Old view/vision

Hormone deficiencies are rare:

• 1 in 40 persons (below the lower reference limit)
• or 1 in 100
• or 1 in 500
• or 1 in 1000
Actual vision/view

Hormone Deficiencies are frequent, very frequent
Facts

We are all born with Hormone Deficiencies:

35 important hormones
....impossible to be optimal in all these hormones at birth
The Endocrine System develops in the embryo.
Facts

Many are born with some degree of Thyroid Deficiency:

... not only in iodine-deficient areas
Map 4.2. Iodine deficiency.
The smile might appear at 26 weeks' development, but the new techniques clearly show limb movements at 8 weeks, the foetus leaping, turning and "jumping" at 11-12 weeks, intricate movement of fingers at 15 weeks & yawning at 20 weeks.
Newborns => ↑ serum PCB’s & pp’DDE’s

SUBJECTS: 68 women/newborns pairs from South Portugal, non-intensive agriculture area

FINDINGS:
• Mean serum PCBs congeners and pp'DDE levels = 1.62 ng/mL ± 0.39 & 1.11 ± 0.69 ng/mL for maternal & 1.45 ± 0.25 ng/mL & 0.85 ± 0.50 ng/mL for cord serum, respectively.
• Congeners distribution pattern followed the order PCB 153>180>130, both for maternal and cord serum).
• Sign. corr. (p<0.05) between maternal & cord serum concentrations. The umbilical cord/maternal serum ratio were 0.90 & 0.76, resp. for ΣPCB and pp'DDE
• Women in urban centers have ↑ PCB levels, while
• Older primiparous women that live at rural area => ↑ pp'DDE
• ↑ Consumption of more fat rich foods => PCBs
• ↑ ingestion of vegetables and fruits => ↑ pp'DDE.

CCL: PCB & pp'DDE => pass the placenta barrier and target the fetus. Even in non-industrialized areas, and in non-intensive agriculture areas, like the Southern Portugal => ↑ risk of organochlorine overexposure during pregnancy.

Organochlorines in maternal serum/milk

=> ↓ T3 RU

Table: Crude and adjusted β-coefficients (95%CI) in thyroid parameters associated with a doubling of pollutant conc. In regression analyses*

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>T3RU</th>
<th>Cord serum</th>
<th>Maternal serum</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Crude</td>
<td>Adjusted&lt;sup&gt;abc&lt;/sup&gt;</td>
</tr>
<tr>
<td>PCB’s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal serum</td>
<td>-0.011**</td>
<td>(-0.021 to -0.002)</td>
<td>-0.012**</td>
</tr>
<tr>
<td>Milk</td>
<td>-0.010**</td>
<td>(-0.019 to -0.001)</td>
<td>-0.010**</td>
</tr>
<tr>
<td>p,p’-DDE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal serum</td>
<td>-0.014**</td>
<td>(-0.024 to -0.003)</td>
<td>-0.016*</td>
</tr>
<tr>
<td>Milk</td>
<td>-0.011**</td>
<td>(-0.019 to -0.002)</td>
<td>-0.014*</td>
</tr>
<tr>
<td>HCB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal serum</td>
<td>-0.014</td>
<td>(-0.032 to 0.003)</td>
<td>-0.014</td>
</tr>
<tr>
<td>Milk</td>
<td>-0.014**</td>
<td>(-0.027 to 0.001)</td>
<td>-0.015*</td>
</tr>
<tr>
<td>transNonachlor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal serum</td>
<td>-0.005*</td>
<td>(-0.010 to -0.001)</td>
<td>-0.006**</td>
</tr>
<tr>
<td>Milk</td>
<td>-0.013*</td>
<td>(-0.020 to -0.006)</td>
<td>-0.016*</td>
</tr>
</tbody>
</table>

- Data adjusted for child’s birth weight and sex and maternal weight gain, age, and smoking during pregnancy. *Multivariate linear regression were used after transforming the variables to fit a normal distribution and log transforming the exposure biomarkers. ‡The T3RU results were unchanged when the final models were adjusted by FT<sub>3</sub> and FT<sub>4</sub> as covariates (data not shown). *p < 0.10; ** p < 0.05; ‡p < 0.01.

- “consistent inverse and monotonic associations between organochlorine exposure and T3RU.
- T3RU was positively associated with improved performance on most of the neuro-psychological tests (at age 5).
- For other thyroid parameters ..findings ...less consistent.”

PARTICIPANTS 60 cryptorchid boys and 76 matched controls => xenobiotics, mainly polychlorinated biphenyls (PCBs), dichloro diphenyl dichloroethylène (DDE), dibutylphthalate, hexachlorobenzene, and bisphenol A.

FINDINGS: significant negative correlation between fT4 and concentrations of polychlorinated biphenyls PCB118, PC180, and dichloro diphenyl dichloroethylène (DDE) in mother’s milk (resp. $r = -0.342, p < 0.03$, $r = -0.296, p = 0.031$, $r = -0.315, p = 0.016$), persisting after adjustment for mode of delivery. There

Neonatal Hypothyroidism

Hypotonicity
Facts

Hypothyroidism since birth aggravates with age and

People without hypothyroidism at birth, gradually become hypothyroid during (childhood or) adulthood ....
Hypothyroidism accelerates aging.

Prenatal:
- Puffy face
  - Flat nose root
  - Swollen tongue
  - Swollen nose
  - Swollen lips

Childhood:

Adult:

Old age
Thyroid Pollutants in body care products

http://suppversity.blogspot.be/2012/08/hypothyroid-cold-tired-depressed-try.html
Accumulation of organo-chlorines => ↓ thyroid function (may be set free by low calorie diet)

**SUBJECTS:** morbidly obese patients => "zero calorie" diets often weeks => release of organochlorines, accumulated in the fat tissue of the dieters over years & are now liberated within months => Self-intoxication! => sudden ↓ thyroid fn (Pelletier, 2002; Tremblay, 2004; Hue, 2006).

Inability to lose further weight by weight loss/toxic/low T3 - induced aggravation of hypothyroidism

http://suppversity.blogspot.be/2012/08/hypothyroid-cold-tired-depressed-try.html
Thyroid Hormone Deficiency is as frequent as an eye disease
Presbyopia in people age ≥ 35 or 40 = 66%-67%

In Nepal: incidence of presbyopia uncorrected near visual impairment (vision of 20/40 or worse measured at 40 cm using a LogMAR near vision tumbling E chart under ambient indoor lighting) in people age 35 or over = 66.1%.


In China: prevalence of functional presbyopia (near vision<20/50): 67.3% (95% CI, 64.30%-70.09%), increasing from
• at 40 to 49 years of age: 27.6% to
• at 60 to 69 years: 81.8%

Astigmatism, Myopia, hyperopia = frequent

Brazil: SUBJECTS: 7654 Brazilians aged >1 year
Prevalence of
• Astigmatism: 59.7%
• Hyperopia: 33.8%
• Myopia: 25.3%.

Many serum TSH, T3 & T4 levels within the reference range are significantly associated with an increased risk of disease or premature death => reflect a degree of hypothyroidism
Hypothyroidism = Only below the reference range?
WHY DO I STILL HAVE THYROID SYMPTOMS?

WHEN MY LAB TESTS ARE NORMAL

A revolutionary breakthrough in understanding Hashimoto's disease and hypothyroidism

Datis Kharrazian, DHSc, DC, MS
Thyroid deficiencies also within the reference range!

Your test indicates that you are in the lower quarter/third/half of the reference interval and thus have an intermediate degree of hypothyroidism.

This explains your fatigue, low mood, overweight, …
Many serum free T4 levels within the reference range = hypothyroidism
Metabolic syndrome feature: ↑ insulin resistance in euthyroid subjects with serum T4 within the lowest tertile (vs upper tertile).

Blood Free T4 level (ng/dL)

Subjects « above »

2.5%

1.8 ng/dl

Optimal = 78 millions of billions T4 (100 µg/day)

Subjects in « normal » range

95%

1.2 ng/dl

Subjects « below »

2.5%

0.7 ng/dL

40 millions of billions T4 (50 µg/day)

Daily production = 100 millions of billions T4 molecules produced per day (130 µg/day)

± 2.5X higher!!!!
Metabolic syndrome feature:
↑ insulin resistance in euthyroid subjects with serum T4 within the lowest tertile (vs upper tertile)

Normal reference range:
Free T4 (ng/dL)
- Middle high quartile
- Highest quartile = 33.3% highest TSH levels of the population

Subjects « above »
- Blood Free T4 level (ng/dL)
  - 25 pmol/L (1.8 ng/dl)
  - 18 pmol/L
  - Normal 95%

Subjects in « normal » range
- Free T4 ref. range
  - Free T4 = 0.94
  - 1.8 ng/dl

Subjects « below »
- Free T4 = 0.75
  - 9 pmol/L

Some labs free T4 ref. range = 0.8 - 2.8 ng/dL

Daily production = 100 millions of billions T4 (130 µg/day) produced per
- Average population:
  - Free T4 = 1.25 ng/dL
  - 70 millions of billions T4 (90 µg/day) produced per

Progressive ↑ in thyroid deficiency
9 pmol/L
25 pmol/L
70 millions of billions T4 (90 µg/day) produced per

Some labs free T4 ref. range = 0.8 - 2.8 ng/dL

2.5% 2.5% 2.5% 2.5%
Metabolic syndrome feature:
↑ insulin resistance in euthyroid subjects with serum T4 within the lowest tertile (vs upper tertile).

T4 levels with ↑ risk of disease = hyperthyroidism?

Subjects « above »

Blood Free T4 level (ng/dL)

Subjects « normal » range

Normal 95%

Free T4 ref. range

Subjects « below »

Minimal risks with T4 levels among the 20% highest = euthyroidism?

T4 levels with ↑ risk of disease = hypothyroidism?

Subjects « above »


Lowest quartile ↑ mortality

T4 levels with ↑ risk of disease = hypothyroidism?
Many serum free T3 levels within the reference range = hypothyroidism
Serum Free T3 levels & T3 production

Subjects « above »
Serum Free T3 level (pg/mL)
5.7 pmol/L
2.5%

Subjects « below »
Subjects in « normal » free T3 range

Daily T3 production:
31 millions of billions T3
(28 µg/day)

T3 UPPER LIMIT
= 3.7 pg/mL = 5.7 pmol/L

21.5 millions of billions T3
(20 µg/day)
Mean patient population T3 = 2.75 pg/mL

T3 LOWER LIMIT
= 1.8 pg/mL = 2.8 pmol/L

12 millions of billions T3
(12 µg/day)
Blood Free T3 level (pg/mL)

- Subjects « above »
  - 2.5%
  - 5.7 pmol/L

- Subjects in « normal » free T3 range
  - 95%

- Subjects « below »
  - Levels of progressive ↑ in risk of disease
  - 2.5%

1.8 pg/mL = 2.8 pmol/L T3

- 3.7 pg/mL = 5.7 pmol/L T3 UPPER LIMIT
- 3.1

- 2.4
  - ↑ left ventr. dysfn & hyper-trophy (Zoccali C 2006)
  - ↑ risk of dying (critically ill patients) (Peeters RP 2005)
  - ↑ severity of coronary artery atherosclerosis (Auer J 2003)
  - ↑ abnormal inflammatory markers (Zoccali C 2005)
  - ↑ breast cancer (postm. women) (Strain JJ 1997)

- 2.3
  - ↑ breast cancer (Takatani O 1989)
  - ↑ intra-abdominal adipose tissue (Kunesova M 2002)

- 2.8
  - ↑ breast cancer (Takatani O 1989)
  - ↓ CD4+ % in children + HIV (Panamonta O 2004)

- 3.1
  - ↑ risk of dying (critically ill patients) (Maldonado LS 1992)

- ↓ CD4+ % in children + HIV (Panamonta O 2004)

- Slow coronary flow (Evrengul H 2006)
Progressively higher number of hypothyroid signs and symptoms at lower serum T3

- Kiesewetter F, Schell H. Cell kinetics of anagen scalp hairs under physiological and pathological conditions. Skin Pharmacol. 1994;7(1-2):55-60. (“In hyperthyroidism an increase of S phase values (10.3%) was found, while it decreased in hypothyroidism (6.1%). A correlation between the height of S phase and plasma triiodothyronine level was noted.”)

- Gaĭdina GA GA, Matveeva LS, Lazareva SP. Reflexometry as a supplementary study method in thyroid hypofunction. Probl Endokrinol (Mosk). 1982 Jan-Feb;28(1):34-8 (“A correlation was established between the time of the Achilles reflex and the biochemical characteristics of thyroid function (total thyroxin and triiodothyronine levels, thyroxin-binding capacity of the blood serum proteins the basal TSH level) in patients with grave and moderately expressed hypothyroidism. This correlation was retained during the substitution therapy: however, the reflex time recovery was retarded as compared to the degree of manifestation of the clinical symptoms and normalization of the biochemical parameters.”)
Many serum TSH levels within the reference range = hypothyroidism
Metabolic syndrome feature:

- ↑ insulin resistance in euthyroid subjects with serum T4 within the lowest tertile (vs upper tertile)

Also:

- ↑ triglycerides
- ↑ total & LDL cholesterol (inverse associations w/T4)

Daily thyroid hormone production:

- 40 millions of billions T4 (50 µg/day)
- 12 millions of billions T3 (12 µg/day)
- 70 millions of billions T4 (90 µg/day)
- 20 millions of billions T3 (20 µg/day)
- 100 millions of billions T4 (130 µg/day)
- 31 millions of billions T3 (28 µg/day)

Serum TSH levels and daily thyroid hormone production
Serum TSH (mUI/mL)

Subjects "above" (2.5%)

TSH > 1.53
- ↑ death by coronary heart disease in women (Asvold 2008)
- Aggravation of hypothyroidism in diabetics (Warren 2004)

TSH > 1.3
- ↑ breast cancer (Thomas 1986)
- ↑ prostate cancer (Lehrer 2005)
- ↑ overweight (BMI) (Nymes 2006)
- Dia/systolic hypertension (Iqbal 2006)
- ↑ serum glucose, triglycerides (Waterhouse 2007)

TSH > 1.0
- Progressive ↑ of hypothyroid symptoms &/or physical signs (Steinmetz 2000, Monzani 1999, Gaidina 1982)
- Progressive ↑ overweight (BMI) (Knudsen 2005)
- Progressive ↑ thyroid cancer in people with enlarged thyroid (Kumar 1999)

TSH > 0.4
- Progressive ↑ of hypothyroid symptoms &/or physical signs (Steinmetz 2000, Monzani 1999, Gaidina 1982)

TSH > 0.2
- Subjects "below" (2.5%)

Mean TSH of a population: 1.3-1.5

TSH levels with ↑ risks = hypothyroidism?

TSH levels with minimal risks if no enlarged thyroid or overweight is found = euthyroidism?

TSH levels with ↑ risks = hyperthyroidism?
Do all these people with thyroid nodules need thyroid treatment to lower their TSH below 0.4 mIU/mL?

Prevalence of thyroid nodules in subjects without radiation exposure or known thyroid disease (%)

**Figure 1.** Prevalence of Palpable Thyroid Nodules Detected at Autopsy or by Ultrasonography (●) or by Palpation (□) in Subjects without Radiation Exposure or Known Thyroid Disease. Data obtained by palpation are from Christensen et al., 4 Brander et al., 6 Rallison et al., 6 Vander et al., 7 and Trowbridge et al., 8 and data obtained at autopsy and by ultrasonography are from Brander et al., 5 Mortensen et al., 9 Lever et al., 10 Brander et al., 11 Horlock et al., 12 and Oertel and Klinck. 13
The TSH reference evaluated in people without thyroid antibodies = < ½ of the TSH reference range of the population: 0.4-2.0 !!
Reference values of thyroid tests?

Evaluated on persons without thyroid abnormalities (no goiter or thyroid nodule, no autoimmune disease, etc.)

The official TSH reference ranges have been evaluated on patients, mainly sick persons, those who go to the laboratory.

Narrower reference range

Too wide ref. range

2,5%

= Statistical references ≠ health values
When data for subjects with positive TPOAb or a family history of autoimmune thyroid disease are excluded, the normal reference interval becomes much tighter, i.e. 0.4–2.0 mU/liter. This tighter reference range may certainly be more applicable to African-Americans, who have a lower mean TSH.


Publications with data to support a more narrow reference range for serum TSH that would be obtained when persons with diffuse hypoechogenicity of the thyroid on ultrasound, a condition that precedes thyroid peroxidase antibody positivity in autoimmune thyroid disease, would be excluded


A study suggests that the serum TSH cut-off point between hypo-1 euthyroidism is 2, not 4 or 5.5

4. Michalopoulou G, Alevizaki M, Piperingos G, Mitsibounas D, Mantzos E, Adampoulos P, Koutras DA. High serum cholesterol levels in persons with 'high-normal' TSH levels: Should one extend the definition of subclinical hypothyroidism? Eur J Endocrinol. 1998 Feb;138(2):141-5*(Treating TPO antibody-positive hypercholesterolemic patients with TSH levels between 2-4 mU/L with low dose levothyroxine normalizes TSH levels and improves the lipid profile)*
Every individual has a personal narrower TSH reference range

= $\frac{1}{2}$ or $\frac{1}{3}$rd of the TSH reference range of the population
Reference ranges = Statistical ranges ≠ Health ranges

TSH reference range in older adults (% of population)

2.5% of the population is below the lower TSH limit

95% of population = 95% confidence interval

2.5% is above the upper TSH limit

Pedro Wesley Rosario, Maria Regina Calsolari. TSH reference range in older adults: a Brazilian study. Arq Bras Endocrinol Metab vol.58 no.4 São Paulo June 2014
Population TSH reference range ≠ Individual TSH reference range

TSH reference range in older adults (% of population)

2.5% of the population is below the lower TSH limit
95% of population = 95% confidence interval
2.5% is above the upper TSH limit

Pedro Wesley Rosario, Maria Regina Calsolari. TSH reference range in older adults: a Brazilian study. Arq Bras Endocrinol Metab vol. 58 no. 4 São Paulo June 2014
The TSH reference range for an INDIVIDUAL is narrower than the range for a population. The value of a population-based reference range is limited to the individual patient-based reference range (i.e. his personal reference range) is narrower.


The individual TSH reference ranges are remarkably narrow within a relatively small segment of the population reference range, i.e. confined to only 25% of a range of 0.3–5.0 mU/liter. A shift in the TSH value of the individual outside of his or her individual reference range, but still within the population reference range, would not be normal for that individual. For example, an individual with a personal range of 0.5–1.0 mU/liter would be at subphysiological thyroid hormone levels at the population mean TSH of 1.5 mU/liter (as explained by Wartofsky 2005)
3. Andersen S, Petersen KM, Brunn NH, Laurberg P. Narrow individual variations in serum T4 and T3 in normal subjects: a clue to the understanding of subclinical thyroid disease. J Clin Endocrinol Metab. 2002;87:1068–72

Studies of twins have data to support that each of us has a genetically determined optimal free T4 (FT4)-TSH set point or relationship.
Every individual has a personal narrower TSH reference range

\[ = \frac{1}{2} \text{ or } \frac{1}{3} \text{rd of the TSH reference range of the population} \]
Individual reference ranges for serum T3 and T4

= are about half the width of population-based reference ranges.

Hence, a test result within the laboratory reference limits is not necessarily normal for the individual. Serum TSH outside the population-based reference range indicates that serum T3 and serum T4 are not normal for the individual. 

Andersen S, Pedersen KM, Bruun NH, Laurberg P. Narrow individual variations in serum T(4) and T(3) in normal subjects: a clue to the understanding of subclinical thyroid disease. J Clin Endocrinol Metab. 2002 Mar;87(3):1068-72. Department of Endocrinology, Aalborg Hospital, Aalborg, Denmark DK-9000. stiga@dadlnet.dk
Individual reference ranges for serum T3 and T4

= are about half the width of population-based reference ranges.

Figure 2.
The distribution of 12 monthly measurements of total T₄ in 15 healthy men (○) and in one individual, number 11 (●). The distribution in one individual is about half the width of the distribution in the group.

Andersen S, Pedersen KM, Bruun NH, Laurberg P. Narrow individual variations in serum T(4) and T(3) in normal subjects: a clue to the understanding of subclinical thyroid disease. J Clin Endocrinol Metab. 2002 Mar;87(3):1068-72.
Department of Endocrinology, Aalborg Hospital, Aalborg, Denmark DK-9000. stiga@dadlnet.dk
Other study that shows that the Intra-individual variations of thyroid function tests in healthy subjects are narrow, about 1/3 pf the population-based ones.

Rinsho Byori. 1996 Feb;44(2):159-62. [Intra-individual and seasonal variations of thyroid function tests in healthy subjects] [Article in Japanese] Nishi I, Ichihara K, Takeoka K, Miyai K, Amino N. Central Laboratory for Clinical Investigation, Osaka University Hospital, Suita. We report intra-individual and seasonal variations of thyroid function tests in healthy subjects. Blood samples were obtained from thirteen healthy males and seven healthy females every two weeks over a period of one year, and totally 25 samplings of each were made. Serum thyrotropin (TSH), free thyroxine (FT4) and free triiodothyronine (FT3) were measured after the completion of the sampling. The 25 samples from each subject were always assayed with the same assay run. Variations of FT4 and FT3 in each subject were narrow and approximately one-third of normal reference ranges. The magnitude of individual variation of TSH values was proportional to the average of TSH in each individual. Serum TSH and FT3 values during winter were significantly higher than those during summer, but such change was not observed on serum FT4.

Study: narrow degree of intra-individual variations of thyroid fn tests in healthy subjects => population-based ref.ranges inadequate for an individual

**DESIGN:** Monthly blood samplings for the assay of the above hormones were collected during one calendar year. in healthy volunteers

**SUBJECTS:** 13 normal men & 13 normal women (mean age 38.7 +/- 13.4 years).

**RESULTS:** Significant annual, four-monthly and biannual rhythms were detected in serum TSH; the lowest TSH values were observed in spring. A significant annual rhythm was detected in TT3, with lower values in spring and summer than in the other seasons. The peak-trough differences in the yearly variation expressed as a percentage of the mean were 29.1% and 8.2% for TSH and TT3, respectively. There were no significant seasonal rhythms in PRL, FT4 or testosterone.

The intraindividual/interindividual CV values: TSH 29.3/48.4%, TT3 9.4/18.5%, FT4 7.1/9.1%, PRL 39.2/65.0%, cortisol 21.7/46.2%, & testosterone 12.6/40.8%.

**CONCLUSIONS:** The degree of individuality measured in the plasma hormones is such that conventional population-based reference ranges may not correctly identify major alterations in these hormones in individual subjects.

The situation is worse: People may have lower thyroid hormone receptors
Fig. 1: The maximal nuclear binding capacity for both T4 & T3 declines with increasing age in mononuclear blood cells in healthy subjects.

Obesity:

the affinity of T4 nuclear receptors => lower in obese persons than in normal weight persons

Kvetny J. Nuclear thyroxine receptors and cellular metabolism of thyroxine in obese subjects before and after fasting Horm. Res. 1985;21(1):60-5. (The maximal specific binding capacity for T4 was decreased in fed obese subjects compared to normal weight persons)
Reduced T3 binding in diabetes mellitus

<table>
<thead>
<tr>
<th>Reduced T3 binding in diabetes mellitus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>there is a decrease (not an increase) in the binding of T₃ to nuclear receptors to T₃ in diabetes mellitus and fasting in the rat</strong></td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Reduced T3-nuclear binding in glial cells in illness (diabetes), not in fasting</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sanchez found that in the brain, starvation did not alter the content or binding capacity for T3, but illness (diabetes) did cause a decrease in the thyroid hormone receptor content &amp; T3 binding capacity of glial cell nuclei</strong></td>
</tr>
</tbody>
</table>

High levels of reverse T3 may cause hypothyroidism.
Reverse T3

= the best measurement of thyroid tissue levels” found in the 2005, volume 90 issue of The Journal of Clinical Endocrinology & Metabolism, it states that “the T3/rT3 ratio is the most useful marker for tissue hypothyroidism and as a marker of diminished cellular functioning

On day 1, rT3 was higher and T3/rT3 was lower in nonsurvivors as compared with survivors (P = 0.001). **Odds ratio for survival of the highest vs. the lowest quartile was 0.3 for rT3 and 2.9 for T3/rT3.** TSH, T4, and T3 were lower in nonsurvivors from d 5 until LD (P < 0.001). TSH, T4, T3, and T3/rT3 increased over time in survivors, but decreased or remained unaltered in nonsurvivors. Liver D1 activity was positively correlated with LD serum T3/rT3 (R = 0.83, P < 0.001) and negatively correlated with rT3 (R = -0.69, P < 0.001). Both liver and skeletal muscle D3 activity were positively correlated with LD serum rT3 (R = 0.32, P = 0.02 and R = 0.31, P = 0.03).

**CCL:** In critically ill patients who required more than 5 d of intensive care, rT3 and T3/rT3 were already prognostic for survival on day 1. **On day 5, T4, T3, but also TSH levels are higher in patients who will survive.** Serum rT3 and T3/rT3 were correlated with postmortem tissue deiodinase activities

Peeters RP, Wouters PJ, van Toor H, Kaptein E, Visser TJ, Van den Berghe G. Serum 3,3',5'-triiodothyronine (rT3) and 3,5,3'-triiodothyronine/rT3 are prognostic markers in critically ill patients and are associated with postmortem tissue deiodinase activities. J Clin Endocrinol Metab. 2005 Aug;90(8):4559-65.
Reverse T3 Suppresses T4 to T3 Conversion

- $rT3 = 100 \times$ more potent inhibitor of T4 to T3 conversion than PTU (propylthio-uracil, antithyroid medication used in hyperthyroidism) at reducing T4 to T3 conversion.

- “Reverse t3 appeared to inhibit the conversion of t4 to T3 with a potency which is about 100 times more than PTU…”

Chopra IJ. Endocrinology 101(2):453-63 A study of extrathyroidal conversion of thyroxine (T4) to 3,3',5-triiodothyronine (T3) in vitro
Ratio rT3 / T3

- **Free T3**: 2.1-4.2 pg/mL

- **Reverse T3**: 9 -24ng/dL = 90-240 pg/mL
  
  => 50 x more reverse T3

**Conclusion**: a ratio of reverse T3 to free T3

- > 10 (in ng/dl for rT3 to pg/mL for T3)
- > 100 (in pg/mL)

may cause hypothyroidism
Presence of thyroid antibodies may reflect an intermediate degree of hypothyroidism.
Thyroid antibodies: their presence or high levels are associated with

An increased risk of depression


An increased risk of overweight, obesity


An increased risk of diabetes

- Karges B, Muche R, Knerr I, Ertelt W, Wiesel T, Hub R, Neu A, Klinghammer A, Aufschild J, Rapp A, Schirbel A, Boehm BO, Debatin KM, Heinze E, Karges W. Levothyroxine in euthyroid autoimmune thyroiditis and type 1 diabetes: a randomized, controlled trial. J Clin Endocrinol Metab. 2007 May;92(5):1647-52. Division of Pediatric Endocrinology and Diabetes, University Children's Hospital, University of Ulm, Ethstrasse 24, D-89075 Ulm, Germany. beate.karges@uniklinik-ulm.de (T4 treatment (1.3 microg/kg daily, 24 months) to biochemically euthyroid children and adolescents with type 1 diabetes and positive thyroid peroxidase antibodies, thyroglobulin antibodies, or both, reduced thyroid volume, but had no effect on thyroid function and serum autoantibody compared to diabetic controls, T4 levels)
Thyroid antibodies: their presence or high levels are associated with

Poor cardiac indices, an increased risk of coronary heart diseases, etc.


An increased risk of dyslipidemia

Thyroid antibodies: their presence or high levels are associated with

An increased risk of progression to overt hypothyroidism:

- Effraimidis G, Strieder TG, Tijssen JG, Wiersinga WM. Natural history of the transition from euthyroidism to overt autoimmune hypo- or hyperthyroidism: a prospective study. Eur J Endocrinol. 2011 Jan;164(1):107-13. Departments of Endocrinology and Metabolism Cardiology, Academic Medical Centre, University of Amsterdam, PO Box 22700, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands. grigoris.effraimidis@gmail.com

CONCLUSION: The presence or high levels of thyroid antibodies often reflects an intermediate degree of thyroid deficiency