New Insights in Integrative Medicine To Support Healthy Thyroid Function

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The most common causes of acquired thyroid disorders are:

- Iodine deficiency
- Autoimmune disease
- Iatrogenic (radiation, surgery and drugs)
- Environmental toxicity, such as heavy metals, halides and xenoestrogens
- Nutritional deficiency

Environmental Hazards:

- PCB’s
- Oestrogenic and growth hormones in food consumption
- Xeno oestrogens in cosmetics, personal care products, household cleaning chemicals
- Halide toxicity

Aoki Y. Polychlorinated biphenyls, polychlorinated dibenzo-p-dioxins, and polychlorinated dibenzofurans as endocrine disrupters--what we have learned from Yusho disease. Environ Res. 2001 May;86(1):2-11
Metametrix USA
(Diagnostic Insights Australia)
- Organophosphates Profile - Urine
- Bisphenol A Profile
- Phthalates & Parabens Profile
- Chlorinated Pesticides
- PCBs
- Volatile Solvents
- Porphyridins Profile
- Toxic Metals – Whole Blood
- BPA, Phthalates & Parabens, and Organophosphates Combo Profile
- BPA and Phthalates & Parabens Combo Profile
- Urinary Halides
The low affinity site could be displaced by hGRF (1-44)-NH2, hGRF (1-29)-NH2 and rGRF (1-29)-NH2. A synthetic growth hormone releasing peptide (GHRP) also interacted with the low affinity GRF binding site. Lead dose-dependently displaced the binding of [125I]GRF to its pituitary receptors. The IC50 of lead for inhibiting [125I]GRF binding was 0.195 mM added lead or 52 pM free lead.

The data suggest that one mechanism by which lead may affect pituitary function is through inhibition of receptor binding.

The effect of cadmium on thyroxine (T4) outer ring monodeiodination was studied *in vivo* and *in vitro* in the rat liver. One microgram of T4 was incubated with rat liver homogenates in 50 mM Tris--HCl buffer, pH 7.4, with or without 0.5, 5, and 50 mM dithiothreitol (DTT) for 60 min in the presence of 10(-8) to 10(-3) M CdCl₂, and the amount of 3,5,3'-triiodothyronine (T3) produced was determined by a specific radioimmunoassay.

*Subcutaneous injection of CdCl₂, 1 mg/kg BW/day, 5 days a week for 10 weeks, to the rats resulted in a significant reduction in serum T3 concentration (by 37%) and hepatic T3 production from T4 (by 78 to 92%).*
In vitro addition of 1 microM to 1 mM CdCl2 to liver homogenates caused a concentration-dependent reduction in T3 generation. Without DTT a 50% reduction in the T4 to T3 converting activity was caused by $4 \times 10^{-6}$ M CdCl2. DTT (0.5 to 50 mM) partially restored T3 generation roughly in a concentration-dependent manner.

These results indicate that cadmium has some effects on the metabolism of thyroid hormone.

Ellingsen et al. (2000) reported finding impaired thyroid function in a group of 47 chloralkali workers exposed to Hg, whom they compared with 47 controls.

The exposed workers showed a statistically significant rise in reverse T3 (rT3), a rise that was dose-related.
Mercury and other dental metals may be playing a role in some cases of thyroid nodules. In 1995 the journal Analyst reported on a recent study showing that heavy metals, including mercury, were found to be high in malignant and benign thyroid nodular tissue. The researchers examined concentrations of antimony, iron, iodine, rubidium, scandium, selenium, mercury, silver, cobalt, chromium and zinc in malignant and benign thyroid nodules (the latter 5 elements are metals commonly used in dentistry).

Zaichick VYe, Tsyb AF, Vtyurin BM. Trace Elements and Thyroid Cancer. Analyst 1995;120(3):817-21
Interestingly, T3 was significantly lower with the longer (210 months) exposure time in comparison with the group having shorter (29 months) exposure duration.

The mean TSH levels were significantly higher in workers exposed in comparison with the control group. This rise in TSH was independent of exposure time, but it was definitely associated with the Pb-B levels. The increase being more pronounced with mean Pb-B levels of 2.66 +/- 0.2 micromole/l (55.4 +/- 4.25 microg/dl) when compared with the group having mean levels of 1.51 +/- 0.30 micromole/l (31.5 +/- 6.20 microg/dl). The rise in TSH associated with Pb-B levels was only statistical valid, however, the levels fall within the normal laboratory range.

**We thus conclude that the Pb-B levels of > or = 2.4 micromole/l (50 microg/dl) enhance the pituitary release of TSH without having any significant alterations in the circulating levels of T3 and T4.**

Elevated cortisol leads to:

- Decreased fT3
- Increase rT3
- Decreased peripheral hormone metabolism by inhibition of the enzyme 5-deiodinase
- Increased risk of auto-antibody production and subsequent increased risks of AITD
Hyperinsulinaemia

- Elevated insulin levels trigger increased production and release of Thyroxine Binding Globulin (TBG) from the liver.
- This results in elevated levels of bound T4 and T3 and a deficiency of free thyroid hormones available to have metabolic cellular activity.
- This will result in symptoms of hypothyroidism but often goes undetected.
In high fat diet induced obesity, instead of increased serum T(3) and T(4) secondary to higher circulating leptin and thyrotropin levels, elevated serum rT3

T3/rT3-ratio, which is supposed to reflect the tissue thyroid hormone metabolism, is significantly increased in insulin resistant subjects. This supports a link between thyroid function and IR.

Diagnostic Evaluation

- Barnes Basal temperature test
- Iodine patch test
- The 24 hour urinary iodine excretion test
  - FFP or Doctors Data
- Thyroid function test (blood work)
- Palpation of thyroid (goitre or nodules)
## Hypothyroidism Blood Labs

<table>
<thead>
<tr>
<th></th>
<th>T4</th>
<th>TSH</th>
<th>T3</th>
<th>Interpretation</th>
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<tbody>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>High</td>
<td>Normal</td>
<td>Mild (subclinical) hypothyroidism</td>
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<td>Low</td>
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<td>Hyperthyroidism</td>
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<tr>
<td>Low or normal</td>
<td>Low</td>
<td>Low</td>
<td>Low or normal</td>
<td>Rare pituitary (secondary) hypothyroidism</td>
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</tbody>
</table>
• TRH
• TSH: if >2, then include:
  • fT4
  • fT3
  • rT3
  • Thyroid antibodies
    • thyroid peroxidase antibody (TPOAb)
    • thyroglobulin antibody (TgAb) and
    • thyroid stimulating hormone receptor antibody (TRAb)
• 25-OH –D (D3)
• Iron studies
• Selenium RBC
• Zinc RBC
• Copper RBC
• Spot urinary Iodine (?)
• Fasting insulin
• Blood Lipid Panel
• AM fasting cortisol (start) or 24 hour urinary cortisol excretion test or ASI
• If Female: Oestradiol (test of day 2-3 of menses)

http://2_thyroid.pdfwww.nacb.org/lmpg/thyroid
Interpretation of TFT

Adults

- **TSH (0.1 - 4 mU/L)**
  - optimal 1-2
  - subclinical hypothyroidism 2-4 mU/L
  - clinical hypothyroidism >4 2-4 mU/L

- **fT3 (3.5 - 6.3 pmol/L)**
  - optimal 5-6 pmol/L

- **fT4 (11 – 19 pmol/L)**
  - optimal 16+ pmol/L

**Interpretation of TFT**

- **rT3**: the ratio of T3/rT3 multiplied by 100 should be between 1.06 to 1.13
  - if this ratio is <1, reverse T3 dominance is present
- **Reverse T3** is virtually inactive having only 1% the activity of T3 and being a T3 antagonist binds to T3 receptors blocking the action of T3
- **Normal physiological production ratio of T4 to T3** is **3.3 : 1**

If reverse T3 dominance is present, then slow release T3 therapy may need to be initiated once adrenal issues, hyperinsulinaemia, nutritional deficiencies, environmental toxicity have been ruled out and/or treated.

- Slow release T3 therapy (S4) – GP Rx only
- Reverse T3 dominance is very often overlooked

Galton VA, Schneider MJ, Clark AS, St Germain DL. Life without thyroxine to 3,5,3'-triiodothyronine conversion: studies in mice devoid of the 5'-deiodinases. Endocrinology. 2009 Jun;150(6):2957-63
Hypothyroidism: Signs and Symptoms

- Slow Pulse
- Lethargy
- Puffy face
- Muscle fatigue
- Loss of eyebrows in outer third
- Carpel tunnel
- Depression
- Headaches
- Menstrual disturbance
- Hyperlipidemia
- Growth retardation in children, delayed teething and slow mental development
- Dull facial expression
- Hoarse voice with slow speech
- Intolerance to cold
- Dry, course skin, hair and nails
- Weight gain
- Drooping eyelid
- TSH levels are high, decreased T3 and T4 count
1,25-Dihydroxyvitamin D3 inhibits thyroid hormone-induced osteocalcin expression in mouse osteoblast-like cells via a thyroid hormone response element

Significantly low levels of vitamin D were documented in patients with AITDs that were related to the presence of anti thyroid antibodies and abnormal thyroid function tests, suggesting the involvement of vitamin D in the pathogenesis of AITDs and the advisability of supplementation.

The nuclear receptors for 1,25-dihydroxyvitamin D3 (VD) and 3,5,3'-triiodothyronine (T3), that is, VDRs and T3Rs respectively, control aspects of homeostasis, cell growth and differentiation. They activate transcription from response elements consisting of direct repeats, palindromes and inverted palindromes of a variety of hexameric core-binding motifs. VDRs bind preferentially to direct repeats spaced by three nucleotides, whereas T3Rs bind to direct repeats spaced by four nucleotides. VDRs and T3Rs can function as homodimers but heterodimerization with retinoid X or retinoic acid receptors increases their affinity for DNA in vitro and resulting transcriptional activity in vivo. We recently observed the formation of VDR-T3R heterodimers. Here we show that the polarity of the binding of such heterodimers to the VD response element of the rat 9K (relative molecular mass 9,000) calbindin gene promoter was 5'-T3R-VDR-3', whereas on the mouse 28K calbindin VD response element this polarity was reversed to 5'-VDR-T3R-3'. We also show that the ligand for the downstream receptor controls the transcriptional activity of the heterodimeric complex. Thus, polarity seems to be an important regulatory property of heterodimeric nuclear receptor complexes.
Ferritin is considered the true indicator of stored iron status

- Reference range of 120-200 ug/L
- Target level > 150 ug/L
- Retest at regular intervals
Copper toxicity displaces zinc and competes for absorption

Copper toxicity related to oestrogen dominance

Oestrogen dominance partially suppresses thyroid function
How Much Iodine is Enough?

<table>
<thead>
<tr>
<th>Population sub-group</th>
<th>Amount</th>
</tr>
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<tbody>
<tr>
<td>Adults</td>
<td>150 µg/day</td>
</tr>
<tr>
<td>Pregnancy and Lactation</td>
<td>200 µg/day</td>
</tr>
<tr>
<td>Children (6-12 years)</td>
<td>120 µg/day</td>
</tr>
<tr>
<td>Infants (0-5 years)</td>
<td>90 µg/day</td>
</tr>
</tbody>
</table>

(µg = micrograms)
Meet the Halides
A study published in May this year suggests that some halogenated phenolics, including current use compounds such as plastic monomers, flame retardants and their metabolites, may disrupt thyroid hormone homeostasis through the inhibition of DI activity in vivo.

## Urinary Halides Test

- **Iodine**
  - Levels include iodine and iodide, oxidized to iodine.
  - Excretion percentage is calculated by dividing the patient's mg/24 hour iodine result by the iodine/iodide dosage (in mg) recorded on the requisition form, then multiplying by 100.
  - **Reference Range:**
    - mg/24 hr: 0.1 - 0.45 mg/24 hr
  - % Excretion/24 hr: 84%

- **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.
  - **Reference Range:**
    - mg/24 hr: < 7 mg/24 hr
    - µg/mg cr: 2.5
    - mg/24 hr: 3.2

- **Fluoride**
  - Levels 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.
  - **Reference Range:**
    - mg/24 hr: < 1.3 mg/24 hr
    - µg/mL: 0.81

- **Creatinine**
  - Reference Range: 600 - 1900 mg/24 hr
  - Urine Creatinine is used to assess the collection completeness in 24-hour collections. For estimation of glomerular filtration rate (GFR), a Creatinine Clearance test is recommended.
  - **Result:** 1300
Sources of Fluoride

- Toothpaste enhanced with fluoride
- Fluoride Supplements
- Fluoridated Water Supplies
- Food processed with fluoridated water
- Mouthwash enhanced with fluoride
The chlorine tree
The assistance and support of the following colleagues is gratefully acknowledged

Associate Professor Kerry Bone
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