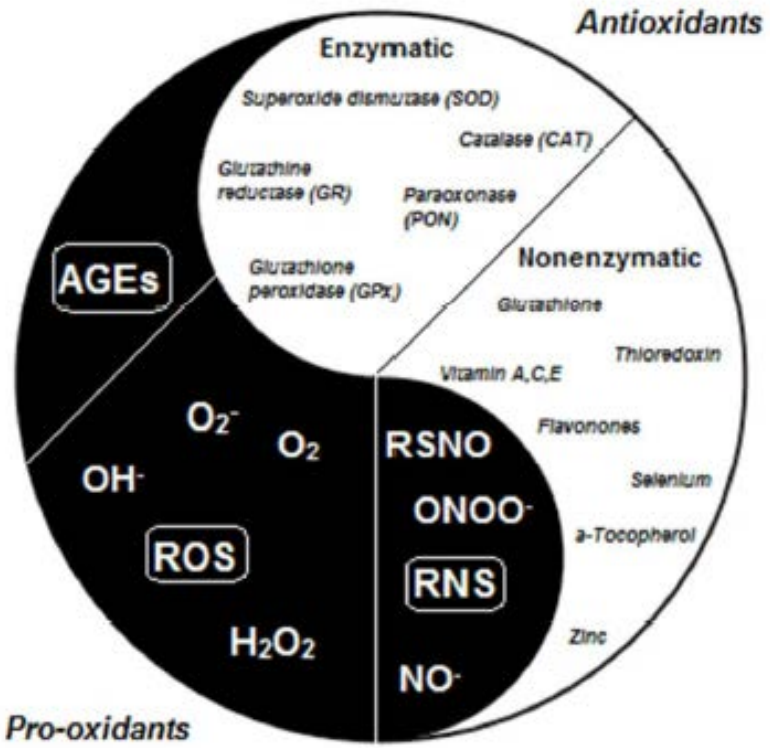
Mikronährstoffe und Vitamine jenseits von Jod

Wels 7.10.2016

Roland Gärtner
Medizinische Klinik IV der Universität München

Redox-System und SD



ROS Ursache für : Mutationen = Knotenbildung
Auslöser für Autoimmunthyreoiditis

Spurenelemente und Schilddrüse (außer Jod)

Selen = als Selenocystein essentiell für Selenoenzyme

Eisen = essentiell für Aktivität der TPO, (Hämgruppe im aktiven Zentrum)

Zink = notwendig für T3-Rezeptor-Aktivierung,
ca 200 Enzyme benötigen Zink (Immunregulation)

Mangan/Kupfer = Superoxid dismutase (Antioxydants)

Cobalt = essentiell für B12 Wirkung, Wirkung auf Schilddrüse kontrovers

Journal of Trace Elements in Medicine and Biology 24 (2010) 106–110

Trace elements status in multinodular goiter

Belma Giray [a,*], Josiane Arnaud [b,c], İskender Sayek [d], Alain Favier [c], Filiz Hıncal [a,*]

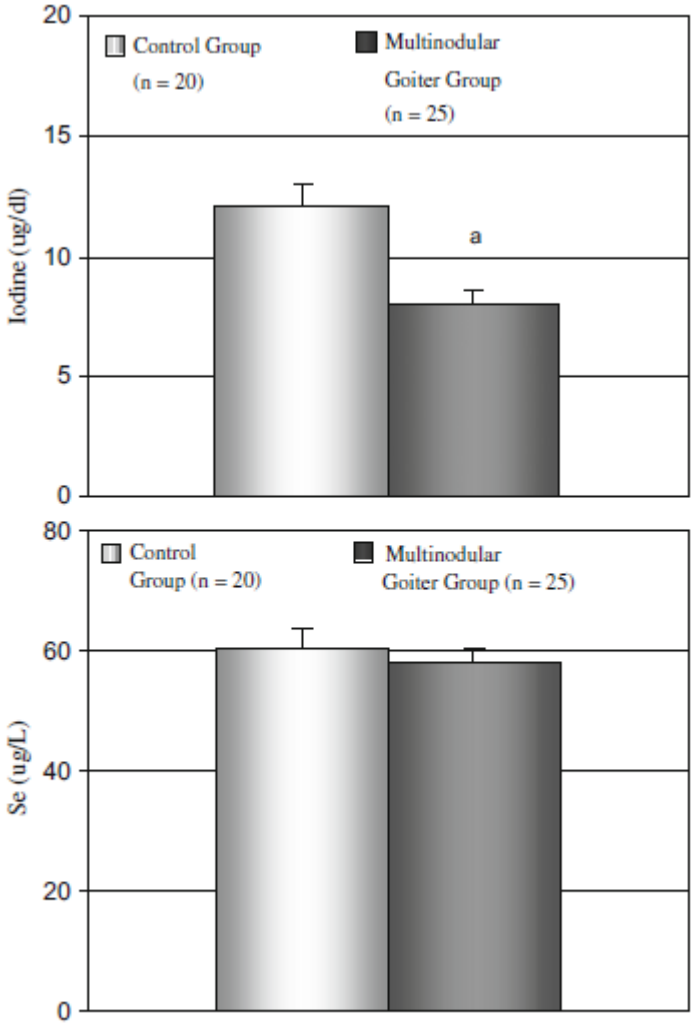


Fig. 1. Urinary iodine and plasma selenium concentrations in the patients with multinodular goiter and control group; [a]$p < 0.05$.

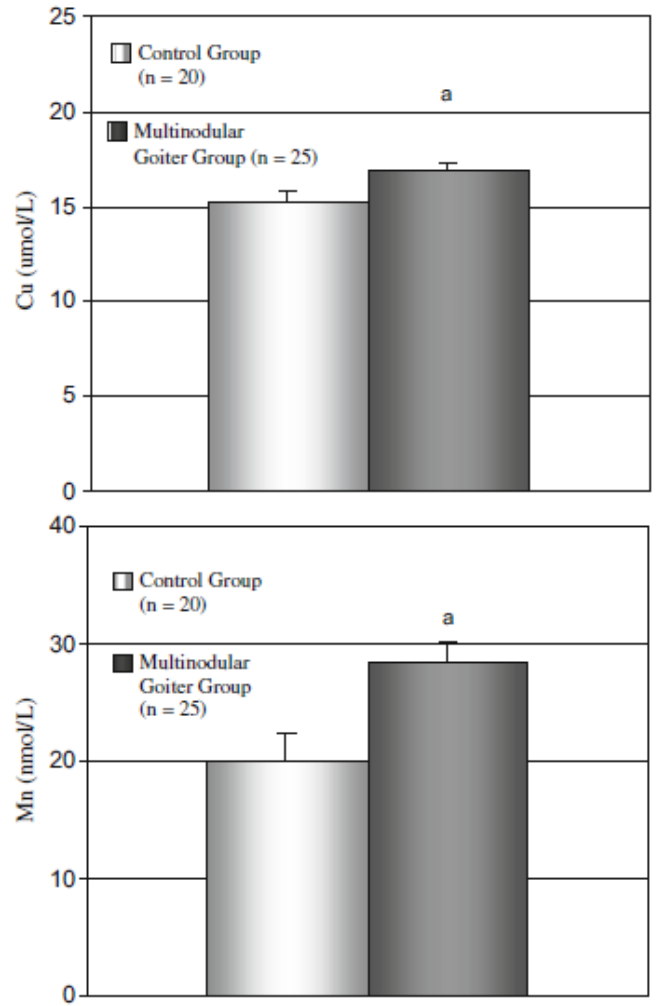


Fig. 4. Plasma copper and manganese concentrations in the patients with multinodular goiter and control group; [a]$p < 0.05$.

Papillary Thyroid Cancer Incidence in the Volcanic Area of Sicily

Pellegriti G et al J Natl Cancer Inst 2009;101:1575–1583

Papillary Thyroid Cancer Incidence in the Volcanic Area of Sicily

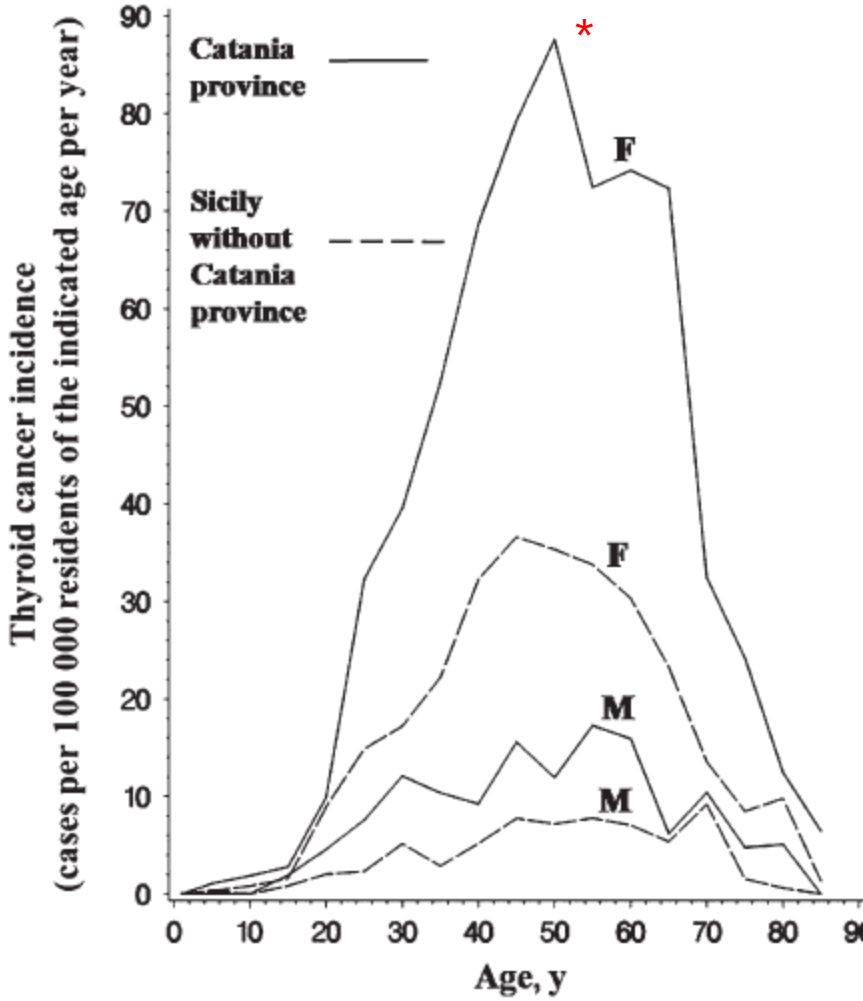
Pellegriti G et al J Natl Cancer Inst 2009;101:1575–1583

Table 4. Contaminants measured in groundwater sources and tap water in the provinces of Catania, Palermo, and Ragusa (localized in north-east, west and south of Sicily, respectively)*

Element	MAC (µg/L)	No. of specimens with concentrations greater than MAC/total No. (maximum value measured)		
		Catania	Palermo	Ragusa
Boron (B)	1000	131/478 (2100)	0/151 (750)	0/73 (218)
Iron (Fe)	200	92/280 (5300)	6/153 (1380)	1/92 (1330)
Manganese (Mn)	50	87/264 (2600)	3/151 (138)	0/92 (14)
Vanadium (V)	50	193/280 (179)	0/142 (<7)	0/73 (20)
^{222}Radon (^{222}Rn)†	11	48/119 (57)	–	–

* MAC = maximum allowed concentration.

† Radiation unit in Bq/L [data from D'Alessandro and Vita (21)].



* BRAF V600E Mutationen ca 57%

The Association between Cobalt Deficiency and Endemic Goiter in School-Aged Children

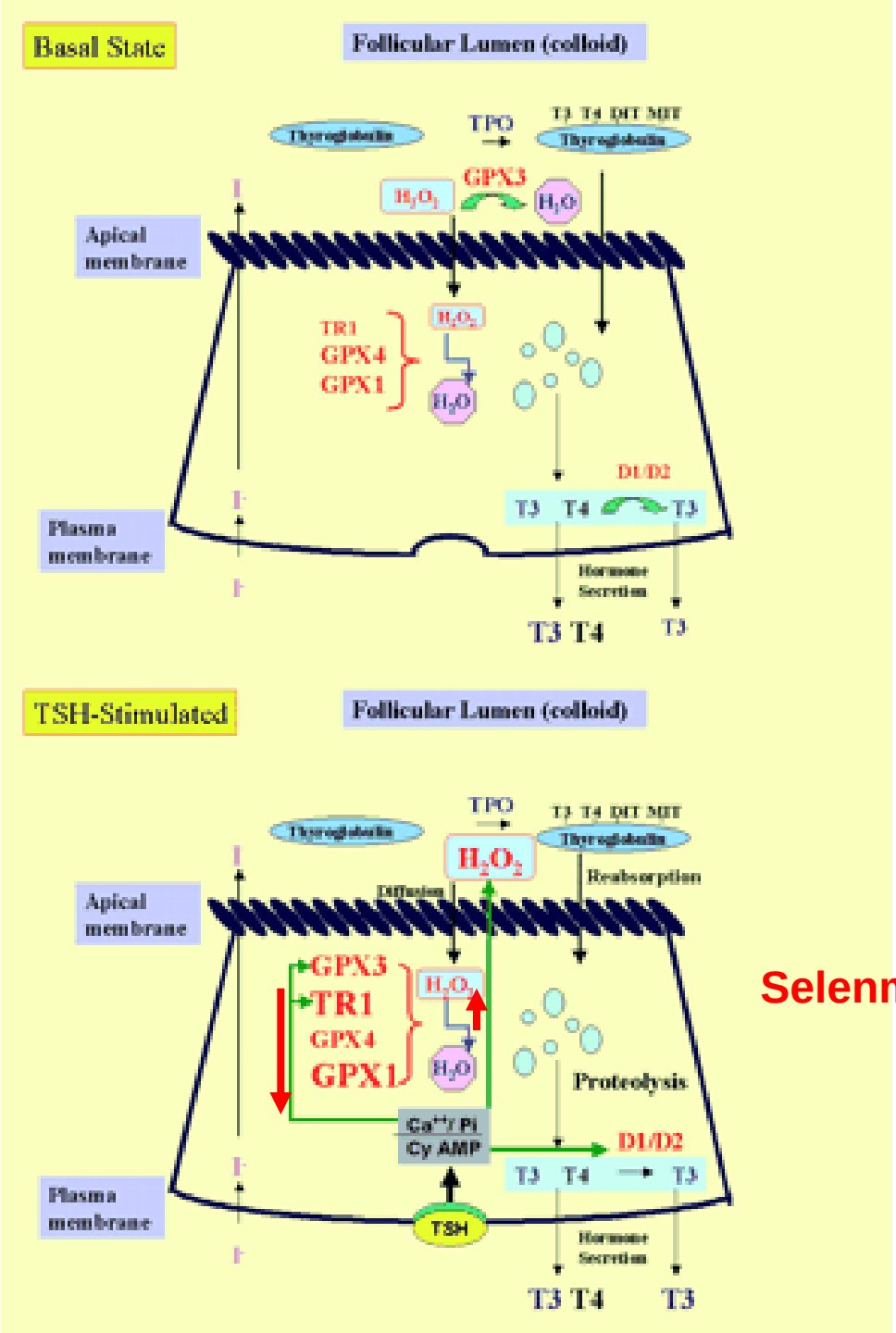
Endocrinol Metab 2014;29:307-311

Mojgan Sanjari[1], Ahmad Gholamhoseinian[2], Akram Nakhaee[3]

Table 2. Characteristics of Goitrous and Nongoitrous Subgroups

Characteristic	Goitrous (n=130)	Nongoitrous (n=40)	P value
Age, yr			0.23
9 yr-old	29 (22)	6 (15)	
10 yr-old	65 (50)	17 (42.5)	
11 yr-old	36 (28)	17 (42.5)	
Mean±SD	10.1±0.7	10.3±0.7	0.11
Serum cobalt, μg/L	4.38±2.91	6.36±2.71	<0.01[a]
Urine iodine, μg/L	198.3±108.3	270.2±91.1	<0.01[a]
Serum T4, μmol/L	8.80±1.89	8.66±1.97	0.68
Serum T3, μmol/L	157.1±31.8	159.6±32.9	0.73
TSH, mU/L	2.38±1.29	2.25±0.94	0.55

Selen und Schilddrüse



Die Gluathionperoxidasen

- schützen die Zelle vor oxidativem Stress und
-tragen mit zur Regulation der Schilddrüsenhormonsynthese bei

-Selenmangel führt zu einer erhöhten Inzidenz von:
- Autoimmunerkrankungen
- Neoplasien

Selenmangel

Selenium and endocrine systems
Beckett GJ, Arthur JR

J Endocrinol. 2005 Mar;184(3):455-65

Wirkungsmechanismen von Selenoenzymen bei Entzündung

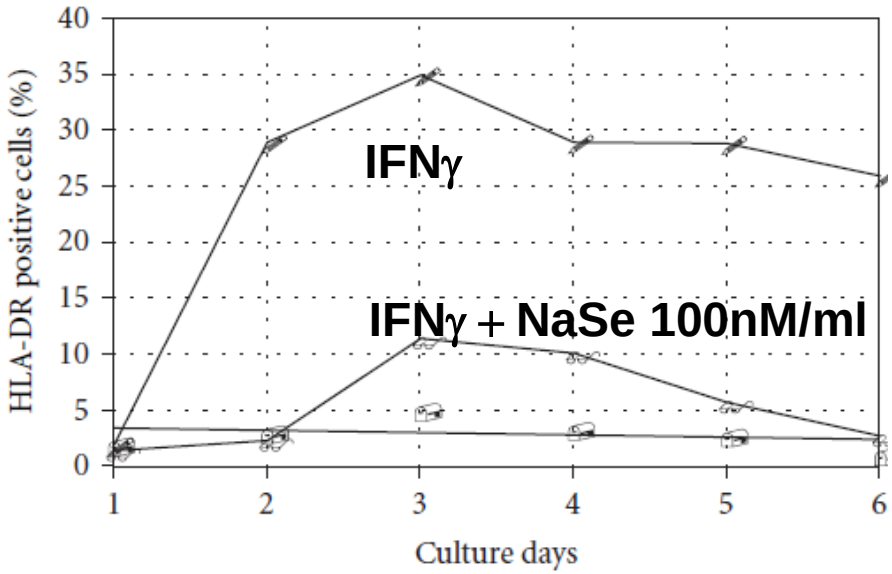
- Verminderte NFKB Translokation und damit weniger Zytokinfreisetzung
- Neusynthese von Selenoprotein P
  - und damit Schutz des Endothels vor oxidativer Schädigung
  - Transport von Selenocystein zur Synthese von Selenoenzymen in die Organe
- Verbesserung des Redox- Homöostase im Plasma, Zytosol und Zellkern

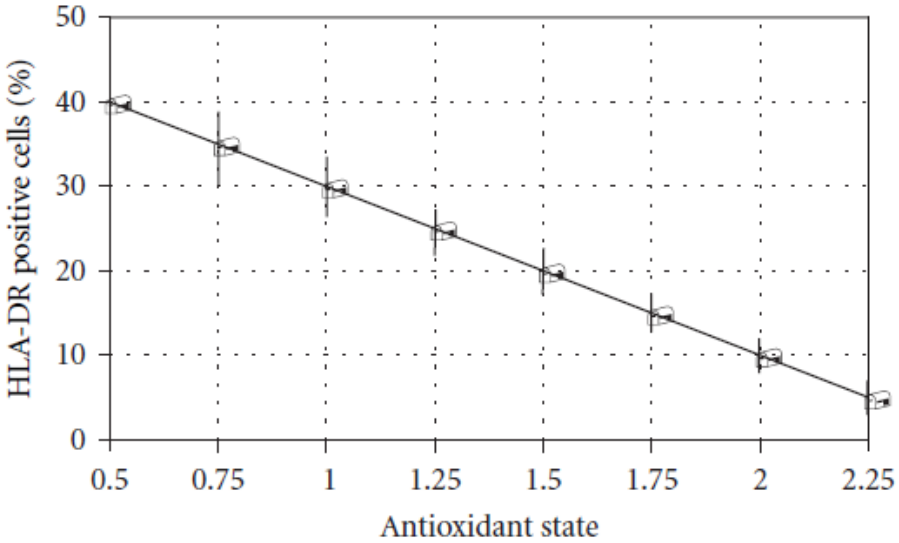
Selen und AIT – Experimentelle Untersuchungen

Effect of Selenium on HLA-DR Expression of Thyrocytes

Autoimmune Diseases
Volume 2012, Article ID 374635, 5 pages

Csaba Balázs and Viktória Kaczur



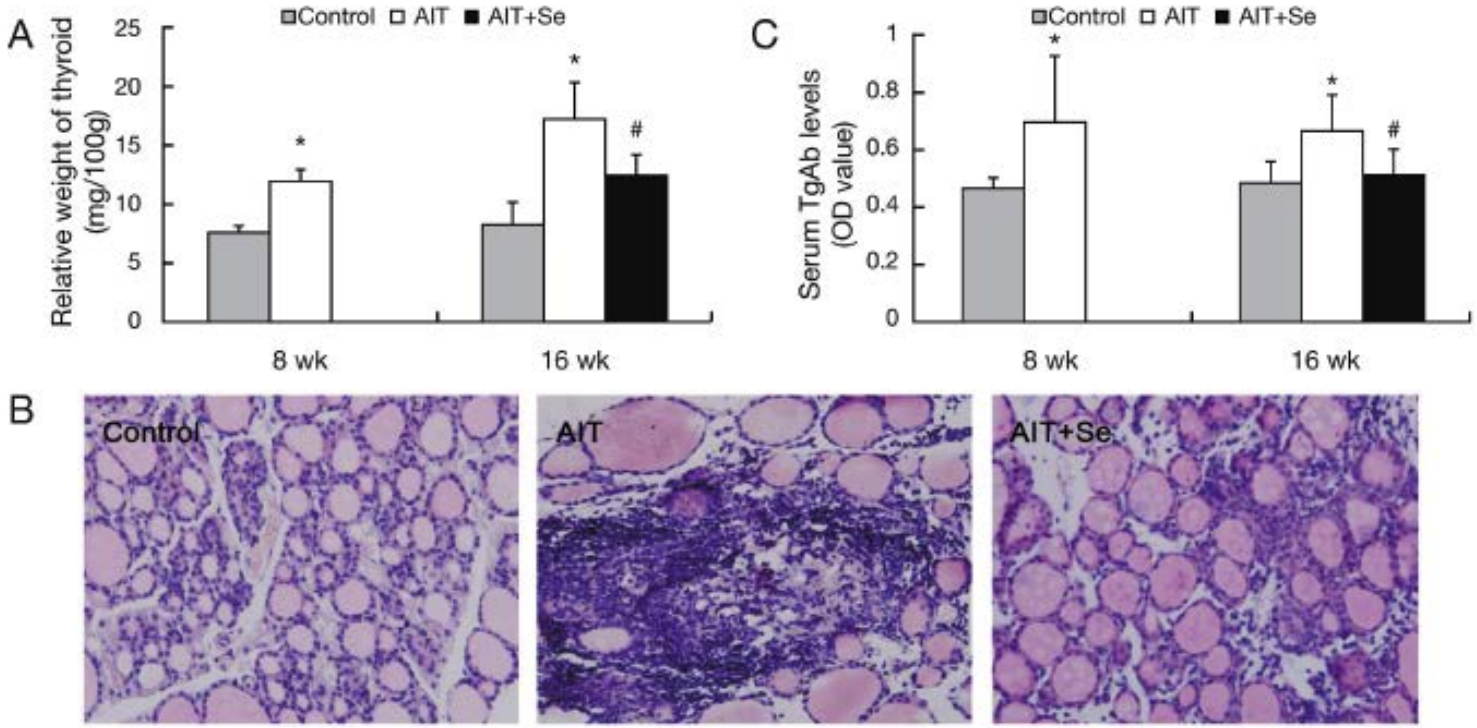


Selen reduziert die durch IFNγ induzierte HLA-DR Expression in humanen Thyreozyten in-vitro

Endocrine Journal 2010, **57** (7), 595-601

Selenium upregulates $CD4^+CD25^+$ regulatory T cells in iodine-induced autoimmune thyroiditis model of NOD.H-2^{h4} mice

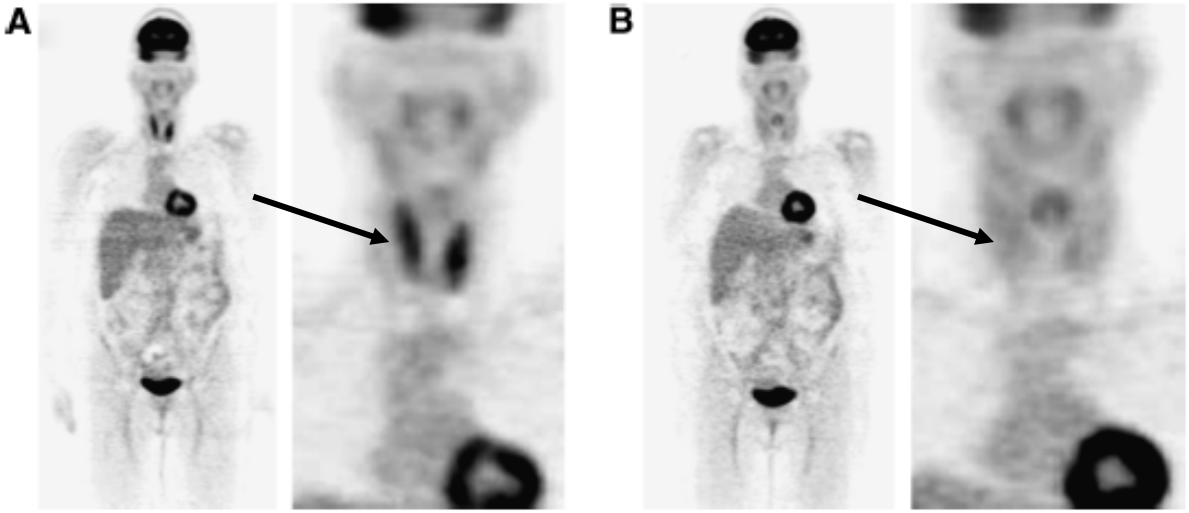
Haibo Xue[1),2)], Weiwei Wang[1)], Yuanbin Li[1),3)], Zhongyan Shan[1)], Yushu Li[1)], Xiaochun Teng[1)], Yun Gao[1)], Chenling Fan[1)] and Weiping Teng[1)]



EAT durch hohe Joddosen induziert

THYROID
Volume 19, Number 11, 2009

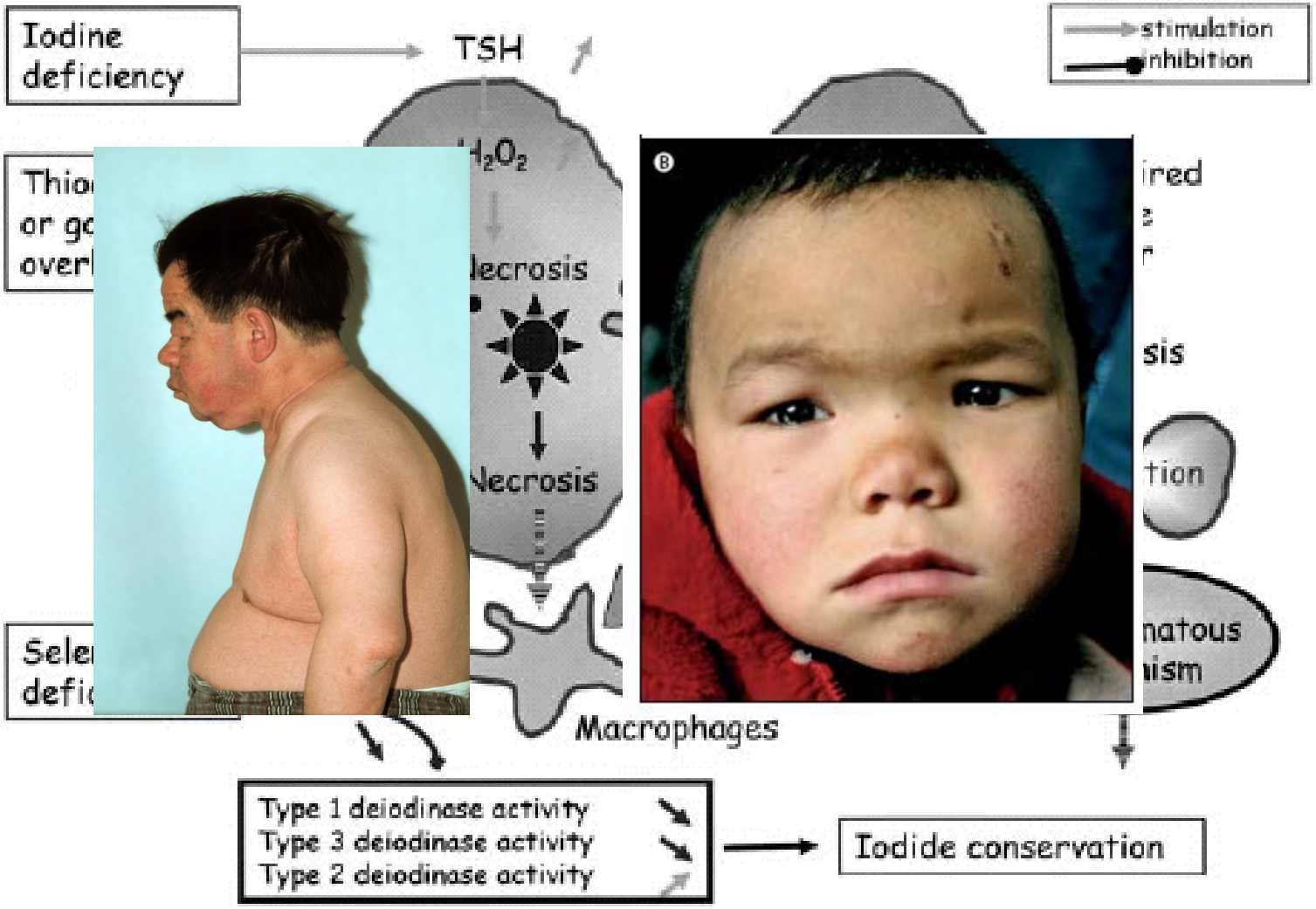
Decline in Thyroid ^{18}Fluorodeoxyglucose Uptake Associated with Selenium Supplementation in a Patient with Autoimmune Thyroiditis



TSH 1,9	1,7 U/L
TPOAk 2860	795 U/L
Se 0,9	1,3 µmol/L

Pathogenesis of Myxedematous Cretinism

The interaction between combined selenium and iodine deficiency



Köhrle J. Thyroid 2005

Low Population Selenium Status Is Associated With Increased Prevalence of Thyroid Disease

J Clin Endocrinol Metab, November 2015, 100(11):4037–4047

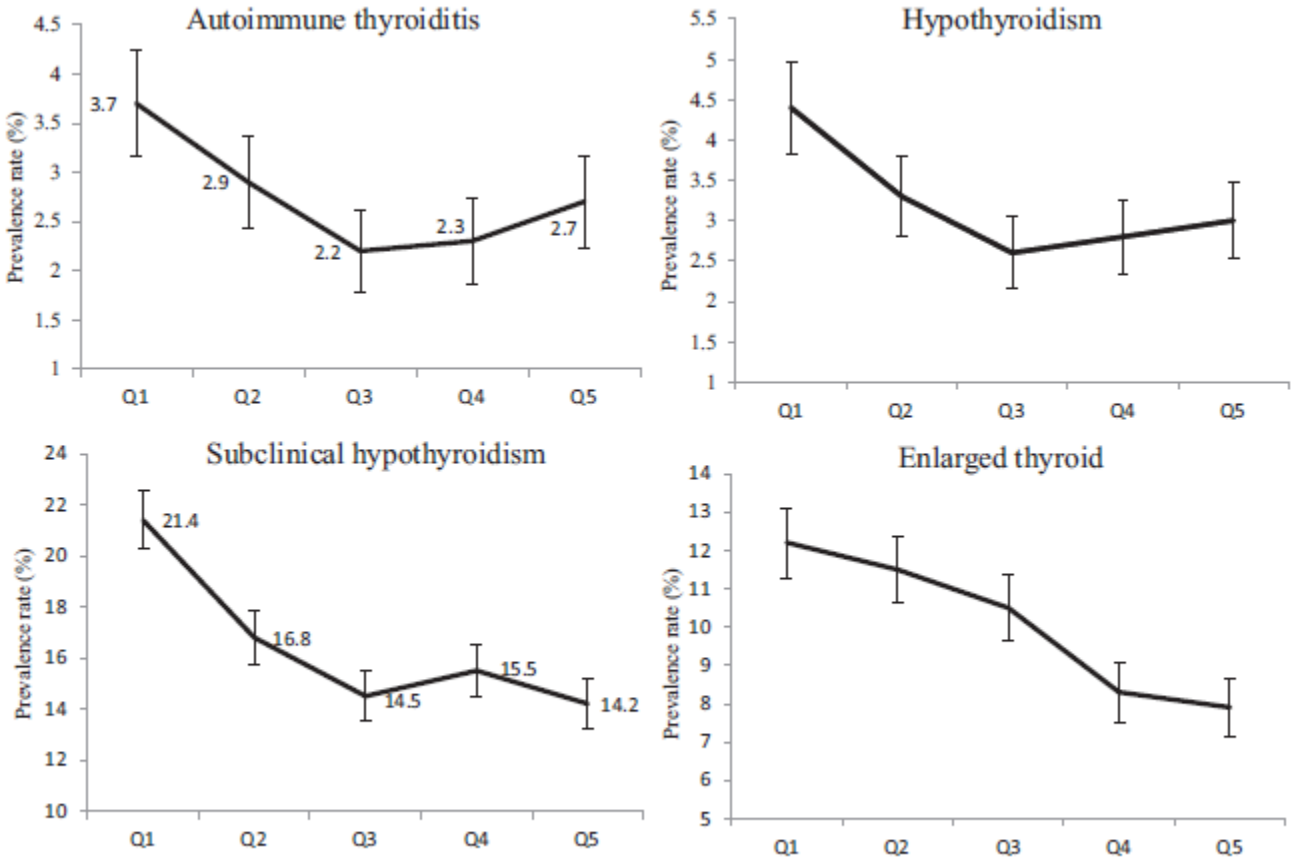
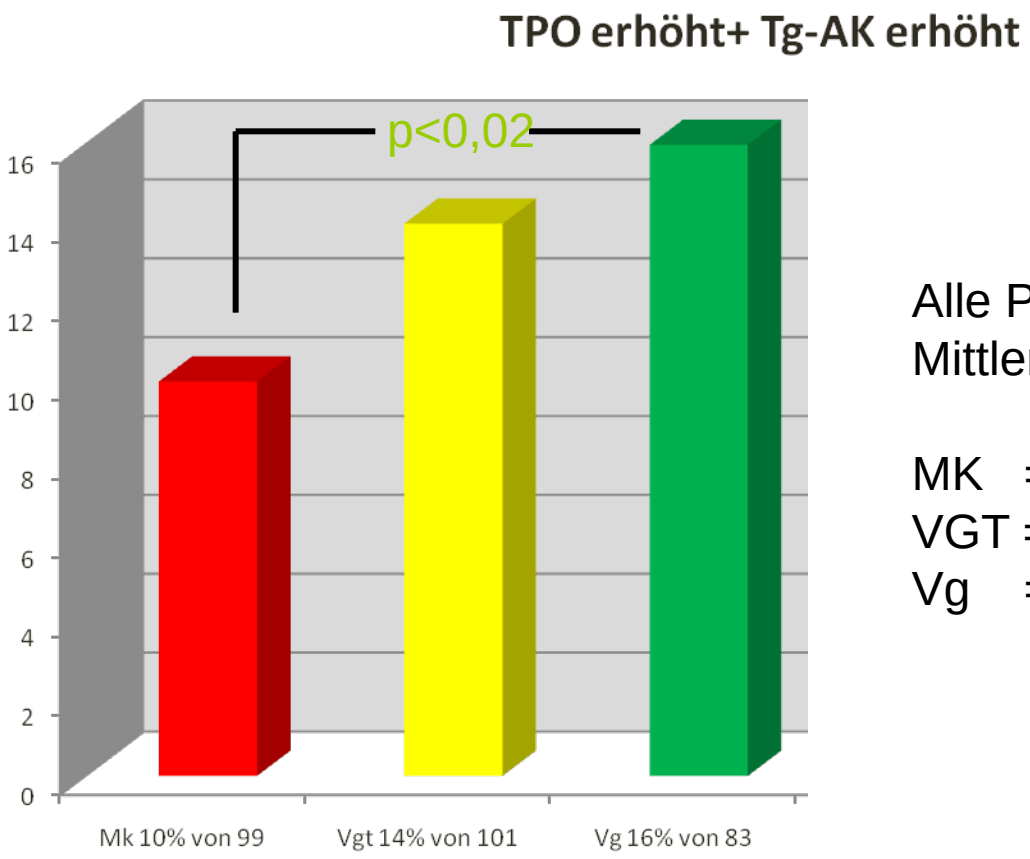


Figure 2. Prevalence rate of thyroid disease by category of serum Se (both counties combined). Participants were divided into quintiles by serum Se: Q1 (quintile 1) <47.00 μg/L; Q2 (quintile 2), 47.00–68.99 μg/L; Q3 (quintile 3) 69.00–90.99 μg/L; Q4 (quintile 4) 91.00–119.99 μg/L, Q5 (quintile 5) ≥120.00 μg/L.

Prävalenz der Autoimmunthyreoiditis bei kombiniertem Jod- und Selenmangel



Alle Probanden euthyreot
Mittleres Alter 34 Jahre

MK = Mischköstler
VGT = Vegetarier
Vg = Veganer

83/50 68/33 56/13 Selen/Jod (µg/L/ Plasma/Urin)

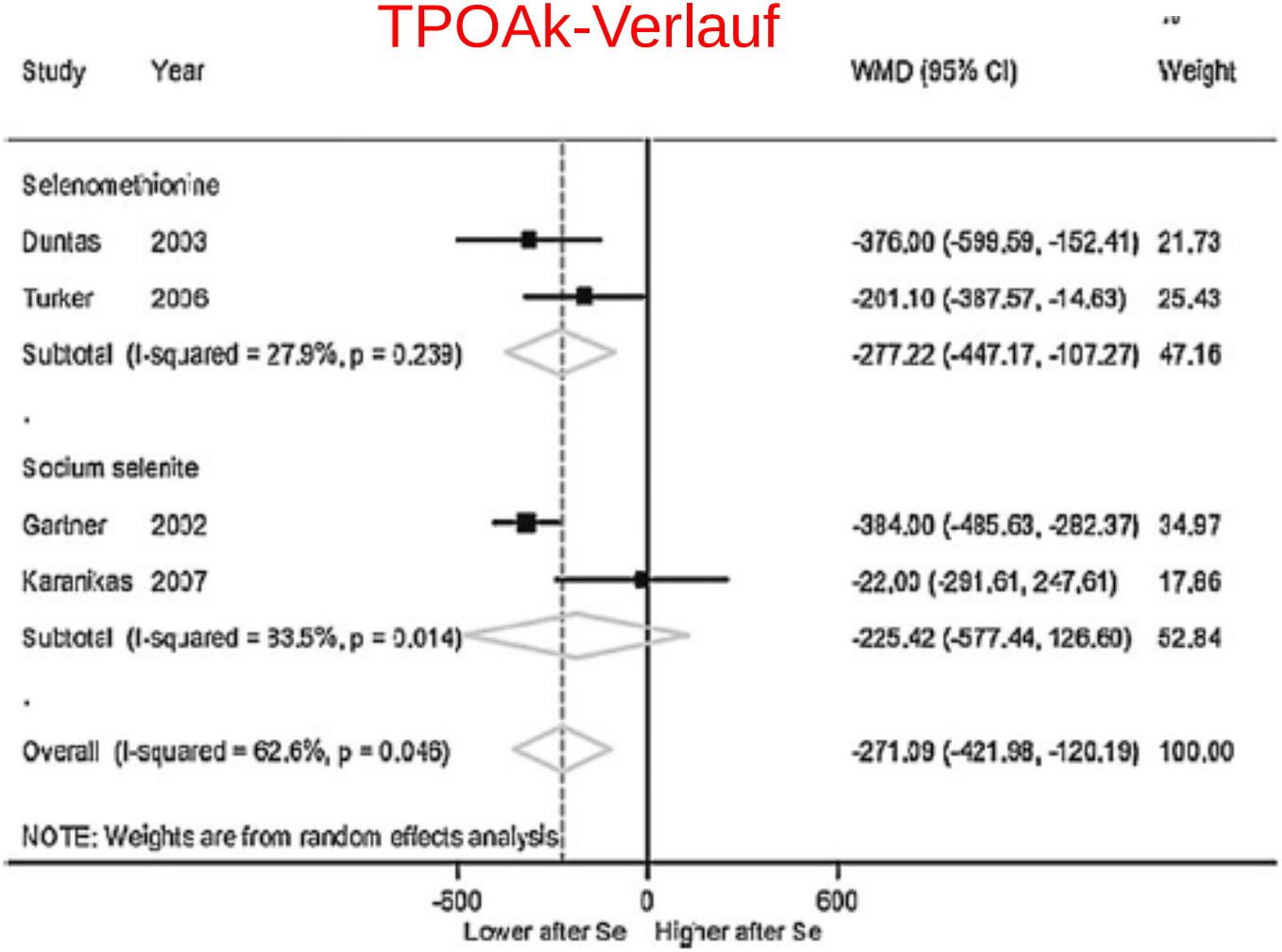
Gärtner et al 2010

THYROID
Volume 20, Number 10, 2010

Selenium Supplementation in the Treatment of Hashimoto's Thyroiditis: A Systematic Review and a Meta-analysis

Konstantinos A. Toulis,[1] Athanasios D. Anastasilakis,[2] Thrasivoulos G. Tzellos,[3]
Dimitrios G. Goulis,[1] and Dimitrios Kouvelas[3]

TPOAk-Verlauf



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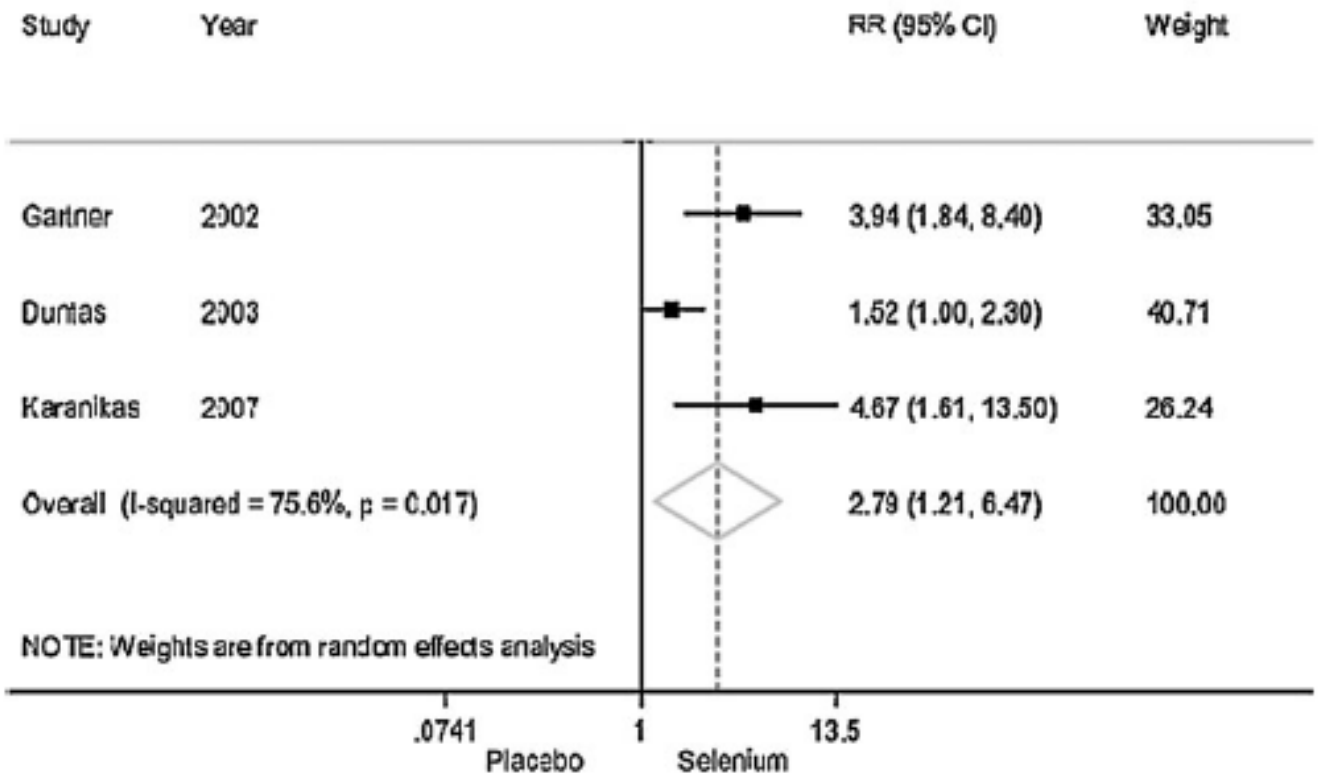
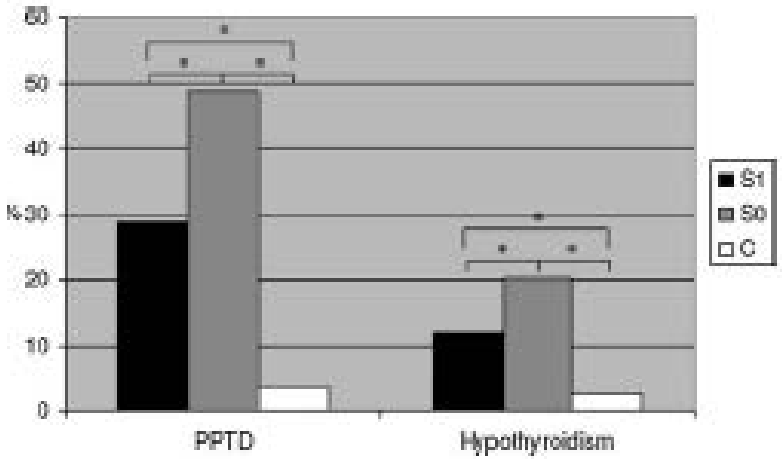
Wohlbefinden/QuL

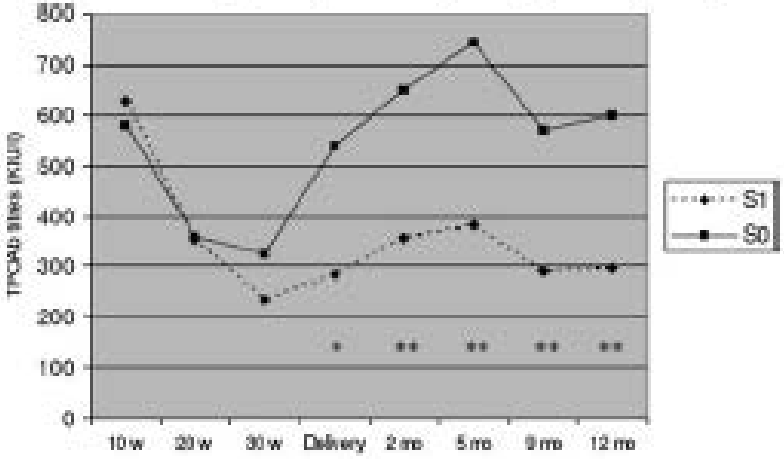


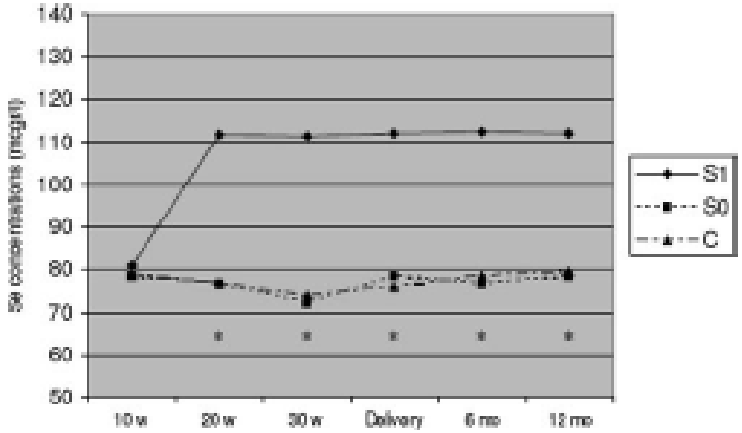
The Influence of Selenium Supplementation on Postpartum Thyroid Status in Pregnant Women with Thyroid Peroxidase Autoantibodies

Roberto Negro, Gabriele Greco, Tiziana Mangieri, Antonio Pezzarossa, Davide Dazzi, and Haslinda Hassan

The Journal of Clinical Endocrinology & Metabolism 92(4):1263–1268
Copyright © 2007 by The Endocrine Society

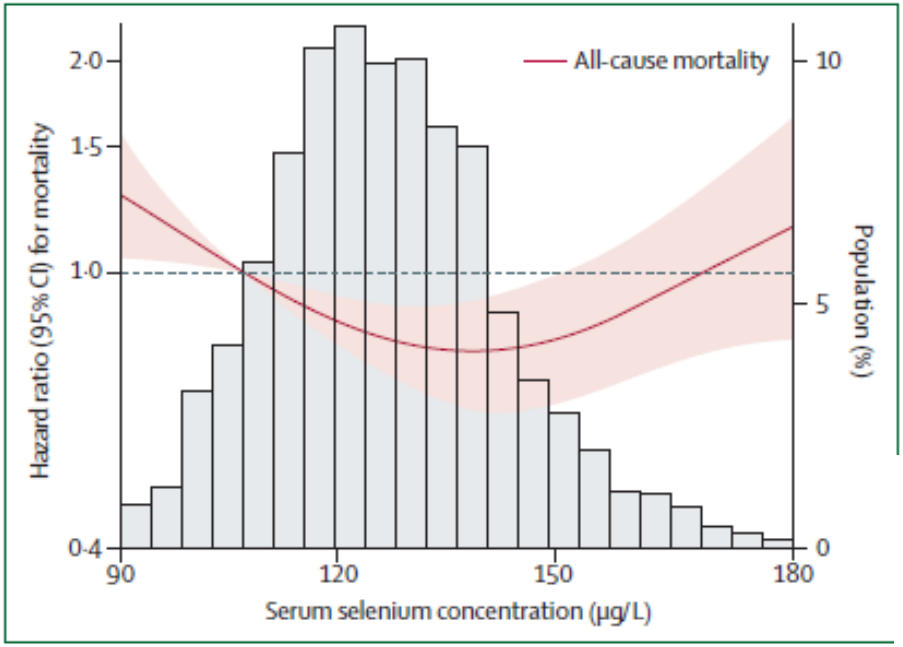


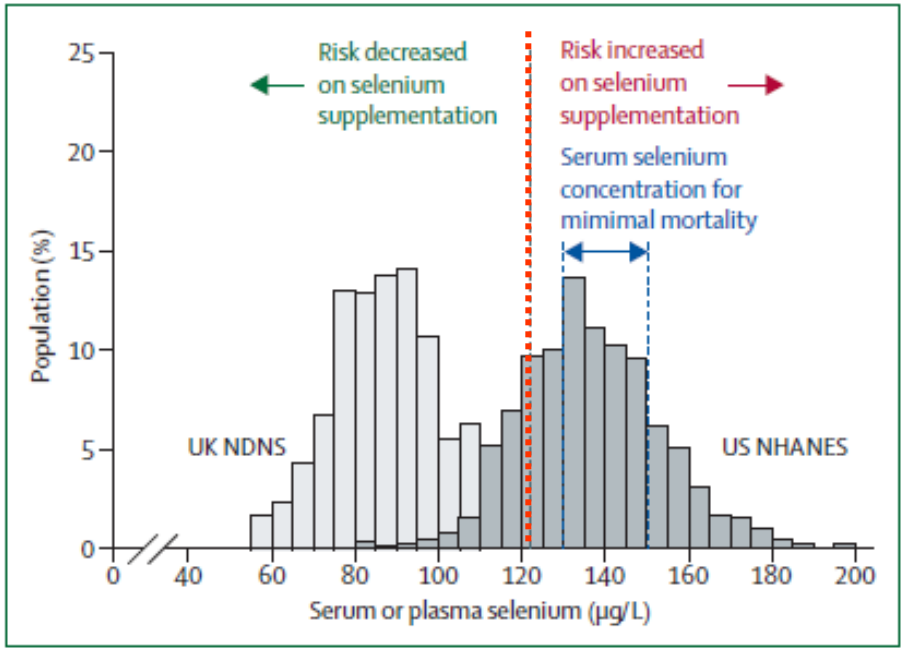




Selenium and human health

Margaret P Rayman ***Lancet* 2012; 379: 1256–68**





Zusammenhang:
Jod und Eisenmangel

Eisenmangel und Schilddrüsenunktion

- Die TPO enthält als aktives Zentrum eine Hämgruppe
- TPO – Aktivität abhängig von der ausreichenden Eisenzufuhr
- Bei Eisenmangel (Ferritin < 20 nmol/l) kann weniger Jod in Schilddrüsenhormone eingebaut werden
- Bei Eisenmangel ist eine Jodidsubstititon nicht wirksam

Zimmermann et al 2002

Addition of microencapsulated iron to iodized salt improves the efficacy of iodine in goitrous, iron-deficient children: a randomized, double blind, controlled study.

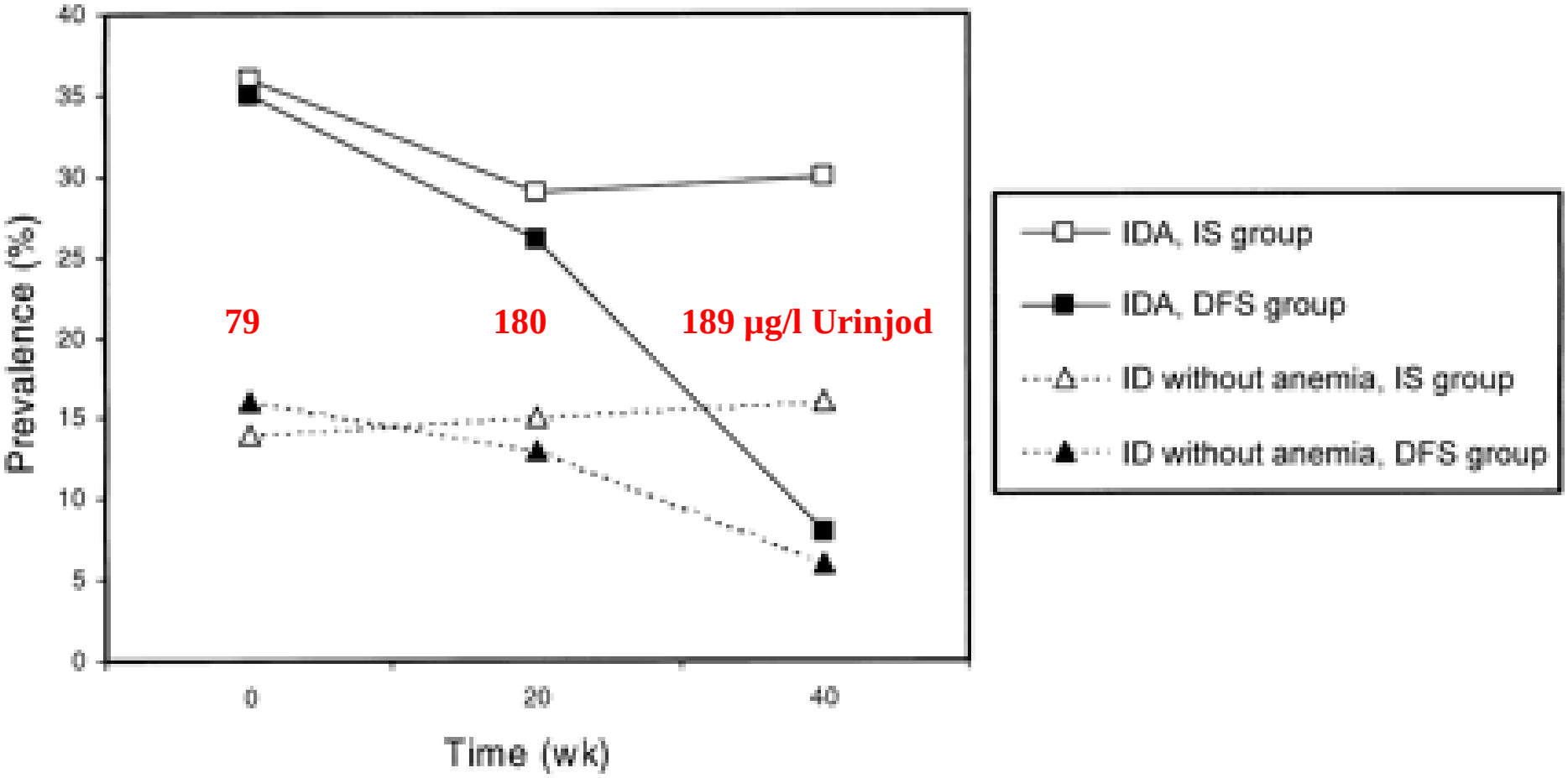
Zimmermann MB et al, EJE 147: 747-753 (2002)

- **Rif Mountains Nord-Marokko: Endemischer Jodmangel**
- **Jodaufnahme 8-12 µg pro Tag**

184 Kinder nur Jodsalz (n=184)
vs. Salz mit Jodid +mikroverkapseltem Eisen (n=183)

Prävalenz Eisenmangelanämie:

	Jodsalz (IS)	Jodid + Eisensalz (DFS)
Baseline:	**36%**	**35%**
20 Wochen	**28%**	**28%**
40 Wochen	**30%**	**8%**
	150-250 µg Jod	**7-12 mg Fe**



Zimmermann MB et al, EJE 147: 747-753 (2002)

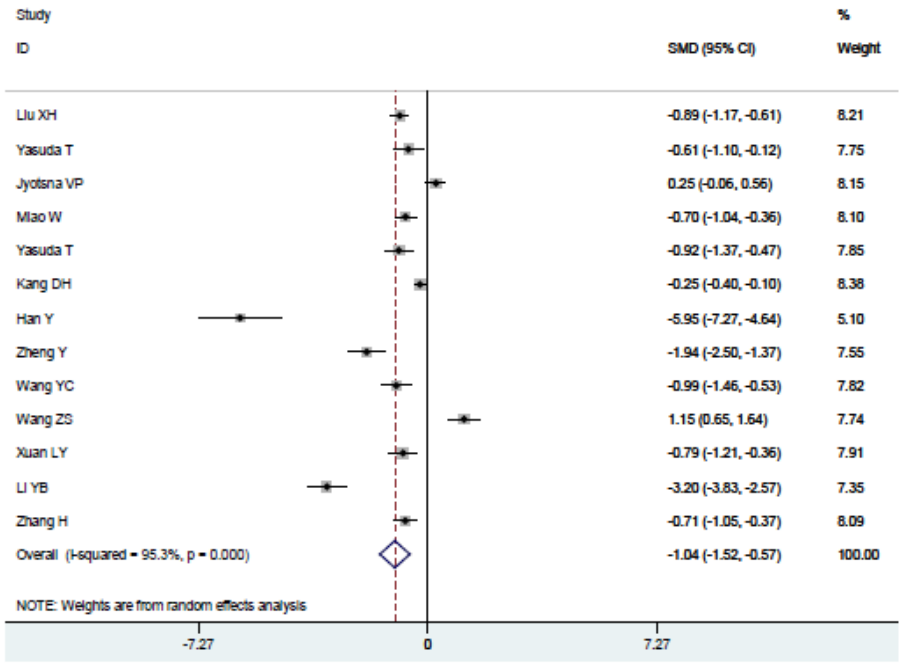
Vitamin D- Einfluss auf AIT

Vitamin A – hemmt ß-TSH Expression

Nutrients **2015**, *7*, 2485-2498; doi:10.3390/nu7042485

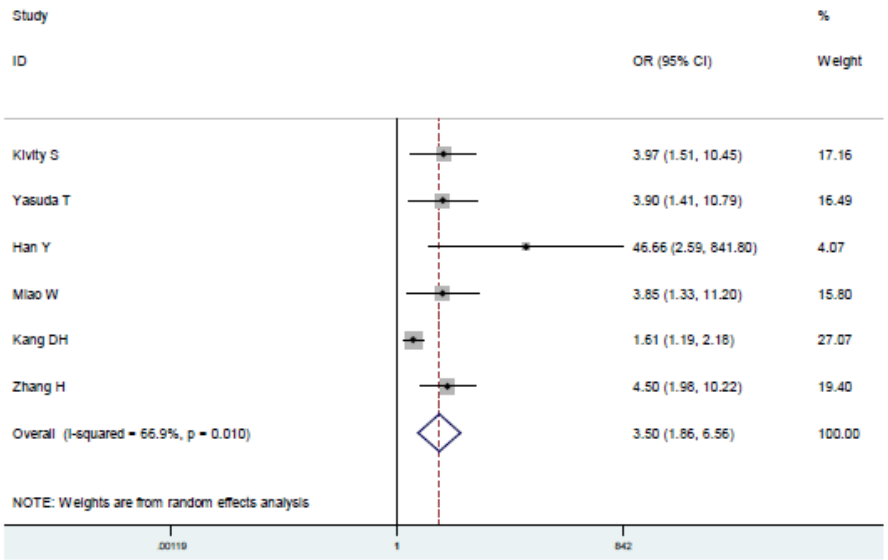
Meta-Analysis of the Association between Vitamin D and Autoimmune Thyroid Disease

Jiying Wang, Shishi Lv, Guo Chen, Chenlin Gao, Jianhua He, Haihua Zhong and Yong Xu *



Pat mit niedrigen Vitamin D Spiegel haben häufiger M. Basedow

Patienten mit M. Basedow haben signifikant niedrigere Vitamin D Spiegel



Nutrients **2015**, *7*, 2485-2498; doi:10.3390/nu7042485

Meta-Analysis of the Association between Vitamin D and Autoimmune Thyroid Disease

Jiying Wang, Shishi Lv, Guo Chen, Chenlin Gao, Jianhua He, Haihua Zhong and Yong Xu *

Diese erste Metaanlyse zeigt, dass sowohl Patienten mit Hashimoto-Thyreoiditis als auch M. Basedow niedrigere Vitamin D Spiegel haben als vergleichbare Gesunde

Und umgekehrt:

Das Risiko eine AITD zu bekommen ist bei Vitamin D Mangel signifikant erhöht

Vitamin D and thyroid disease: to D or not to D?

European Journal of Clinical Nutrition **69**, 291-296 (March 2015)

Although observational studies support a beneficial role of vitamin D in the management of thyroid disease, randomized controlled trials are required to provide insight into the efficacy and safety of vitamin D as a therapeutic tool for this dysfunction.

VDR-Polymorphismen

Systematic review and meta-analysis on vitamin D receptor polymorphisms and cancer risk

Yeqiong Xu · Bangshun He · Yuqin Pan · Qiwen Deng · Huiling Sun · Rui Li · Tianyi Gao · Guoqi Song · Shukui Wang

Tumor Biol. (2014) 35:4153–4169

Single nucleotide polymorphisms in the vitamin D pathway associating with circulating concentrations of vitamin D metabolites and non-skeletal health outcomes: Review of genetic association studies

David A. Jolliffe*, Robert T. Walton, Christopher J. Griffiths, Adrian R. Martineau*

Journal of Steroid Biochemistry & Molecular Biology xxx (2015) xxx–xxx

Fazit

Für die extraskeletalen Effekte des Vitamin D Metabolismus sind sehr wahrscheinlich Polymorphismen des VDR entscheidender als der Vitamin D Serumspiegel

Am J Clin Nutr 2007;86:1040–4.

Vitamin A supplementation in iodine-deficient African children decreases thyrotropin stimulation of the thyroid and reduces the goiter rate[1–3]

Michael B Zimmermann, Pieter L Jooste, Ngoako Solomon Mabapa, Serena Schoeman, Ralf Biebinger, Linda F Mushaphi, and Xikombiso Mbhenyane

IS = 191 mg Lipiodol
VAS = 200 000 E Vitamin A

TABLE 4
Thyroid volume (Tvol), whole-blood thyrotropin (TSH) and thyroglobulin (Tg), and serum total thyroxine (TT_4) in children who received, at baseline and after 3 mo, 1 of 4 treatments[1]

	Group			
Measure	Placebo (n = 88)	IS (n = 100)	VAS (n = 115)	IS+VAS (n = 101)
Tvol (mL)				
Baseline	3.19 (1.10–9.03)[2]	3.23 (1.12–13.43)	3.25 (1.04–10.28)	3.18 (1.22–8.33)
3 mo	3.26 (0.97–9.69)	3.09 (0.98–12.25)	2.97 (1.01–10.39)	3.10 (0.96–7.74)
6 mo	3.29 (1.08–10.08)[a]	2.34 (0.87–9.97)[b,3]	2.91 (0.88–8.96)[c,4]	2.50 (1.01–8.18)[b,3]
TSH (mU/L)				
Baseline	1.4 (0.9–4.3)	1.6 (0.6–14.1)	1.5 (0.5–5.0)	1.7 (0.6–8.8)
3 mo	1.6 (0.6–4.8)[a]	0.9 (0.4–4.7)[b,4]	1.0 (0.4–2.6)[b,4]	0.7 (0.4–3.8)[b,3]
6 mo	1.7 (0.7–4.1)[a]	0.6 (0.3–4.6)[b,3]	1.1 (0.5–2.9)[c,4]	0.5 (0.4–2.9)[b,3]
Tg (μg/L)				
Baseline	16.7 (7.7–79.7)	17.8 (6.1–73.4)	17.4 (5.8–60.9)	16.6 (5.6–50.6)
3 mo	17.6 (7.9–74.1)[a]	6.9 (1.4–31.7)[b,3]	12.9 (7.7–79.7)[c,4]	5.7 (0.7–28.9)[b,3]
6 mo	18.3 (6.3–69.2)[a]	4.3 (1.1–18.8)[b,5]	13.1 (7.7–79.7)[c,4]	4.0 (0.8–20.3)[b,5]
TT_4 (nmol/L)				
Baseline	96 ± 19[6]	105 ± 23	97 ± 15	97 ± 18
3 mo	101 ± 15	105 ± 19	99 ± 17	102 ± 18
6 mo	99 ± 19	100 ± 17	97 ± 16	102 ± 18

Fazit für die Praxis

- Obgleich es Hinweise darauf gibt, dass verschiedene Spurenelemente und Vitamine Einfluss auf den Schilddrüsenhormonstoffwechsel haben, gibt es für die Praxis wenig therapeutische Ansätze, außer für
  - Selen
  - Eisen
  - Vitamin D
- Eisen und Selenmangel, möglicherweise Vitamin A Mangel, sind assoziiert mit einem erhöhten Risiko für Strumen,
- Selenmangel und Vitamin D Mangel mit AITD
- Diese Mängel sollten gegebenfalls als adjuvante Therapie in Erwägung gezogen werden

Vielen Dank für Ihre Aufmerksamkeit !

Fragen?

Kommentare?