# Iodine and Thyroid Function

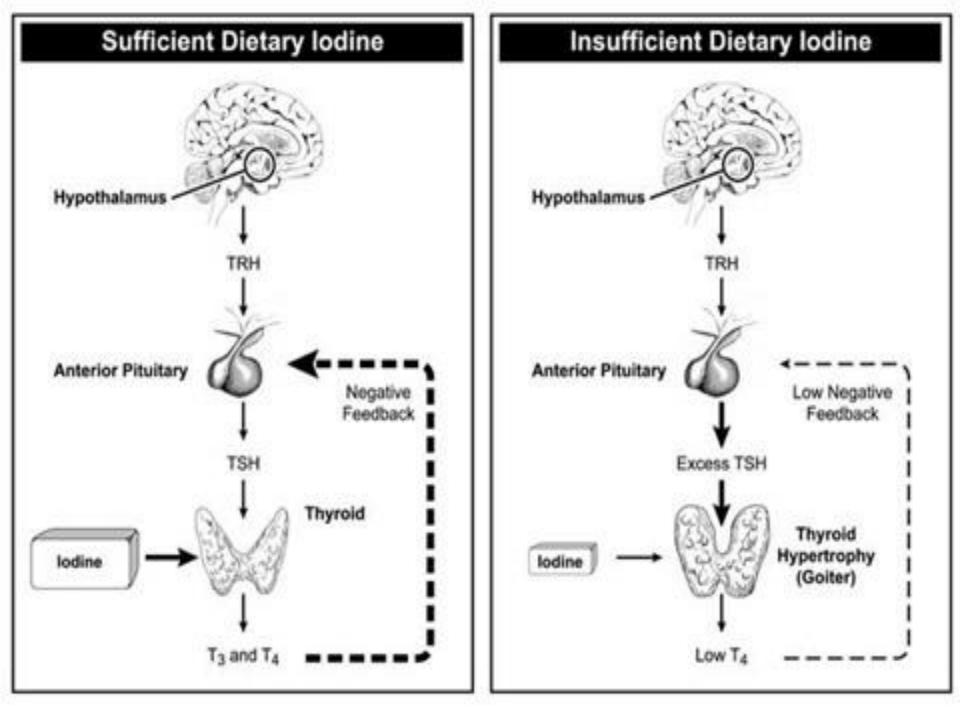
A Question of Balance

### Swiss Physician J.F. Coindet 1812

Had success treating goiter (extreme hypothyroidism) with seaweed and reasoned elemental iodine was the primary reason for his patient's improvement. He tried tincture of iodine at 250 mg per day with great success in 150 goiter patients

#### French Physician Gene Lugol 1829

Devised his formula of 12.5 to 37.5 mg of iodine with potassium iodide in water as the most efficient and sufficient dose. Addition of potassium iodide increased the solubility of iodine sufficiently to be more clinically valuable.



# IODINE

 Iodine is the one halogen the body requires for many biochemical processes.

- chlorine, bromine and fluorine are the others in order of increasing oxidizing potential
- 0.05 mg/day of iodine is necessary to prevent goiter but is not enough for optimal health
- One gram of salt contains 77 mcg of iodine. Because of the high chloride content in table salt, some experts estimate that only about 10% of the iodine in iodized salt is actually absorbed.
- Even though the chloride in table salt is a competing halide (chlorine - halogen) there is enough uptake of iodine in iodized salt from the potassium iodide to prevent goiter.
- The recommended daily allowance (RDA) of iodine is 150 mcg
  - somewhat higher for pregnant women and certain other groups

### **Iodine Containing Foods**

- Iodized salt, sea salt, and salty foods
- All dairy products (milk, sour cream, cheese, cream, yogurt, butter, ice cream)
- Margarine
- Egg yolks
- Seafood (fish, shellfish, seaweed, kelp)
- Foods that contain carrageen, agar-agar, algin, or alginate all of these are made from seaweed
- Many prepared and/or cured meats (ham, bacon, sausage, corned beef, etc)
- Fresh chicken or turkey with broth or additives injected
- Dried fruit
- Canned vegetables
- Commercial bakery products
- Chocolate
- Molasses
- Soy products (soy sauce, soy milk, tofu)
- Any vitamins or supplements that contain iodine
- FD&C red dye #3 this appears in many foods or pills that are red or brown, including colas

# **Medications Containing Iodine**

- Amiodarone
- Cordarone®
- Pacerone®
- Iodoquinol
- Yodoxin®
- Vytone®
- Potassium iodide
  - SSKI® (Lugol's solution)
- x-ray dyes
  - CAT scans
  - IVP's
  - arteriograms
  - Myelograms

- Medicated Douches
  - Bet adine® Medicated Douche
  - Massengil® Medicated Douce
  - povidone- iodine douches
  - **Iodine topical ointments** 
    - Povidone-
    - Betadine® ointment
- KI Syrup®
  - Pediacof Syrup®
  - Pima Syrup®
- Kelp

# IODIDE TRAPPING

The basil membrane of the thyroid cell has the specific ability to pump iodine into the interior of the thyroid cell. This is called *Iodide Trapping*.

In a normal gland the iodine pump concentrates the iodide to about 30 times the concentration in blood. The rate of trapping is influenced by TSH in a negative feedback control method. (17)

### Sodium – Iodide Symporter

- An integral membrane protein that resides in the membrane of thyroid epithelial cells
- Simultaneously transports both Na+ and I- ions from extracellular fluid (i.e. blood) into the thyroid epithelial cell
- Abnormalities in expression or function of the symporter can lead to thyroid disease
- Most highly expressed in thyroid epithelial cells
  - Lower levels of expression can be detected in mammary gland, salivary gland, stomach and colon
  - None of these tissues is known to organify iodide
  - Presence of the symporter in mammary gland leads to secretion of iodine in milk, which is probably important for thyroid function in neonatal animals

#### Sodium – Iodide Symporter

- One atom of iodine is transported into the cells for every 2 atoms of sodium via the sodium/iodine symporter (NIS)
- There is also a chloride/iodide symporter called pendrin
- Goitrogens can bind to the NIS receptor and damage it preventing iodine from entering the cell
- Normal saliva/serum iodide ratio is about 42. Less than 20 may be due to toxins or very high levels of bromine/fluorine binding to the symporter

 The receptor can possibly be repaired with vitamin C (3000 mg/day) and Celtic (unrefined) sea salt. (16)

# CHEMICAL GOITROGENS

- Bromine
  - from fruit fumigants and processed bakery products
- Chlorine
  - chloramine byproduct from drinking water chlorination
- Ammonium perchlorate
  - rocket fuel found in tap water
- Fluorine
  - naturally occurring in well water plus drinking water fluoridation
- Thiocyanate
  - from cigarette smoke

# DIETARY GOITROGENS

#### Cruciferous vegetables including:

- Broccoli
- Brussel sprouts
- Cabbage
- Cauliflower
- Kale
- Kohlrabi
- Mustard
- Rutabaga
- Turnips

#### Other Foods Containing Goitrogens

- Millet
- Peaches
- Peanuts
- Radishes
- Soybean and soy products, including tofu
- Spinach
- Strawberries

# **Dealing with Dietary Goitrogens**

- The goal is not to eliminate goitrogenic foods from the meal plan, but to limit intake so that it falls into a reasonable range.
- Limiting goitrogenic intake is often much more problematic with soy foods than with cruciferous vegetables, since soy appears in so many combination and packaged food products in hidden form. Ingredients like textured vegetable protein (TVP) and isolated soy concentrate may appear in foods that would rarely be expected to contain soy.
  - Isoflavones like genistein appear to reduce thyroid hormone output by blocking activity of an enzyme called *thyroid peroxidase*. This enzyme is responsible for adding iodine onto the thyroid hormones.
- A standard, one cup serving of cruciferous vegetables 2-3 times per week, and a standard, 4-ounce serving of tofu twice a week is likely to be tolerated by many individuals with thyroid hormone deficiency. It's worth it to try and include these foods in a meal plan because of their strong nutritional value and great track record in preventing many kinds of health problems.
- Cooking does appear to help inactivate the goitrogenic compounds found in food. Both isoflavones (found in soy foods) and isothiocyanates (found in cruciferous vegetables) appear to be heat-sensitive, and cooking appears to lower the availability of these substances. In the case of isothiocyanates in cruciferous vegetables like broccoli, as much as one third of this goitrogenic substance may be deactivated when broccoli is boiled in water.

#### Salivary, Urinary or Serum Iodine ?

- There is ample evidence of renal iodine clearance in the literature in Dr. Abraham's references and some evidence of salivary uptake from other sources.
- According to Mr. Zareba under a NASA grant, the mean correlation coefficient (*r*) between iodine elimination for blood/saliva was 0.99, for blood/urine, 0.95, and for saliva/urine, 0.97.
- The absolute value of iodine concentrations in urine revealed marked variability, which was corrected by adjusting for creatinine levels. (15)
- With a normal symporter there is excellent correlation between the iodine concentration increase in serum and saliva. However, the timing is different.

#### Salivary, Urinary or Serum Iodine ?

- From Bruger and Member, thyroxine was not concentrated from the blood to saliva but elemental potassium iodide (KI) was from 5 to 7 times that of the blood.
- The maximal amount of iodine concentrated in the saliva occurred 1 to 2 ½ hours after ingestion of KI peaking to 1200 times the initial salivary iodide. The salivary/blood iodine ratio in the control period was 6 and reached a maximum of 28, 8 hours after ingestion of the iodide. (18)
- Obviously measuring salivary iodide within several hours of supplementation will result in a very high unusable reading. This effect has been verified by our own tests.
  - Note that normal iodide trapping in the thyroid is about 30 times that in the blood.

#### Salivary, Urinary or Serum Iodine ?

The hypothesis is that since the salivary iodide uptake from the interstitium and thyroid trapping iodide from the blood is approximately the same order over time, the saliva uptake can be a rough indication of thyroid uptake.

If this is true then the saliva/urine ratio can be a rough indication of thyroid iodide sufficiency.

There is some anecdotal evidence from nontraditional research to suggest this relationship.

### IODINE AND CHRONIC FATIGUE

- Dr. Brownstein writes: "The illnesses that iodine/iodide has helped are many. These conditions include fibromyalgia, thyroid disorders, chronic fatigue immune deficiency syndrome, autoimmune disorders as well as cancer. Most patients who are deficient in iodine will respond positively to iodine supplementation.
- In fact, I have come to the conclusion that iodine deficiency sets up the immune system to malfunction which can lead to many of the above disorders developing. Every patient could benefit from a thorough evaluation of their iodine levels." (2)

#### Iodine and Fibrocystic Breast Disease

Mainland Japanese women have a very low incidence and prevalence of FDB and breast cancer. (13) Several investigators have proposed that the essential element I was the protective factor in mainland Japanese. (4 - 10)If indeed, the essential element I is the postulated protective factor, the administration of I to American women in amounts equivalent to that consumed by mainland Japanese women would be expected to protect them from breast cancer and improve FDB, as previously proposed by Stadel for breast cancer and confirmed for FDB by Ghent et al. (7)

 Based on data supplied by the Japanese Ministry of Health, the average daily I intake in mainland Japanese is 13.8 mg. (6)

### IODINE and BREAST CANCER

- The administration of thyroid hormones to I-deficient women may increase further their risk for breast cancer.
- In a group of women undergoing mammography for screening purposes (14) the incidence of breast cancer was twice as high in women receiving thyroid medications for hypothyroidism (most likely induced by I deficiency) than women not on thyroid supplement.
- The mean incidences were 6.2% in controls and 12.1% in women on thyroid hormones.
- The incidence of breast cancer was twice as high in women on thyroid hormones for more than 15 years (19.5%) compared to those on thyroid hormones for 5 years (10%).

#### **Case Examples**

■ J was supplementing Iodoral® (7.5 mg KI + 5 mg Iodine per tab) at the rate of 50 mg/day for nine months (without adverse effect) encouraged by the idea of clearing mercury toxicity (a dental assistant) and tested at 25 PPM saliva and 60 PPM/urine iodide. One would expect that after nine months supplementation at this dosage, iodine sufficiency would have been reached. The saliva/urine ratio of

< 1 suggests this conclusion.

### **Case Examples**

- Dr. T supplementing for many years with an organic bound iodine in seaweed extract tested 17 PPM saliva and 15 PPM urine. The supplementation will continue but one would expect sufficiency with this long term supplementation. Again the ratio approached 1.
  B supplementing 6 months 12.5 mg/day Iodoral® tested 9 PPM saliva and 6 PPM urine
  - suggesting a higher dosage could be used to approach higher residual levels and a lower ratio suggesting sufficiency as not reached.

The 24 urine iodine loading test would be appropriate.

#### **Case Examples**

B supplementing 6 months 12.5 mg/day Iodoral® tested 9 PPM saliva and 6 PPM urine suggesting a higher dosage could be used to approach higher residual levels and a lower ratio suggesting sufficiency is not reached.

The 24 urine iodine loading test would be appropriate.

- M was not supplementing but ate substantial amounts of seafood and mostly Mexican foods but very little US produced processed foods. M's saliva tested 17 PPM and urine 15 PPM.
- 20 other subjects were tested who were not supplementing except for iodized salt and multivitamin tabs with iodine in the 100 ug range. None were consuming substantial ocean dwelling foods. Usual tests were 1 PPM saliva and 0.1 PPM urine. The absolute values are very low and the ratio is 10.
  - A 24 hour urine loading tests would probably support this conclusion.
- Testing was performed in the morning with no fast required. It is recommended that a 12 hour fast, 8:00 PM to 8:00 AM for example, be required in order to minimize the effects of hydration.

PT	thyroid	volume	TSH	MIU/L	T4	Mcg/dl	FT4	Ng/dl	FT3	Pg/dl
	pre	post	pre	post	pre	post	pre	post	pre	post
1	4.35	3.6	7.8	1.4	9.2	7.9	0.85	1.3	2.9	2.5
2	5.5	5.5	2.0	2.2	10.7	8.9	1.1	1.1	2.5	2.5
3	4.7	5.6	3.4	5.1	9.6	6.4	1.1	1.1	2.7	2.8
4	5.9	12	2.7	6.1	8.7	0.8	1.2	1.2	3.0	3.2
5	5.7	8.9	1.4	1.1	6.3	6.3	1.0	1.2	2.9	2.9
6	11.6	9.5	1.0	0.34	7.5	6.9	1.2	1.1	2.9	2.7
7	7.0	6.1	1.4	2.3	8.2	6	1.0	0.84	2.9	2.7
8	6.7	7.5	2.3	1.3	9.4	7.4	1.0	1.15	2.7	3.1
9	15.8	14.7	0.76	0.53	9.7	8	1.2	1.3	3.1	3.4
10	9.2	7.7	21.5	11.9	8.3	5.4	1.2	0.9	2.8	2.6
MEA N	7.7	8.1	4.4	3.2	8.8	7.1	1.1	1.1	2.8	2.8
SD	3.6	3.3	6.34	3.6	1.3	1.1	0.12	0.16	0.17	0.31
р		0.29		0.18	6	<.01		0.34		0.50

Effect of Iodide Supplementation in daily amount of 12.5 mg for 3 consecutive months on thyroid volume and thyroid function tests

# **IODINE OR NO IODINE**

- Iodine increases thyroid function if the individual is iodine deficient
- Iodine decreases thyroid function if the individual is sufficient
- We don't know the optimal dose or what individual factors affect outcome



#### Thyrodine Quantitative Fluid Analyzer for Iodide

An instrument that precisely measures iodide concentrations in body fluids. The analyzer will very accurately report these parameters:

- In saliva as an indirect measurement of the interstitial indirect measureme
- Indice in whole blood as an indirect measurement of the sodium/iodine symporter efficiency.
- Indine in urine as an indicator of the body's indine sufficiency

# **Future Studies**

- The Thyrodine Device does not purport to provide sensitivities less than 0.1 mg/L (PPM) but is sensitive enough to measure the uptake effects of iodine supplementation whether in Lugol's formula (as Iodoral® of 7.5 mg potassium iodide and 5 mg elemental iodine) or other organic form such as kelp, dulse or seaweed extract.
- The hypothesis of measuring the ratios of saliva vs urine iodine as a measure of sufficiency and blood vs. urine as an indicator of availability of iodine for the tissues (iodine symporter) is unproven except from anecdotal information.
- We have started a clinical trial to evaluate iodine supplementation and thyroid function. We will see what levels of bromide, chloride and fluoride are in the urine as well as iodine and hope to find out if there is some competition between halides and if iodide supplementation above sufficiency levels cause thyroid dysfunction.



- 1. Hintze, G., Emrich, D., Kobberling, J., Treatment of endemic goitre due to iodine deficiency with iodine, levothyroxine or both: results of a multicentre trial. European Journal of Clinical Investigation, 19:527-534, 1989.
- 2. Brownstein, D., Clinical experience with inorganic, non-radioactive iodine/iodide. The Original Internist, 12(3):105-108, 2005
- 3. Eskin B., Bartuska D., Dunn M., Jacob G., Dratman M., Mammary Gland Dysplasia in Iodine Deficiency, JAMA, 200:115-119, 1967.
- 4. Eskin, B., Iodine Metabolism and Breast Cancer. Trans. New York, Acad. of Sciences, 32:911-947, 1970.
- 5. Funahashi, H., Imaj, T., Tanaka, Y., et al, Suppressive Effect of Iodine on DMBA-Induced Breast Tumor Growth in the Rat. Journal of Surgical Oncology, 61:209-213, 1996.
- 6. Ghent, W., Eskin, B., Low, D., Hill, L., Iodine Replacement in Fibrocystic Disease of the Breast, Can. J. Surg., 36:453-460, 1993. 7. Derry, D., Breast Cancer and Iodine, Trafford Publishing, Victoria B.C., 92, 2001.
- 8. Vishnyakova, V.V., Murav'yeva, N.L., On the Treatment of Dyshormonal Hyperplasia of Mammary Glands, Vestn Akad Med Navk SSSR, 21:19-22, 1966.
- 9. Cann S., Netten J., Netten C., Hypothesis: Iodine, selenium and the development of breast cancer, Cancer Causes and Control 11:121-127, 2000.
- 10. Ghandrakant, C., Kapdim MD, Wolfe, J.N., Breast Cancer. Relationship to Thyroid Supplements for Hypothyroidism. JAMA, 238:1124, 1976. 11. Epstein, S.S., Steinman, D., Breast Cancer Prevention Program. Macmillan, NY, 1998, pg 5.
- 12. Waterhouse, J., Shanmvgakatnam, K., et al, Cancer incidence in five continents. LARC Scientific Publications, International Agency for Research on Cancer, Lyon, France, 1982.

#### References

- 13. Stadel B., Dietary Iodine and Risk of Breast, Endometrial, and Ovarian Cancer, The Lancet, 1:890-891, 1976.
- 14. Ghandrakant, C., Kapdim MD, Wolfe, J.N., Breast Cancer. Relationship to Thyroid Supplements for Hypothyroidism. JAMA, 238:1124, 1976.
- 15. Grazyna Zareba, Elsa Cernichiari, Lowell A. Goldsmith, and Thomas W. Clarkson., Biological Monitoring of Iodine, a Water Disinfectant for Long-Term Space Missions. (1) Center for Space Environmental Health, (2) Department of Dermatology, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 USA, (3) Department of Environmental Medicine, University of Rochester School of Medicine and Dentistry, Rochester School of Medicine and Dentistry of Rochester School of Medicine, University of Rochester School of Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY 14642 USA16.
- 16. David Brownstein, MD., Iodine. Why You Need It Why You Can't Live Without It. 2nd Ed. 2006
- 17. Guyton & Hall, Textbook of Medical Physiology 10th ed.:858, 859)
- 18. Maurice Berger, Samuel Member, On The Excretion of Iodine in the Saliva, From the Research Laboratory, Department of Medicine, New York Post-Graduate Medical School and Hospital, Columbia University
- 19. De la Vieja A, Dohan O, Levy O, Carrasco N: Molecular Analysis of the Sodium/Iodide Symporter: Impact on Thyroid and Extrathyroid Pathophysiology. Phys Rev 80:1083-1105, 2000.
- 20. Dohan O, De la Vieja A, Paroder V, etc: The sodium/iodide symporter (NIS): Characterization, regulation and medical significance. Endocrine Reviews 24:48-77, 2003.
- 21. Fugiwara H, Tatsumi K, Miki K et al: Congenital hypothyroidism caused by a mutation in the Na+/I- symporter. Nature Genetics 16:124, 1997.
- 22. Spitzweg C, Heufelder AE: The sodium iodide symporter: its emerging relevance to clinical thyroidology. Europ J Endocrinol 138:374, 1998.