial bread products as potassium bromate (a dough conditioner). In the 1960's bromide replaced potassium iodate creating a lower supply of iodine in our food and increasing thyroid-blocking halides.

Fluoride Sources



Fluoride exposure can come from many sources such as public drinking water, toothpaste, and lesser known items like processed cereal, fruit juices, wine, beer, soda and tea.

Many psychoactive drugs including Prozac, Paxil and Luvox (Littleton) are fluorinated medications.

How to Test for Urine Halides?

Urine Halides; Pre & Post Loading

Iodine	$\mu\text{g}/\text{mg cr}$	$\text{mg}/24 \text{ hr}$	Reference Range	Iodine levels include iodine and iodide oxidized to iodine. Excretion percentage is calculated by dividing the patient's $\text{mg}/24\text{hour}$ iodine result by the iodine/iodide dosage (in mg) recorded on the requisition form, then multiplying by 100.
Sample 1 PRE	17		0.1- 0.45 $\mu\text{g}/\text{mg cr}$	
Sample 2 POST	43	25	0.1- 0.45 $\text{mg}/24 \text{ hr}$	
% Excretion/24 hr		50%		

Bromine	$\mu\text{g}/\text{mg cr}$	$\text{mg}/24 \text{ hr}$	Reference Range	Bromine levels represent total bromine plus bromide, as measured by ICP-MS. Bromide is antagonistic to iodide, and is abundant in commercially produced baked goods, soft drinks, pesticides, brominated chemicals and some medications.
Sample 1 PRE	1.7		< 7 $\mu\text{g}/\text{mg cr}$	
Sample 2 POST	2.8	8	< 7 $\text{mg}/24 \text{ hr}$	

Fluoride	$\mu\text{g}/\text{mL}$	$\text{mg}/24 \text{ hr}$	Reference Range	Fluoride in urine is measured using an ion specific electrode. Fluoride is neurotoxic, compromises integrity of bone, and interferes with iodide metabolism. Primary sources of fluoride include fluoridated water, beverages, toothpaste/mouth washes, dental treatments and some medications.
Sample 1 PRE	1.3		< 1.1 $\mu\text{g}/\text{mL}$	
Sample 2 POST	1.5	0.86	< 1.3 $\text{mg}/24 \text{ hr}$	

Creatinine	Result	Reference Range	Urine Creatinine is used to account for urinary dilution effects in less than 24-hour collections and to assess the collection completeness in 24-hour collections. For estimation of glomerular filtration rate (GFR), a Creatinine Clearance test is recommended.
Sample 1 PRE	38	35- 225 mg/dL	
Sample 2 POST	570	600- 1900 $\text{mg}/24\text{hr}$	

The Urine Halides test provides comprehensive assessment of iodine sufficiency and retention of antagonistic halides in a single test. The test requires a spot urine specimen (first morning void preferred) for determination of baseline halide levels.

An oral loading dose of **iodine/iodide (Iodoral)** is ingested and all urine is collected for the subsequent 24 hours. Iodine and displaced bromide and fluoride are measured in the urine and the results for each element are reported as $\mu\text{g}/\text{gm}$ creatinine and $\mu\text{g}/24$ hours. Iodine

status is assessed by evaluation of the percentage of the ingested dose that is excreted. Low iodine excretion is suggestive of greater bodily retention and need.



The specific halides are analyzed in urine.

Clinical Protocol

There are simple ways of lowering the levels of bromine and fluoride in the body.

1. **Stop ingesting bromine and fluoride** containing food and medicines
2. **Take iodine.** The use of iodine will also cause bromine and fluoride to be released from other tissues in the body in addition to the thyroid. Taking iodine in physiologic doses can help to competitively inhibit the binding of bromine and fluoride
3. **Eat unrefined salt (NaCl).** Salt can also help with the removal of bromine and fluoride. The chloride in salt is part of the halide family (iodide, chloride, fluoride and bromide). Chloride can competitively inhibit bromine and fluoride and help the kidneys excrete bromine and fluoride. A low-salt diet will exacerbate bromine and fluoride toxicity.

When rats are subjected to a low-salt diet, the half-life of bromine is prolonged 833% as compared to rats given a normal salt diet. Unrefined salt is an effective tool to help lower bromine and fluoride levels in the body.

Use clinical judgment with patients with hypertension.