Tireopatia e nutraceutica: facciamo chiarezza

Dott. Giuseppe Pasimeni

Firenze, 21 maggio 2016

DEFINIZIONE

Nutraceutica è un **neologismo sincratico** da **"nutrizione" e "farmaceutica**" e si riferisce allo studio di alimenti che si suppone abbiano una funzione benefica sulla salute umana. Il termine è stato coniato dal Dr. Stephen DeFelice nel 1989

Gli alimenti nutraceutici vengono comunemente anche definiti alimenti funzionali o alicamenti

Nutraceutico: integratore alimentare che contiene una forma concentrata di una sostanza bioattiva, derivata da un alimento, presente in una matrice non alimentare ed a dosaggi superiori a quella ottenibile con i normali alimenti

Alimento funzionale: alimento che associa componenti nutrizionali selezionate per caratteristiche, quali l'alta digeribilità e l'ipoallergenicità, alle proprietà curative di principi attivi naturali.

Nutraceutici e tiroide

Iodio

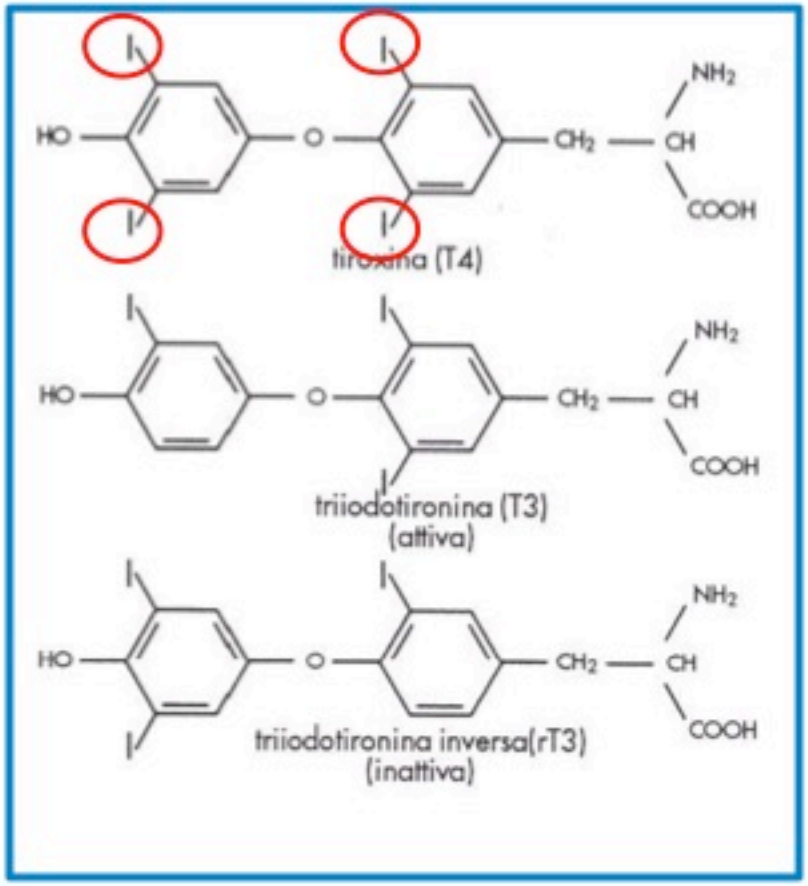
Selenio

Selenio+Inositolo

Interferenti funzione ghiandolare

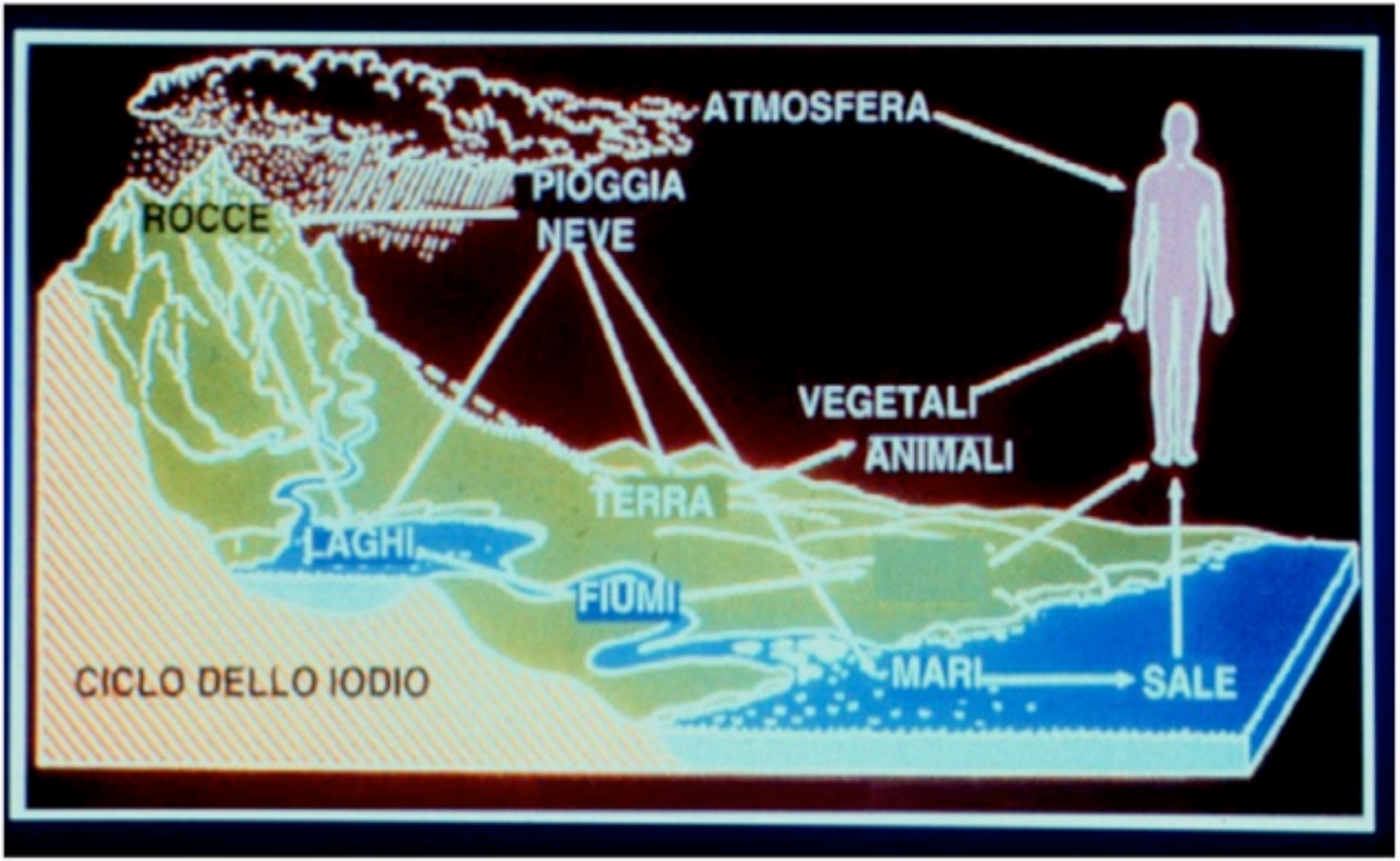
IODIO

L'importanza biologica dello iodio deriva dal fatto che questo elemento è il costituente essenziale degli ORMONI TIROIDEI



Un adeguato apporto nutrizionale di iodio è essenziale per assicurare la normale crescita e lo sviluppo degli organismi animali e dell'uomo

CICLO DELLO IODIO IN NATURA



METABOLISMO DELLO IODIO

I_2 alimentare

$I_2 \longrightarrow I^-$

Assorbimento gastrointestinale

POOL PLASMATICO DELLO IODIO

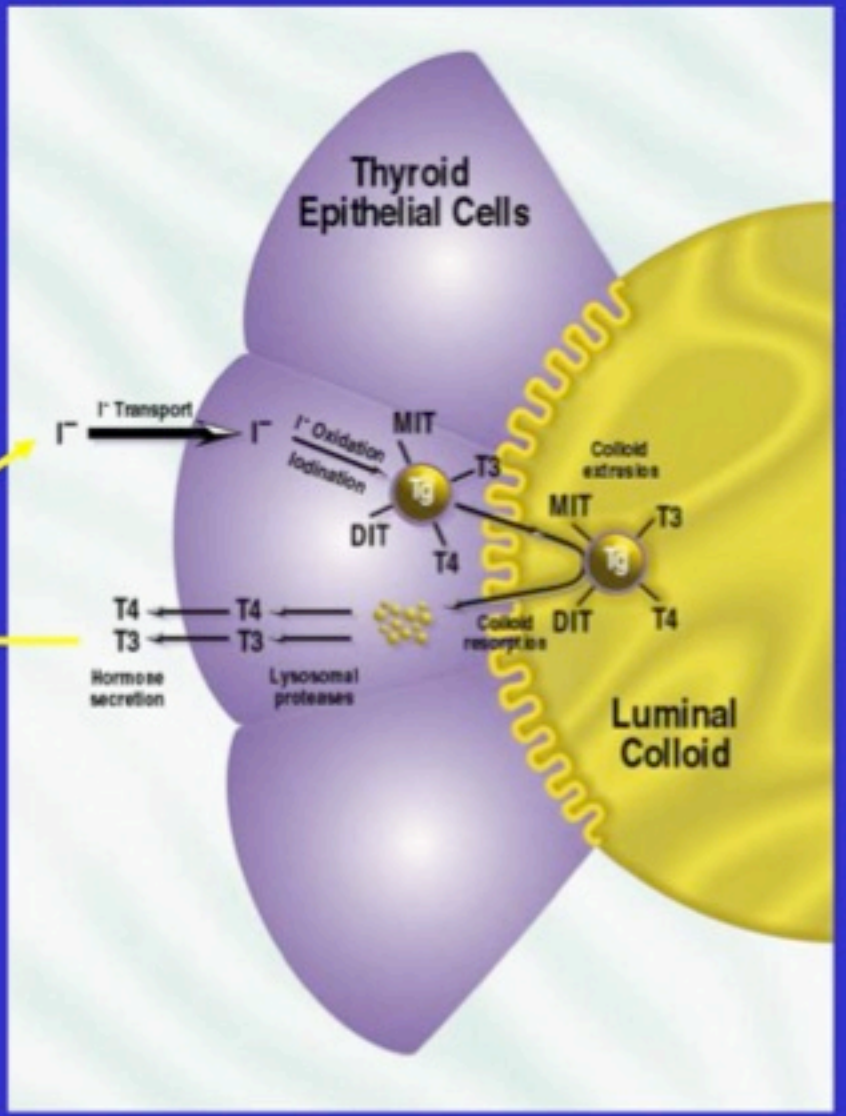
deiodazione

Escrezione renale

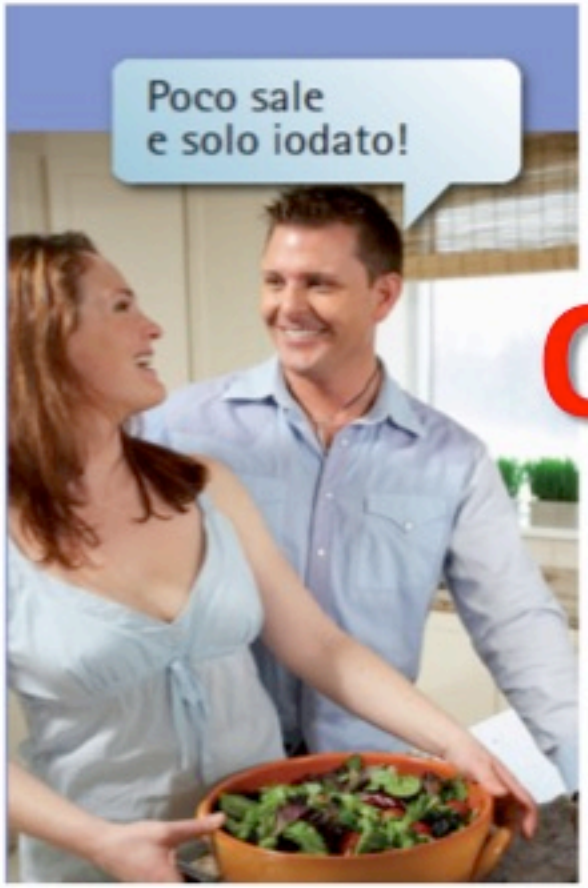
98%

Escrezione fecale, sudore, aria espirata

circa 2%



Legge n. 55 del 2005: « Disposizioni finalizzate alla prevenzione del gozzo endemico e di altre patologie da carenza iodica»



- Presenza di sale iodato obbligatoria nei punti vendita;
- Fornitura del sale comune solo su specifica richiesta del consumatore;
- Uso di sale arricchito di iodio nella ristorazione collettiva;
- Possibilità di utilizzazione nella preparazione e nella conservazione dei prodotti alimentari

OSNAMI

Circa il 30% della popolazione mondiale è affetto da carenza iodica

www.associazionemediciendocrinologi.it

ame flash
nr. 14 - luglio 2015

L'APPORTO OTTIMALE DI IODIO

Responsabile Editoriale
Vincenzo Toscano

Tabella 1
RDA e ULs per lo iodio

Età	RDA (µg/die)	ULs (µg/die) Upper intake levels	
		DGS&C-EU	IMS
0 – 12 mesi	Non stabilito *	Non stabilito *	Non stabilito *
1 – 3 anni	90	200	200
4 – 6 anni	90	250	300
7 – 8 anni	90	300	300
9 – 10 anni	120	300	600
11 – 13 anni	120	450	600
14 anni	150	450	900
15 – 17 anni	150	500	900
Adulto	150	600	1100
Gravidanza	220	600	14 – 18 anni: 900 ≥ 19 anni: 1100
Allattamento	290	600	14 – 18 anni: 900 ≥ 19 anni: 1100

* Il cibo e/o il latte artificiale dovrebbero costituire le uniche fonti di iodio in questa fascia d'età

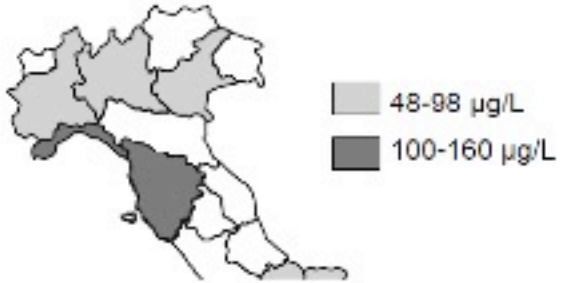


Tabella 2
Livelli mediani di *Urinary Iodine Excretion* (UIE) proposti dall'OMS

	UIE mediana	Apporto iodico
Popolazione generale	< 20 µg/L	Insufficiente (grave)
	20–49 µg/L	Insufficiente (moderato)
	50–99 µg/L	Insufficiente (lieve)
	100–199 µg/L	Adeguato
	200–299 µg/L	Più che adeguato
	≥ 300 µg/L	Eccessivo
Donne in gravidanza	< 150 µg/L	Insufficiente
	150–249 µg/L	Adeguato
	250–499 µg/L	Più che adeguato
	≥ 500 µg/L	Eccessivo
Donne in allattamento e bambini < 2 anni	< 100 µg/L	Insufficiente
	≥ 100 µg/L	Adeguato

Figura 4. Valori mediani di ioduria in gravidanza (2006-2011) (la ioduria mediana attesa in donne in gravidanza con adeguato apporto iodico rientra in un range pari a 150-249 µg/L)

Olivieri A Rapporti ISTISAN 2014

Indicatori di efficacia di iodoprofilassi

- Volume tiroideo in bambini in età scolare (% di gozzo inferiore al 5%)

-TSH neonatale (da effettuarsi ad almeno 48 ore dalla nascita)

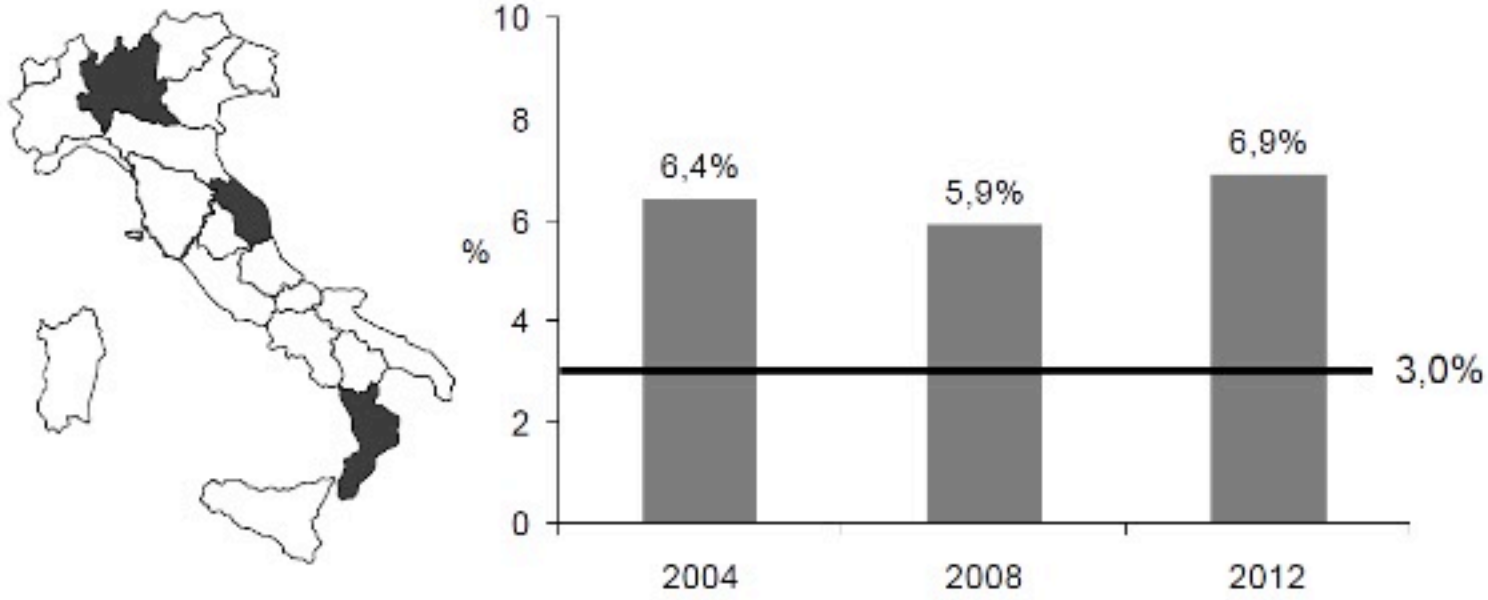


Figura 5. Frequenza di TSH >5 µUI/mL in Italia

Indicatori di efficacia di iodoprofilassi

- Tireoglobulina sierica (cut-off 13 µg/L nei bambini in età scolare)

THYROID
Volume 24, Number 8, 2014

DOI: 10.1089/thy.2014.0052

REVIEWS and SCHOLARLY DIALOG

Thyroglobulin as a Biomarker of Iodine Deficiency: A Review

Zheng Feei Ma and Sheila A. Skeaff

LA CARENZA ALIMENTARE DI IODIO compromette la funzione tiroidea e si traduce in quadri morbosi che variano a seconda del periodo della vita interessato da questo deficit

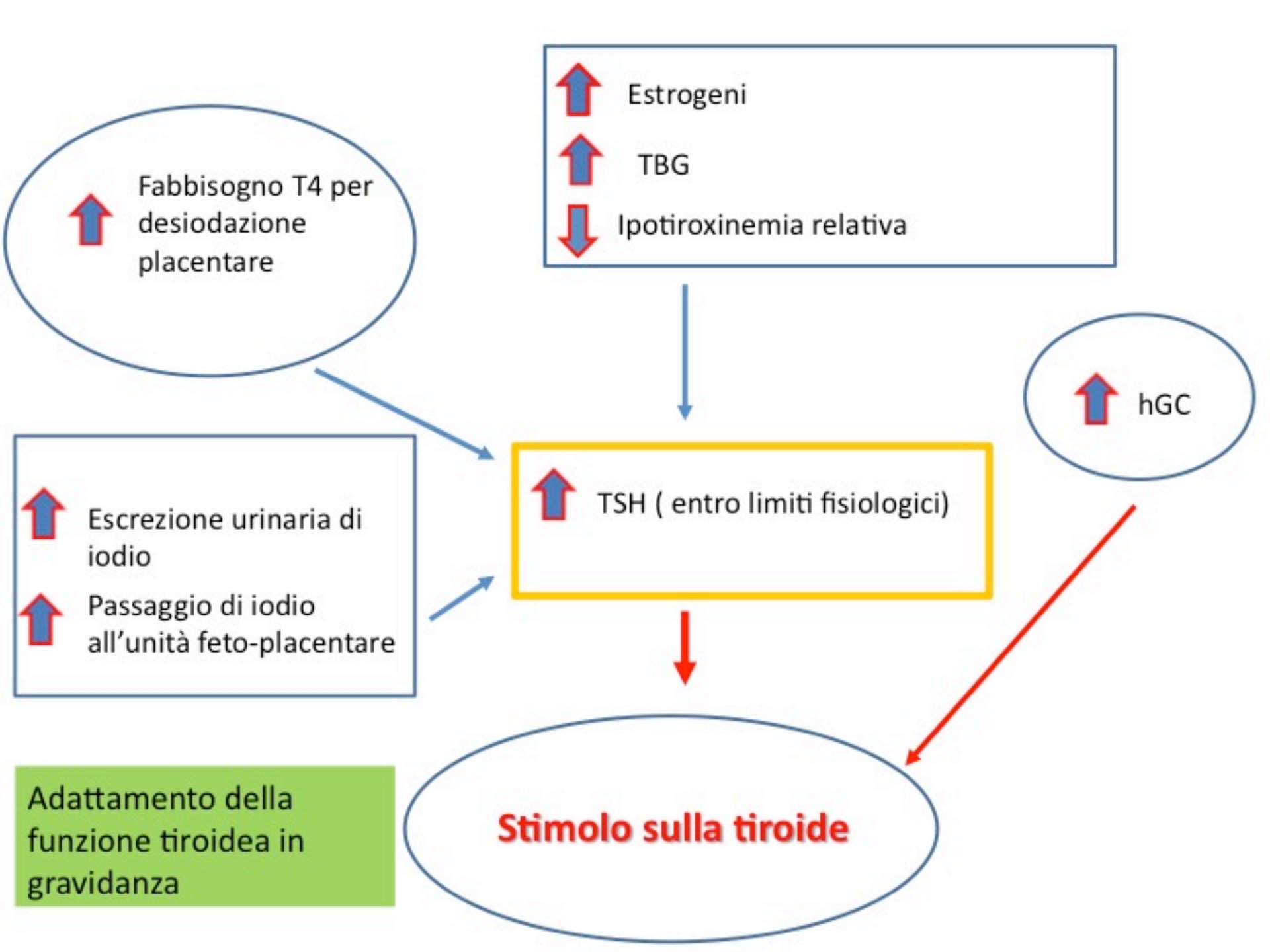
In tutte le età	Gozzo
Nel feto e nel neonato	Aborto, mortalità perinatale, cretinismo, ipotiroidismo, difetti psicomotori
Nel bambino e nell'adolescente	Ipotiroidismo subclinico e franco, ritardo di sviluppo psicosomatico
Adulto	Gozzo nodulare, ipertiroidismo da gozzo nodulare

Modificata da ICCIDD, UNICEF WHO 2001

Difetti neuropsicologici in neonati e bambini in età scolare residenti in aree dell'Europa a lieve o moderata carenza iodica

Regione	Test	Risultati	Autori
Spagna	Baylely McCarthy modificati	Capacità psicomotorie e sviluppo mentale ridotti	Bleichrodt 1989
Italia-Sicilia	Bender-Gestalt	Ridotte capacita' motorie percettive ed integrative; anomalie neuromuscolari e neurosensoriali	Vermiglio 1990
Toscana	Wechsler Raven	Ridotte QI verbale; basse capacità percettive e motorie	Fenzi 1990
Toscana	WISC	Ridotta risposta motoria Tempo di reazione agli stimoli visivi	Vitti 1992 Aghini Lombardi 1995

Modificata da Aghini Lombardi et al J. Endocrinol. Invest.1995


Estrogeni
TBG
Ipotiroxinemia relativa
Fabbisogno T4 per desiodazione placentare
hGC
Escrezione urinaria di iodio
Passaggio di iodio all'unità feto-placentare
TSH (entro limiti fisiologici)
Stimolo sulla tiroide
Adattamento della funzione tiroidea in gravidanza

Iodine Prophylaxis Using Iodized Salt and Risk of Maternal Thyroid Failure in Conditions of Mild Iodine Deficiency

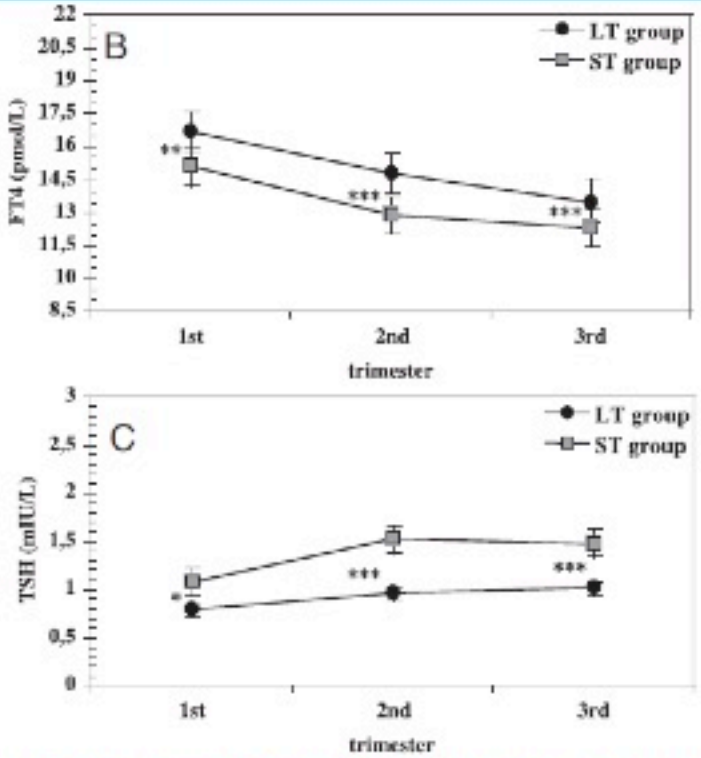


FIG. 1. Average values of maternal T_3 to T_4 molar ratio, FT4, and TSH at first, second, and third trimester of gestation in both LT and ST groups. *, $P < 0.05$; **, $P < 0.001$; ***, $P < 0.0001$.

The overall prevalence of MTF over the entire study period was almost 6-fold higher in ST than LT women **(36,8 vs 6,4 % P<0,0005)**

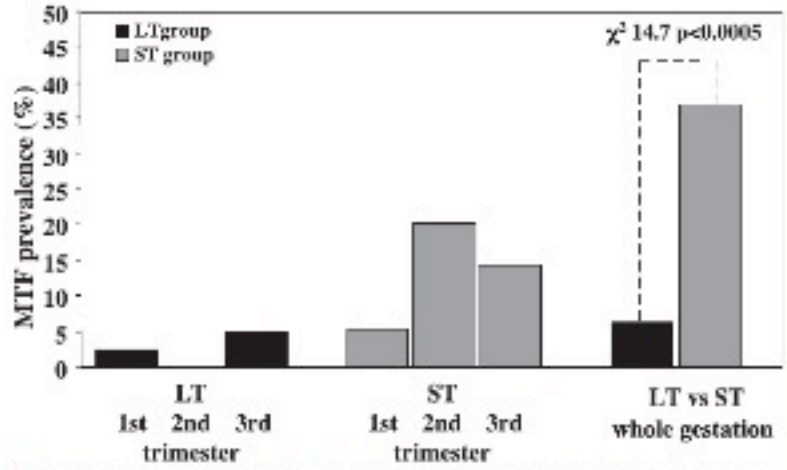


FIG. 3. Prevalence of maternal thyroid failure at the first, second, and third trimester or whole gestation in both LT and ST groups.

Moleti M. et al JCEM 2008

The Effect of Voluntary Iodine Prophylaxis in a Small Rural Community: The Pescopagano Survey 15 Years Later

F. Aghini Lombardi, E. Fiore, M. Tonacchera, L. Antonangeli, T. Rago, M. Frigeri, A. M. Provenzale, L. Montanelli, L. Grasso, A. Pinchera,+ and P. Vitti

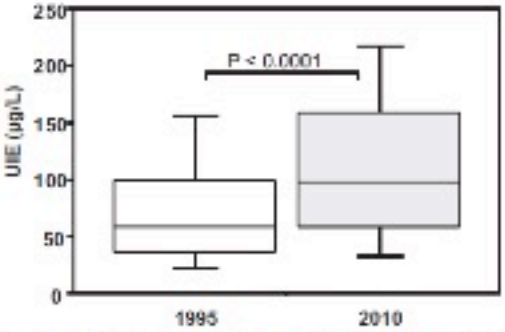


Figure 1. Box-whisker plot of UIE measured in 1995 (n = 1186) and in 2010 (n = 453). Results are reported as median values (black lines), interquartile (25 to 75 percentiles) range (boxes), and 10th to 90th percentiles (whiskers). UEI was significantly higher in 2010 than in 1995 (Mann Whitney *U* test: $P < .0001$).

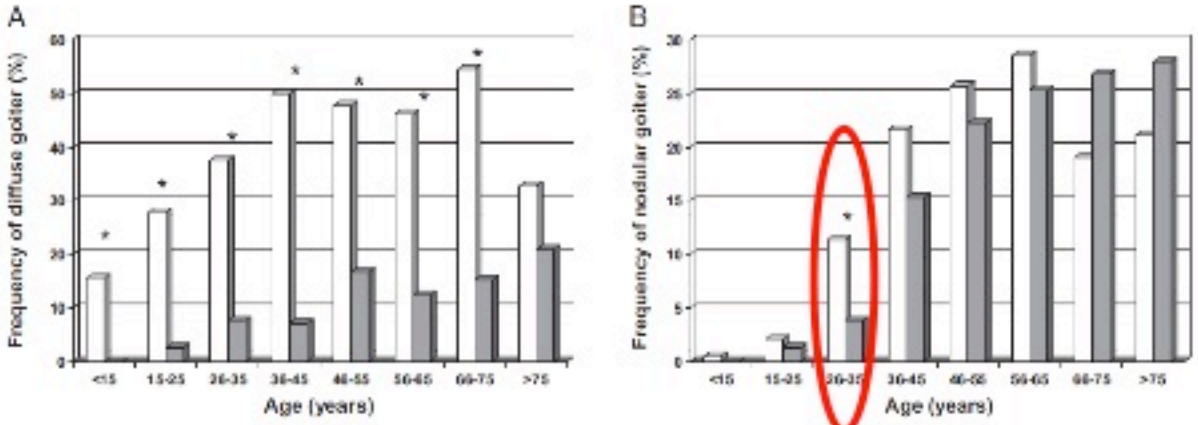


Figure 2. Frequency of diffuse goiter (panel A) and nodular goiter (panel B) in subjects resident in Pescopagano in 1995 (white columns) and in 2010 (gray columns). The prevalence of diffuse goiter progressively increased with age both in 1995 and 2010 and in each class of age was significantly lower in 2010 compared with 1995, with the exception of subjects older than 75 years. The frequency of nodular goiter was significantly lower in 2010 than in 1995 in patients aged 26–35 years, whereas no difference was observed in older classes of age. *χ^2 $P < .05$). The number of subjects included in each class of age is reported in *Subjects and Methods*.

ORIGINAL ARTICLE
Endocrine Care

The Effect of Voluntary Iodine Prophylaxis in a Small Rural Community: The Pescopagano Survey 15 Years Later

F. Aghini Lombardi, E. Fiore, M. Tonacchera, L. Antonangeli, T. Rago, M. Frigeri, A. M. Provenzale, L. Montanelli, L. Grasso, A. Pinchera,+ and P. Vitti

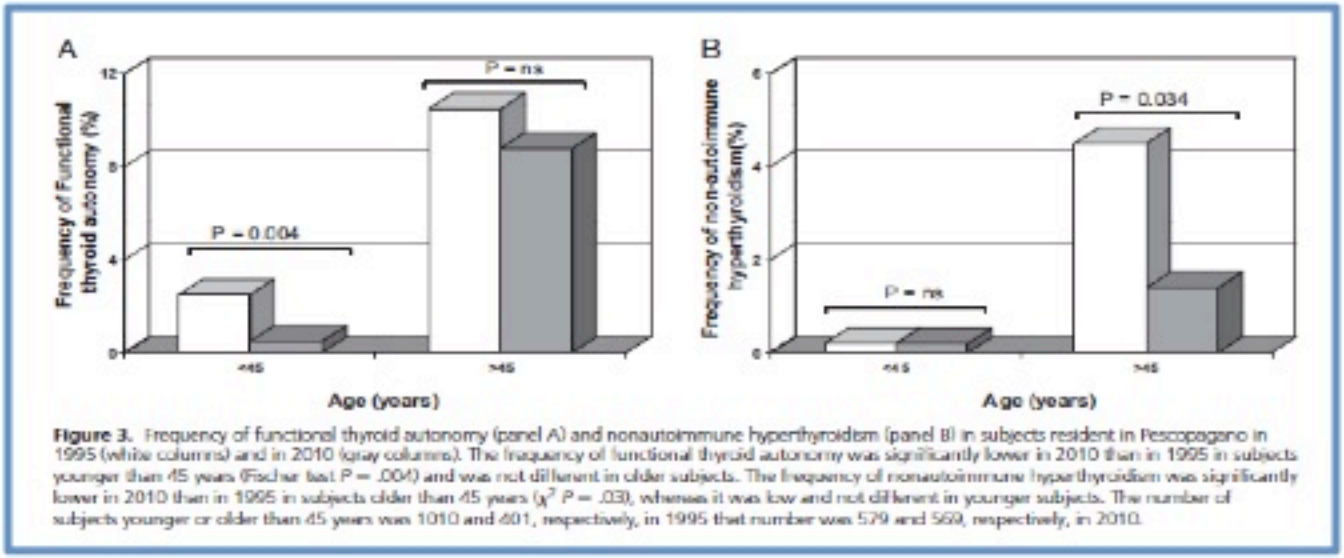


Figure 3. Frequency of functional thyroid autonomy (panel A) and nonautoimmune hyperthyroidism (panel B) in subjects resident in Pescopagano in 1995 (white columns) and in 2010 (gray columns). The frequency of functional thyroid autonomy was significantly lower in 2010 than in 1995 in subjects younger than 45 years (Fischer test $P = .004$) and was not different in older subjects. The frequency of nonautoimmune hyperthyroidism was significantly lower in 2010 than in 1995 in subjects older than 45 years (χ^2 $P = .03$), whereas it was low and not different in younger subjects. The number of subjects younger or older than 45 years was 1010 and 401, respectively, in 1995 that number was 579 and 569, respectively, in 2010.

JCEM 2013

The Effect of Voluntary Iodine Prophylaxis in a Small Rural Community: The Pescopagano Survey 15 Years Later

F. Aghini Lombardi, E. Fiore, M. Tonacchera, L. Antonangeli, T. Rago, M. Frigeri, A. M. Provenzale, L. Montanelli, L. Grasso, A. Pinchera,[4] and P. Vitti

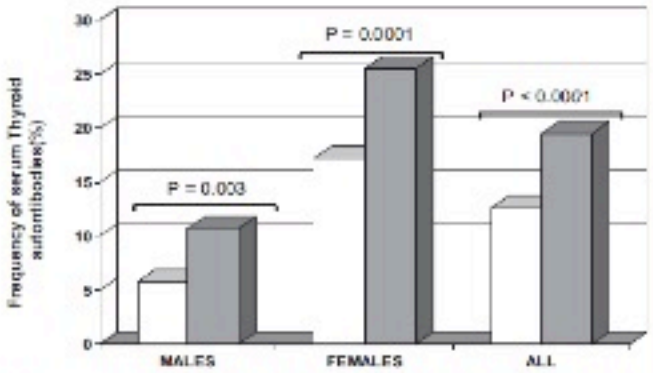
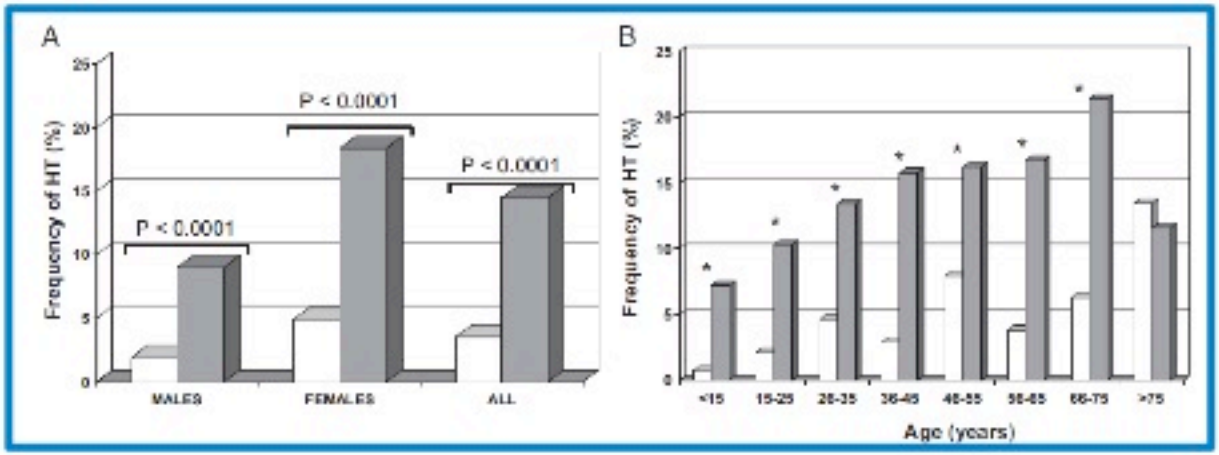


Figure 4. Frequency of TAbs in resident subjects in Pescopagano in 1995 (white columns) and in 2010 (gray columns). The frequency of positive TAb was significantly higher in 2010 than in 1995 in both females and males (χ^2 P value reported in figure). The number of males and females was 634 and 777, respectively, in 1995 and 468 and 680, respectively, in 2010.

changed between the 2 surveys. Iodine intake strongly affects the pattern of thyroid diseases, but the benefits of correcting iodine deficiency (decreased prevalence of goiter and thyroid autonomy, mainly in younger subjects and reduced frequency of nonautoimmune hyperthyroidism in older subjects) far outweigh the risk of development of thyroid autoimmunity and mild hypothyroidism in youngsters.



JCEM 2013

Reduction of Thyroid Nodule Volume by Levothyroxine and Iodine Alone and in Combination: A Randomized, Placebo-Controlled Trial

M. Grussendorf, C. Reiners, R. Paschke, and K. Wegscheider, on behalf of the LISA investigators

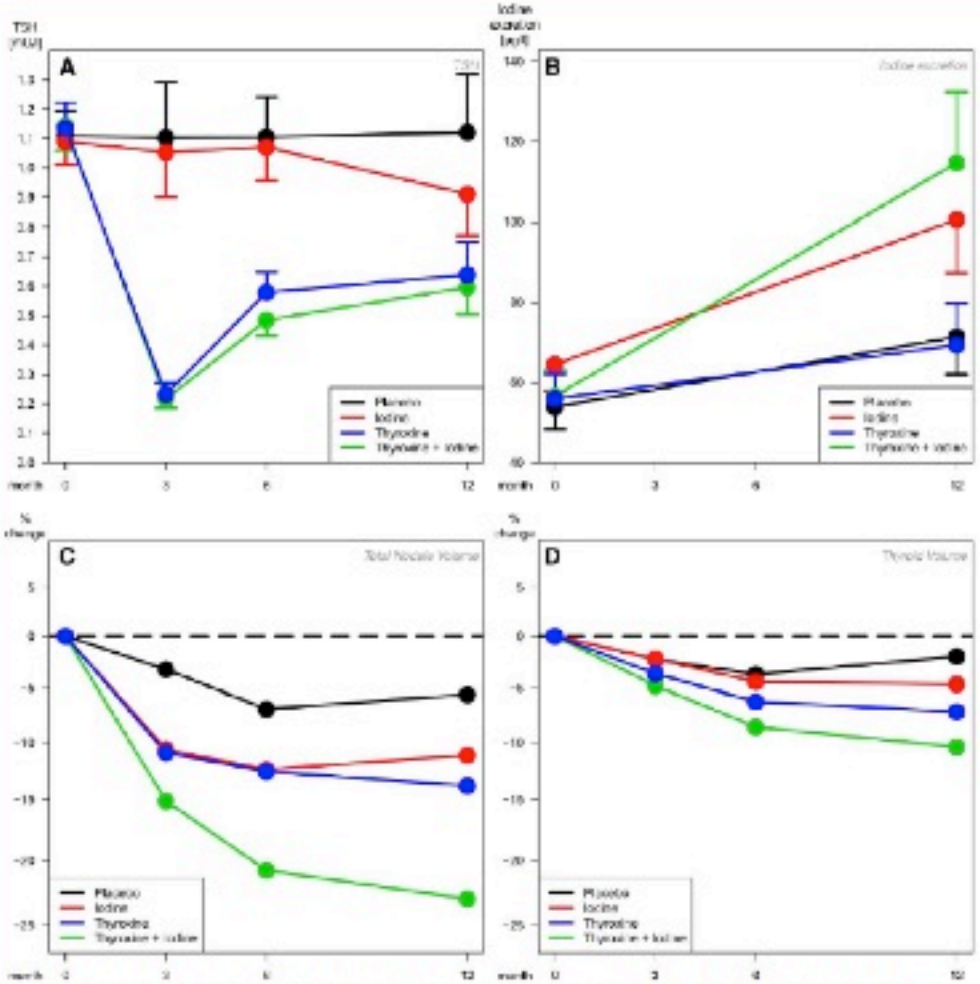


FIG. 1. Changes of TSH (A) and iodine (B) levels and corresponding percent changes from baseline of nodule (C) and thyroid (D) volumes in different treatment groups. Marginal means from longitudinal mixed models, with 95% CI (A and B) or presented as percent change from group specific baseline mean (C and D) intention to treat population, missing value imputation by direct maximum likelihood.

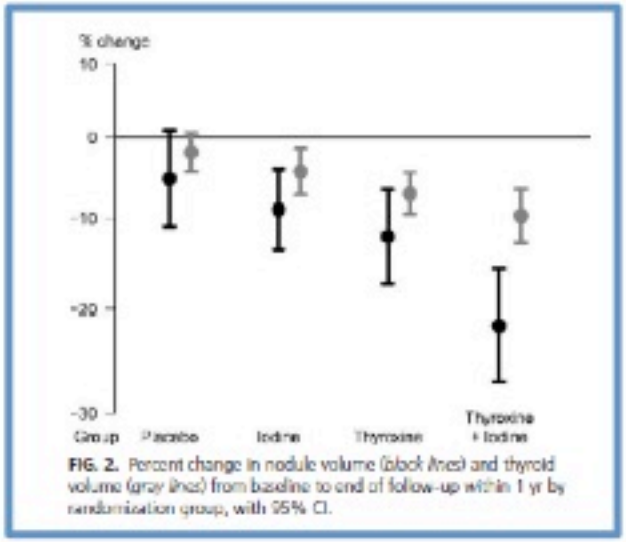


FIG. 2. Percent change in nodule volume (black lines) and thyroid volume (gray lines) from baseline to end of follow-up within 1 yr by randomization group, with 95% CI.

Nodule volume reductions: T4+I therapy was significantly superior to T4 (P=0 0,018) or I (P=0,003);

Thyroid volume reductions: T4+I was significantly superior to I (P=0,034) but not to T4 (P= 0,190)

JECM 2011

Nutraceutici e tiroide

Iodio

Selenio

Selenio+Inositolo

Interferenti funzione ghiandolare

Il **Selenio** è un "minerale traccia" scoperto per la I volta nel 1817 da un chimico svedese Berzelius

Esiste in natura e la sua presenza nell'organismo umano è fondamentale per il funzionamento di molti processi vitali

La principale fonte di reperimento di selenio per l'uomo è l'alimentazione. Gli alimenti fonte naturale principale di selenio sono: fegato, pesce, molluschi, crostacei, latte e derivati, noci, arachidi, frutta, vegetali, funghi, riso, lievito di birra e carne.

Le verdure sono il mezzo principale attraverso cui il selenio raggiunge la catena alimentare umana ed il loro contenuto di selenio dipende da quello del suolo.

Negli alimenti il selenio può essere presente in due forme diverse:

1) forma organica (**seleno-metionina**): non direttamente disponibile per la sintesi di specifiche selenoproteine, incorporato come selenoalbumina

2) forma inorganica (**selenite**): prontamente utilizzabile

La concentrazione di selenio plasmatico varia tra i 60 ed i 120 mcg/L

Selenio e funzioni biologiche

Azione immunostimolante

(Incremento proliferazione cellule T attivate,citotossicità umorale mediata dai linfociti, ed attività cellule NK)

Azione antiossidante/ immunomodulante

(a mezzo di selenoproteine determinanti nella risposta immune organo-specifica)

Azione di contrasto nei confronti di radicali liberi la cui azione distruttiva è rivolta verso componenti cellulari (lipidi,proteine, DNA etc)

Antiossidanti endogeni:

✓Non enzimatici (Acido urico, glutatione, bilirubina, tioli, albumina)

✓Enzimatici (SOD,Catalasi,GPx)

Antiossidanti esogeni:

✓Vitamine (C,E,B-carotene etc)

✓Elementi traccia (Cu,manganese,zinco e **Se**)

✓Sostanze di origine vegetale (isoflavoni,flavonoidi, polifenoli catechine)

La maggior parte degli effetti biologici del selenio mediati da selenoproteine

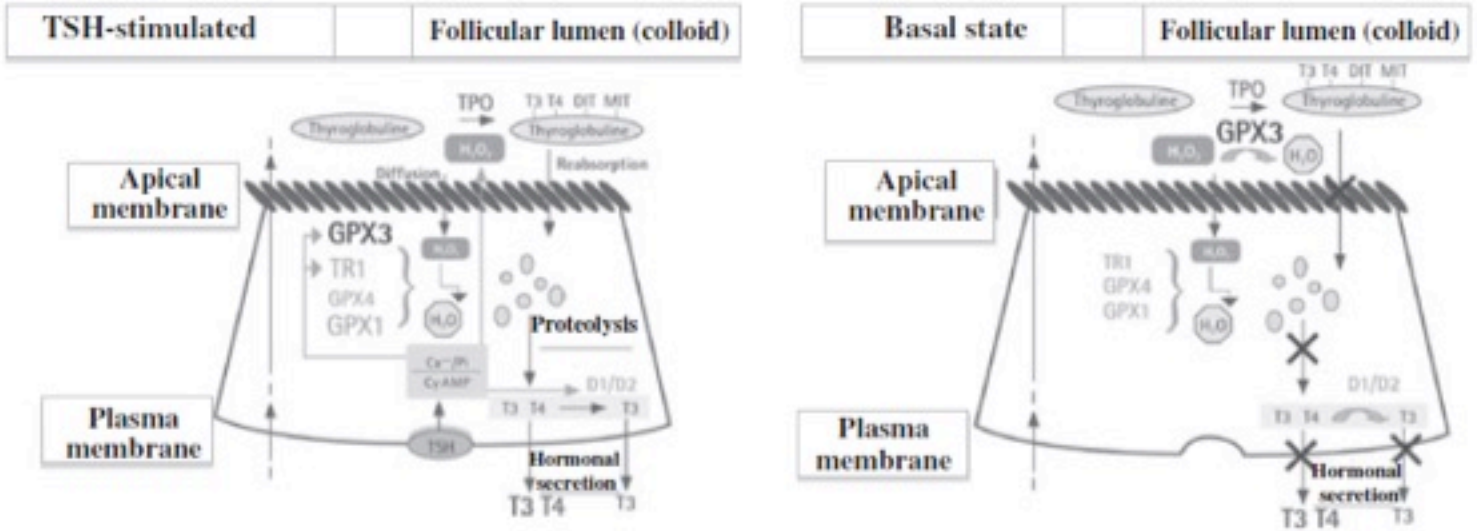
The principal selenoproteins and their functions in humans

Selenoproteins	Proposed functions
Gluthatione peroxidases (GPXs)	
GPX1	Cytosolic antioxidant, type of reserve?
GPX 2	Digestive tract antioxidant
GPX 3	Plasma and extracellular space antioxidant, significant thyroid expression
GPX 4	Mitochondrial membrane antioxidant, structural protein of sperm, apoptosis?
GPX 5	Unknown
GPX 6	GPX1 homologue?
Thioredoxin reductase (TRs)	Sustain the oxidation-reduction systems within the body, regulates certain transcription and cell growth factors
TR1	Principally cytosolic, ubiquitous
TR2	Testes expression
TR3	Principally mitochondrial, ubiquitous
Deiodinases	
Type 1 deiodinase (D1)	Conversion of T4 into T3 and rT3, and T3 into rT3 or T2
	Localisation: liver, kidneys, thyroid gland, pituitary gland
Type 2 deiodinase (D2)	Conversion of T4 into T3, and T3 into T2
	Localisation: thyroid gland, CNS, pituitary gland, skeletal and heart muscles
Type 3 deiodinase (D3)	Conversion of T4 and T3 into rT3 and T2
	Localisation: gravid uterus, placenta, foetal liver, foetal and neonatal brain, skin of newborns
Other selenoproteins	
Selenoprotein P	Transportation of selenium, endothelial antioxidant
Selenoprotein W	Heart and skeletal muscle antioxidant
Selenophosphate synthetase	Synthesis of selenophosphate for selenoproteins
15-kDa selenoprotein	Protection against cancer?
Selenoproteins H, I, K, M, N, O, R, S, T, V	Function unknown

Incorporato sotto forma di seleniocisteina

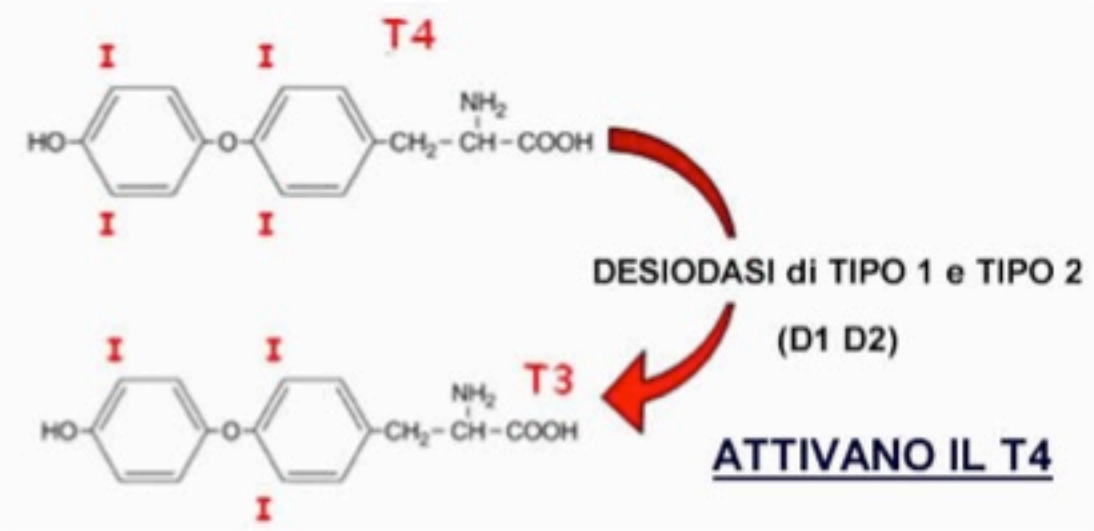
Drutel A. et al Clinical Endocrinology 2013

Ruolo di specifiche selenoproteine nella sintesi degli ormoni tiroidei



Drutel A. et al Clinical Endocrinology 2013


tirosina
HO
NH2
CH2 - CH - COOH
TPO
I
MIT
TPO
Si formano MIT e DIT


T4
I
HO
O
NH2
CH2 - CH - COOH
DESIODASI di TIPO 1 e TIPO 2
(D1 D2)
T3
ATTIVANO IL T4

Impact of selenium repletion on thyroid metabolism in controlled, randomised clinical trials carried out in industrialised countries

Reference of the study	Characteristics of the study population	Study duration	Groups studied and sample sizes	Final levels of total T4 (nmol/l)*	Final levels of TSH (mUI/l)	Final levels (or change/start of study) of plasma selenium levels (µg/l)	Final levels of plasma erythrocyte GPX levels (UI/g Hb)
Olivieri *et al.*[27] 1995 Italy	Elderly subjects in good health (86 years ± 7)	3	Placebo = 17	68·5 + 10·4	0·99 + 0·71	60·0 + 15·8	4·1 + 1·1
			100 µg Se/day = 19	62 + 10 ($P < 0·005$)	1·18 + 0·58 (NS)	105·8 + 23·7 ($P < 0·05$)	7·78 + 2 ($P < 0·05$)
Rayman *et al.*[30] 2008 England	Elderly subjects in good health (60–74 years)	6	Placebo = 90	87·2 + 18	1·23 + 0·72	−2·6 (95% CI: −5·9 to 0·6)	ND
			100 µg Se/day = 99	87·0 + 16·4	1·23 + 0·70	54·9 (95% CI: 49·5–60·4) ($P < 0·001$) 99·0 (95% CI: 91·6–106·4) ($P < 0·001$) 133·2 (95% CI: 123·1–143·3) ($P < 0·001$)	ND
			200 µg Se/day = 95	83·5 + 14·5	1·27 + 0·69		ND
			300 µg Se/day = 84	81·6 + 14·4 (NS)	1·18 + 0·69 (NS)		ND
Duffield *et al.*[28] 1999 New Zealand	Selenium-deficient adult subjects (19–59 years)	5	Placebo = 10	99 + 30	ND	66·3 + 12·6	ND
			10 µg Se/day = 10	93 + 10	ND	83·7 + 17·4	ND
			20 µg Se/day = 11	($P < 0·05$)	ND	($P < 0·005$)	ND
			30 µg Se/day = 10	88 + 15 (NS)	ND		ND
			40 µg Se/day = 11	90 + 17 (NS)	ND		ND
				89 + 19 (NS)			
Thomson *et al.*[29] 2005 New Zealand (Study A)	Selenium-deficient adult subjects (19–52 years)	5	Placebo = 30	91 + 32	ND	79·7 + 12·6	ND
			100 µg Se/day = 30	98 + 33 (NS)	ND	105·0 + 11·8 ($P < 0·001$)	ND
Thomson *et al.*[29] 2005 New Zealand (study B)	Healthy adults (18–65 years)	5	Placebo = 81	88 + 23	ND	90 + 14·2	ND
			200 µg Se/day = 82	84 + 22 (NS)	ND	172·9 + 23·7 ($P < 0·001$)	ND
Hawkes *et al.*[31] 2008 United States	Men (18–45 years)	12	Placebo = 20	92 + 18	2·21 + 1·1	ND	ND
			300 µg Se/day = 22	92 + 22 (NS)	2·0 + 0·9 (NS)	ND	ND

Selenio e Tireopatie

- ✓Tiroidite cronica autoimmune
- ✓Malattia di Basedow Graves'
- ✓Orbitopatia di Graves'

Selenio e Tireopatie

- ✓**Tiroidite cronica autoimmune**
- ✓Malattia di Basedow Graves'
- ✓Orbitopatia di Graves'

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The Journal of Clinical Endocrinology & Metabolism 87(4):1687–1691

Selenium Supplementation in Patients with Autoimmune Thyroiditis Decreases Thyroid Peroxidase Antibodies Concentrations

ROLAND GÄRTNER, BARBARA C. H. GASNIER, JOHANNES W. DIETRICH, BJARNE KREBS, AND MATTHIAS W. A. ANGSTWURM

Department of Endocrinology, Medizinische Klinik Innenstadt, University of Munich, D-80336 Munich, Germany

TABLE 1. Thyroid-specific antibody concentrations before and after treatment with 200 μg (2.53 μmol) sodium selenite/d (verum) or placebo for 3 months

Group	Before	After	Significance	% change
TPOAb				
Verum	904 ± 205	575 ± 146	$P = 0.013$*	−36
Placebo	1090 ± 277	959 ± 267	$P = 0.95$	−12
TgAb				
Verum	1507 ± 390	1375 ± 484	$P = 0.33$	−9
Placebo	1089 ± 255	742 ± 161	$P = 0.015$*	−32

* Significant decrease (Wilcoxon's matched pairs test).

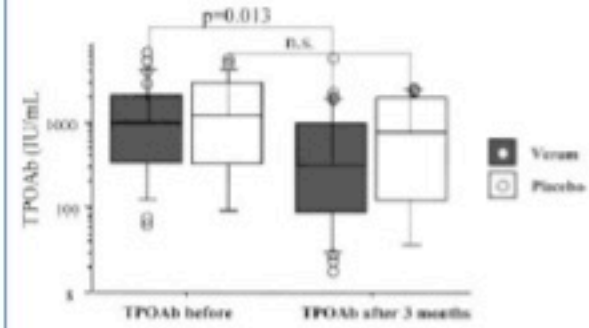

FIG. 1. TPOAb concentrations at study entry and 3 months after treatment with 200 μg (2.53 μmol) sodium selenite or placebo. *P* values are calculated by Wilcoxon's matched pairs, signed-rank test.

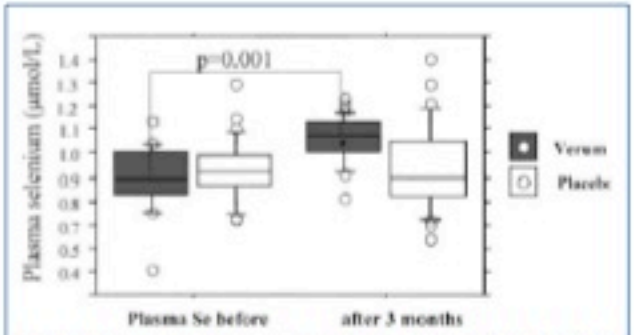

FIG. 2. Plasma selenium concentrations at study entry and 3 months after treatment with 200 μg (2.53 μmol) sodium selenite or placebo. *P* values are calculated by Wilcoxon's matched pairs, signed-rank test.

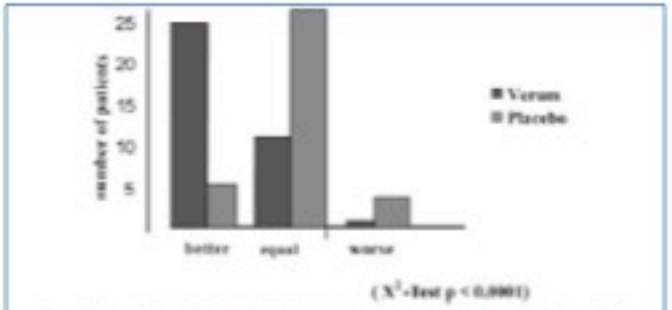

FIG. 3. Quality of life (SF 12) of patients treated with 200 μg (2.53 μmol) sodium selenite or placebo for 3 months.

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CLINICAL STUDY

Effects of a six month treatment with selenomethionine in patients with autoimmune thyroiditis

Leonidas H Duntas, Emilia Mantzou and Demetrios A Koutras

Endocrine Unit, Evgenidion Hospital, University of Athens Medical School, 20 Papadiamantopoulou Str, 11528 Athens, Greece

(Correspondence should be addressed to Leonidas H Duntas; Email: ledunt@otenet.gr)

Table 1 TSH, FT_4, T_3 and anti-Tg serum concentrations (mean±S.D.) in patients with autoimmune thyroiditis treated either with selenomethionine plus LT_4 (Gr I) or with LT_4 plus placebo (Gr II) over a period of 6 months.

	Months					
	Gr I			*Gr II*		
	0	3	6	0	3	6
TSH mU/l (nr: 0.3-4 mU/l)	9.8±3.6	1.4±0.6	0.7±0.2	9.5±3.8	1.1±0.5	0.8±0.3
FT_4 pmol/l (nr: 9–25 pmol/l)	12.4±1.1	15.9±1.2	16.7±1.3	11.9±1.2	16.4±1.7	16.8±1.5
T_3 nmol/l (nr: 0.9–2.7 nmol)	1.7±0.2	2.1±0.2	2.2±0.2	1.7±0.2	2.2±0.2	2.2±0.2
Anti-Tg (<100 U/l)	1724±412	1672±392	1638±404	1807±482	1750±386	1697±417

Table 2 Overall decrease in percentage of serum anti-TPO concentrations after 6 months of treatment with selenomethionine plus LT_4 (Gr I) or with LT_4 and placebo (Gr II) over a period of 6 months.

	Months					
	Gr I			*Gr II*		
	0	3	6	0	3	6
Anti-TPO (<100 U/l)	1875±1039	1013±382*	844±227**	1758±917	1389±520	1284±410***

* $P < 0.0001$ vs t_0; ** $P < 0.05$ vs t_3; *** $P < 0.001$ vs t_0.

Clinical Endocrinology (2010) 73, 535–539 doi: 10.1111/j.1365-2265.2009.037

ORIGINAL ARTICLE

Influence of physiological dietary selenium supplementation on the natural course of autoimmune thyroiditis

Davide Nacamulli*·[1], Caterina Mian*·[1], Daniela Petricca*, Francesca Lazzarotto*, Susi Barollo†, Dina Pozza*, Stefano Masiero*, Diego Faggian‡, Mario Plebani‡, Maria E. Girelli*, Franco Mantero* and Corrado Betterle*

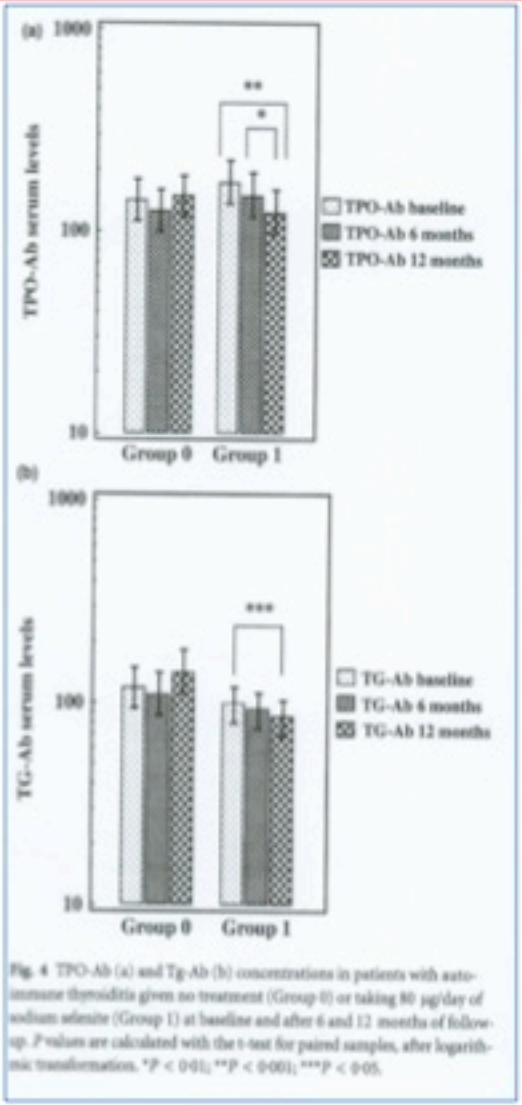

Fig. 4 TPO-Ab (a) and Tg-Ab (b) concentrations in patients with autoimmune thyroiditis given no treatment (Group 0) or taking 80 μg/day of sodium selenite (Group 1) at baseline and after 6 and 12 months of follow-up. *P* values are calculated with the t-test for paired samples, after logarithmic transformation. *$P < 0.01$; **$P < 0.001$; ***$P < 0.05$.

Table 1. Serum concentrations of TSH and fT4 in patients with autoimmune thyroiditis given no treatment (Group 0) or taking 80 μg/day of sodium selenite (Group 1) at the baseline and after 6 and 12 months of follow-up. All values are expressed as mean ± SD

	Group 0			Group 1		
	Baseline	6 months	12 months	Baseline	6 months	12 months
TSH mIU/l (n.v.:0·27–4·2)	3·2 ± 2·1	2·7 ± 1·8	1·8 ± 0·9	3·4 ± 1·86	2·93 ± 1·47	2·92 ± 1·5
fT4 pmol/l (n.v.:12–22)	14·5 ± 10	14 ± 1·9	17·5 ± 6·7	14·5 ± 2·1	14·5 ± 2·2	15·6 ± 8·4

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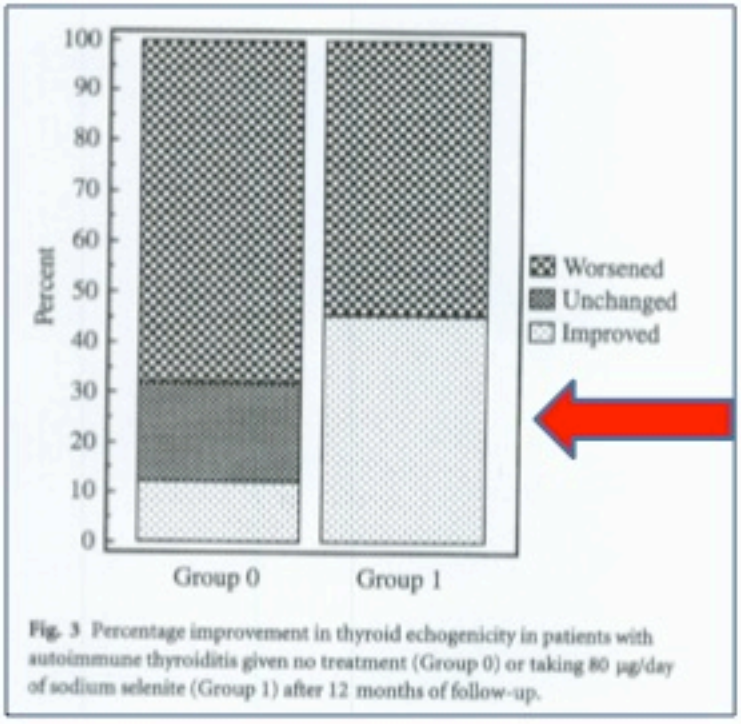
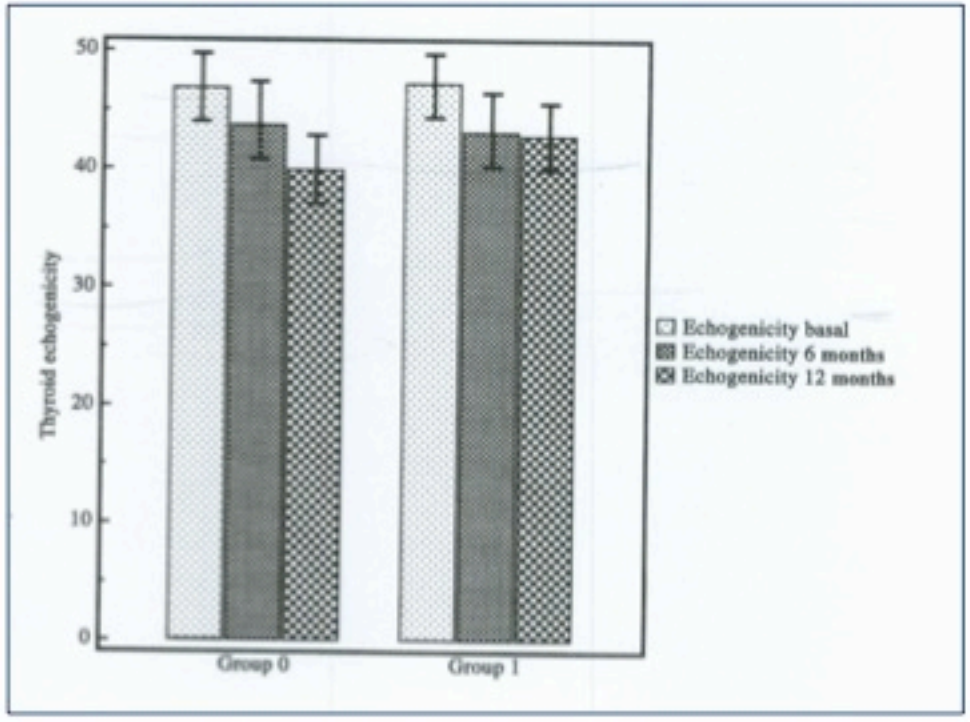


Fig. 3 Percentage improvement in thyroid echogenicity in patients with autoimmune thyroiditis given no treatment (Group 0) or taking 80 μg/day of sodium selenite (Group 1) after 12 months of follow-up.

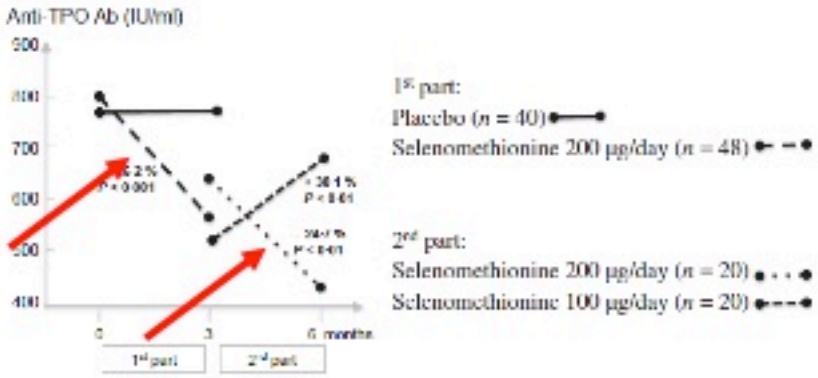


Selenium treatment in autoimmune thyroiditis: 9-month follow-up with variable doses

Omer Turker, Kamil Kumanlioglu[1], Inanc Karapolat[2] and Ismail Dogan

Table 1 Initial age, serum TSH, FT3, FT4, TPOAb, and TgAb levels (mean ± S.D.) of group C (receiving LT4 alone) and group S2 (receiving LT4 + 200 μg L-selenomethionine/day). There was no significant difference in age, TSH, or TPOAb levels between the groups ($P > 0.05$)

	Group C	Group S2
Age (year)	39·2 ± 14·4	40·8 ± 12·5
TSH (mIU/l)	1·58 ± 0·50	1·57 ± 0·61
FT3 (pM)	3·8 ± 0·5	3·4 ± 0·7
FT4 (pM)	17·0 ± 3·6	17·1 ± 3·2
TPOAb (IU/ml)	770·3 ± 406·2	803·9 ± 483·8
TgAb (IU/ml)	195·9 ± 129·9	154·2 ± 217·3



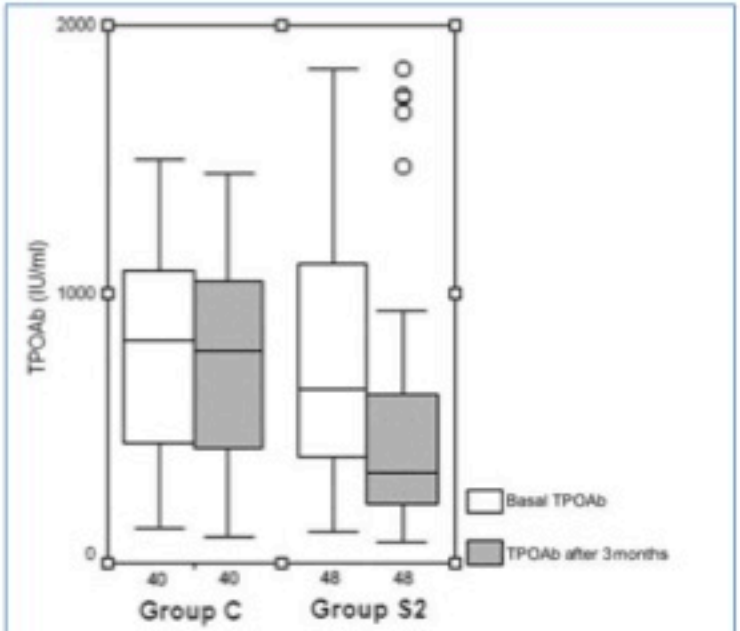


Figure 1 TPOAb concentrations at the beginning of the study and 3 months after treatment with 200 mg L-selenomethionine/day (group S2) or placebo (group C). *P* values were calculated by Wilcoxon's matched pairs, signed-ranks test.

Journal of Endocrinology 2006

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

Department of Endocrinology (R.N., G.G.), Azienda Ospedaliera LE/1, P.O. "V. Fazzi," 73100 Lecce, Italy; Department of Obstetrics and Gynecology (T.M.), Casa di Cura "Salus," 72100 Brindisi, Italy; Department of Internal Medicine (A.P.), Ospedali Riuniti, 43100 Parma, Italy; Department of Internal Medicine (D.D.), Azienda Ospedaliera PR, "Vaio" Hospital, 43036 Fidenza, Italy; and Endocrine Unit (H.H.), Raja Isteri Pengtran Anak Saleha Hospital, Bandar Seri Begawan BA 1000, Brunei

TABLE 1. Characteristics of patients

	Group S1 (n = 77)	Group S0 (n = 74)	Group C (n = 81)	*P* value
Age (yr)	28 ± 6	28 ± 5	27 ± 5	ns
Parity status (0/≥1)	60/17	56/18	59/22	ns
Baseline TSH (mIU/liter)	1.6 ± 0.6[a]	1.7 ± 0.7[a]	0.9 ± 0.4[b]	<0.01
Baseline FT_4 (ng/liter)	12.4 ± 2.2	12.2 ± 2.1	14 ± 2.1	ns
First endocrinological visit (wk)	9.6 ± 3.2	9.4 ± 2.5	9.5 ± 2.8	ns
Time of Se/placebo start (wk)	12.7 ± 0.9	12.6 ± 1.0	12.7 ± 1.1	ns
Patients requiring LT_4 during pregnancy (%)	19.4[a]	21.6[a]	2.5[b]	<0.01
Hypothyroid after delivery (%)	5.2	6.8		ns

ns, Not significant.
[a] Higher than [b].

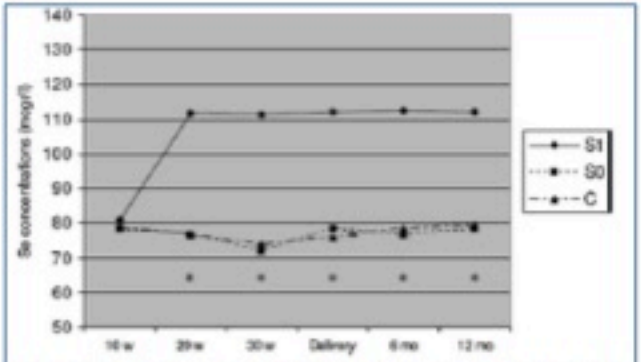


FIG. 3. Se concentrations during and after pregnancy in TPOAb(+) women who received Se (group S1) or placebo (group S0) and in TPOAb(−) women (group C). *, $P < 0.01$. mo, Months; w, weeks.

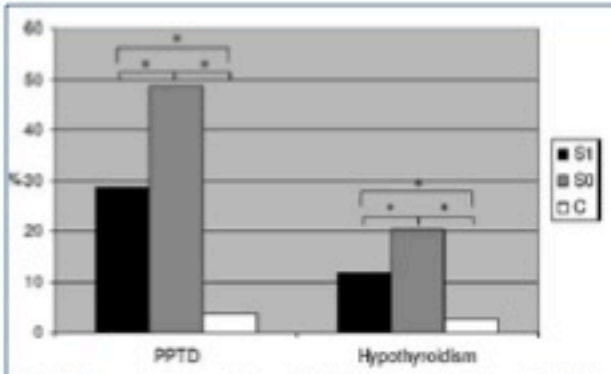


FIG. 1. Percentage of patients who had PPTD (*left*) and hypothyroidism (*right*) develop in TPOAb(+) women who received Se (group S1) or placebo (group S0), and in TPOAb(−) women (group C). *, $P < 0.01$.

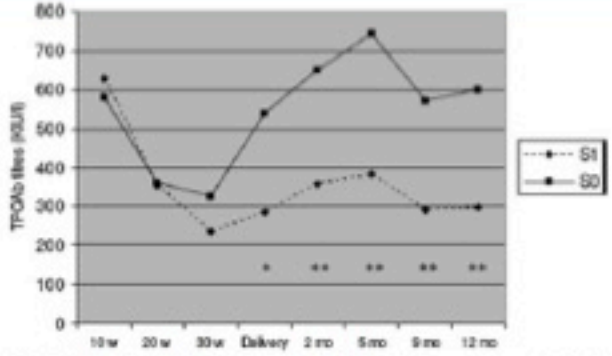
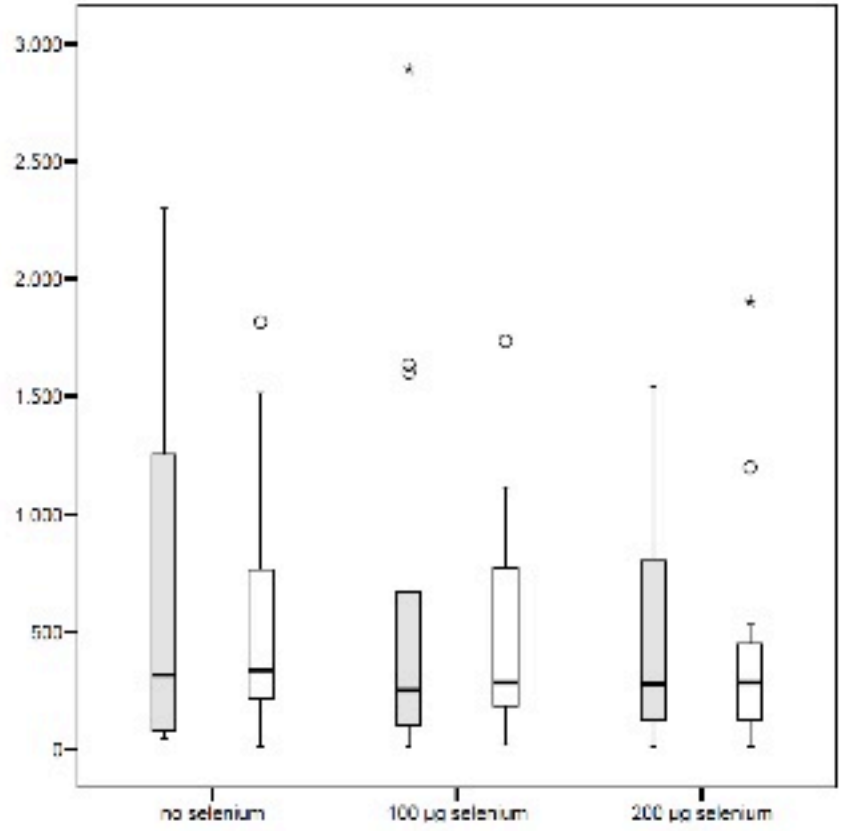


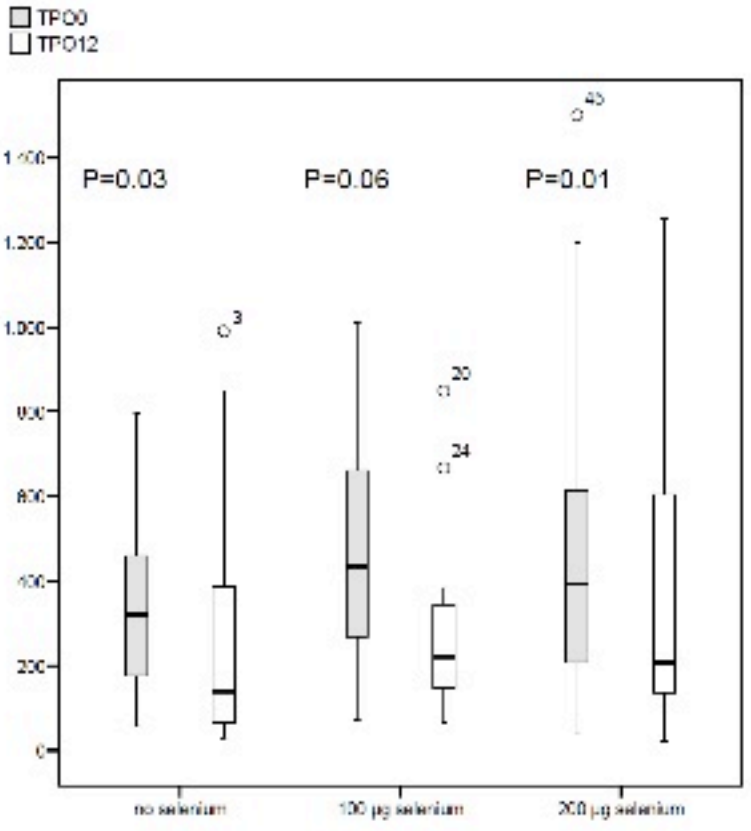
FIG. 2. Trends in TPOAb titers in TPOAb(+) women who received Se (group S1) or placebo (group S0). *, $P < 0.05$. **, $P < 0.01$. mo, Months; w, weeks.

Furthermore, when comparing the echogenicity patterns of groups S1 and S0, the Se-supplemented group displayed a significantly lower percentage of grade 2–3 thyroiditis at the end of the postpartum period (*P 0.01*).

Selenium Supplementation does not Decrease Thyroid Peroxidase Antibody Concentration in Children and Adolescents with Autoimmune Thyroiditis

W. Bonfig[1,*], R. Gärtner[2], and H. Schmidt[1]





Scientific World Journal 2010

Selenio e Tireopatie

✓Tiroidite cronica autoimmune

✓**Malattia di Basedow Graves'**

✓Orbitopatia di Graves'

Original Research Article

Antioxidants in the Treatment of Graves Disease

Liliana N. Guerra,[2,3] Silvia Moiguer,[1] Mirta Karner,[1] Ma del Carmen Ríos de Molina,[3] Claudia M. Sreider,[2,4] and José A. Burdman[1,2,4]

Table 1
Effect of treatment on signs and symptoms of hyperthyroidism

	Before treatment $n = 56$	Group A $n = 23$		Group B $n = 20$	Group C $n = 13$
		4 weeks	8 weeks		
Nervousness, insomnia	96	70	12	0	12
Diarrhea	79	53	12	0	0
Hotness, sweat	80	65	12	0	0
Weight loss	84	82	6	0	0
Tremor	70	88	12	6	0

The results are the percentage of patients presenting the sign or symptom after different treatments.
Period of treatment:
Group A = MMI 4 or 8 weeks.
Group B = Larotabe 4 weeks.
Group C = Larotabe + MMI 4 weeks.

Table 2
Effect of treatment on the clinical score in hyperthyroidism

	4 weeks treatment clinical score	8 weeks treatment clinical score
Group A ($n = 23$)	3–5	0–2
Group B ($n = 20$)	0–1	0*
Group C ($n = 13$)	0–1	ND

All patients had clinical score 5 before treatment.
*Patients were treated with LAROTABE + MMI after week 4.
ND: not determined.

Effect of treatment on thyroid hormones levels in sera of hyperthyroid patients

	Before treatment			4 weeks treatment			8 weeks treatment		
	T3 nmol/l	T4 nmol/l	TSH UU/ml	T3 Nmol/l	T4 nmol/l	TSH μU/ml	T3 nmol/l	T4 nmol/l	TSH μU/ml
Group A	5.72 ± 2.90	236.0 ± 56.7	0.22 ± 0.16	4.50 ± 1.90	206.4 ± 43.9	0.39 ± 0.33	2.43 ± 1.30 *	116.1 ± 77.4 *	1.89 ± 2.21
Group B	4.54 ± 1.24	236.1 ± 52.9	0.44 ± 0.38	4.73 ± 0.74	239.9 ± 38.7	0.38 ± 0.37	1.57 ± 1.3[a] *	52.8 ± 12.3[a] *	15.6 ± 7.2[a] *
Group C	5.38 ± 2.15	258.0 ± 50.3	0.26 ± 0.26	2.15 ± 0.75 *#	82.9 ± 25.8 *#	2.85 ± 3.2 *#	1.20 ± 0.33 *	49.0 ± 11.6 *	22.6 ± 11.7 *

*$P < 0.05$ vs. values before treatment.
#$P < 0.05$ vs. values of 4 weeks treatment group A.

IUBMB Life 2001

Original Research Article

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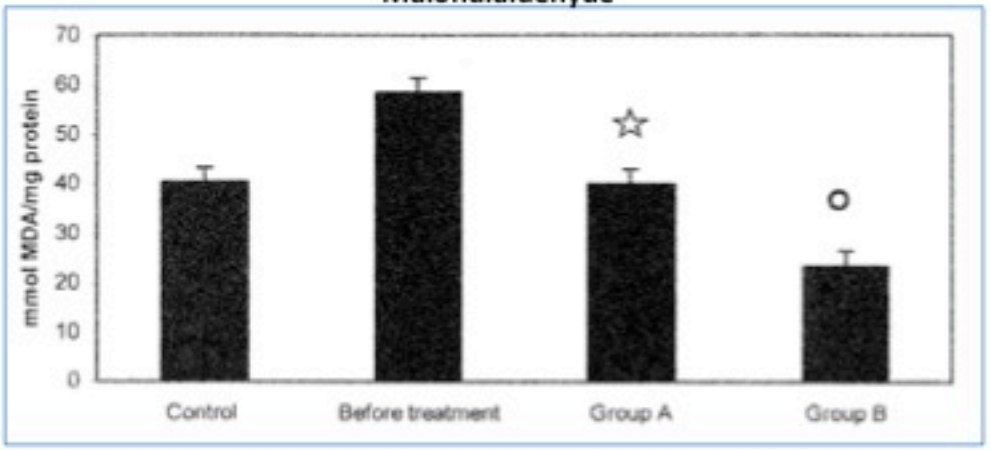
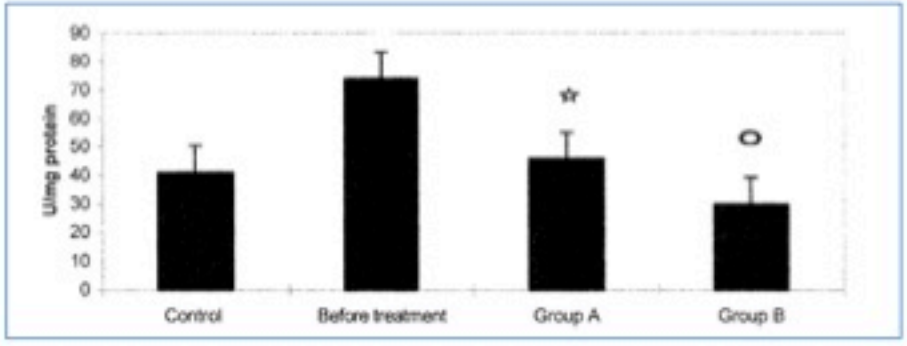
Malondialdehyde



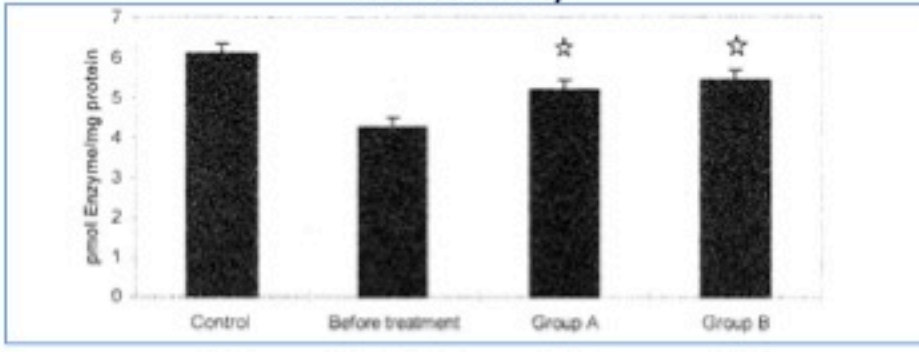
☆ $P < 0.05$ vs. values before treatment, ○ $P < 0.01$ vs. values before treatment.

Superoxide dismutase activity



☆ $P < 0.05$ vs. values before treatment, ○ $P < 0.01$ vs. values before treatment.

Catalase activity



☆ $P < 0.05$ vs. values before treatment.

IUBMB Life 2001

Serum selenium levels in patients with remission and relapse of graves' disease.

OBJECTIVE:

Selenium (Se) in the form of selenocysteine is an essential component of the family of the detoxifying enzymes glutathione peroxidase (Gpx) and of the iodothyronine selenodeiodinases that catalyze the extrathyroidal production of tri-iodothyronine (T(3)). Thus, Se deficiency may seriously influence the generation of free radicals, the conversion of thyroxine (T(4)) to T(3) and a thyroidal autoimmune process. The aim of this study was to investigate whether serum Se levels may influence the outcome of Graves' disease (GD).

DESIGN AND METHODS:

83 patients (77 women, 6 men) with active GD were **retrospectively** analyzed (mean age 40,0 years). Twenty-four GD patients went into remission and were euthyroid during follow-up (median follow-up: 20.1 months), whereas 59 patients did not go into remission or developed relapse over the following 24 months. TSH receptor autoantibodies (TRAb) were measured using the second generation assay on the basis of human TSH receptor. Se levels were determined at the first visit in our outpatient clinic and were correlated with TRAb levels and clinical outcome of these patients.

RESULTS:

Median TRAb levels in the group of remission were significantly ($p<0.0001$) lower than TRAb values in the relapse group (2.1 as compared to 8.6 IU/l). By comparing mean serum Se levels in the remission and relapse group no significant differences were seen (73.0 vs. 71.7 microg/l). **Detailed analyses of both groups of patients, however, revealed that highest serum Se levels (>120 microg/l) were seen in the remission group, indicating a positive effect of Se levels on the outcome of GD.** In addition, we also compared these results with TRAb levels of these patients. We could show that TRAb levels and serum Se values were positively correlated in the relapse group, whereas a negative correlation of both parameters were seen in the remission group, supporting the idea of a positive effect of Se on thyroidal autoimmune process.

CONCLUSION:

Our data indicate that high serum Se levels (>120 microg/l) may influence the outcome of GD. This is important, as Se administration trials in GD, which are under discussion need to be performed with Se supplementation at higher dosages than used in autoimmune thyroiditis.

Wertenbruch T et al Med Chem 2007

Selenio e Tireopatie

- ✓Tiroidite cronica autoimmune
- ✓Malattia di Basedow Graves
- ✓**Orbitopatia di Graves**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Selenium and the Course of Mild Graves' Orbitopathy

Claudio Marcocci, M.D., George J. Kahaly, M.D., Gerasimos E. Krassas, M.D., Luigi Bartalena, M.D., Mark Prummel, M.D.,* Matthias Stahl, M.D., Maria Antonietta Altea, M.D., Marco Nardi, M.D., Susanne Pitz, M.D., Kostas Boboridis, M.D., Paolo Sivelli, M.D., George von Arx, M.D., Maarten P. Mourits, M.D., Lelio Baldeschi, M.D., Walter Bencivelli, Ph.D., and Wilmar Wiersinga, M.D., for the European Group on Graves' Orbitopathy

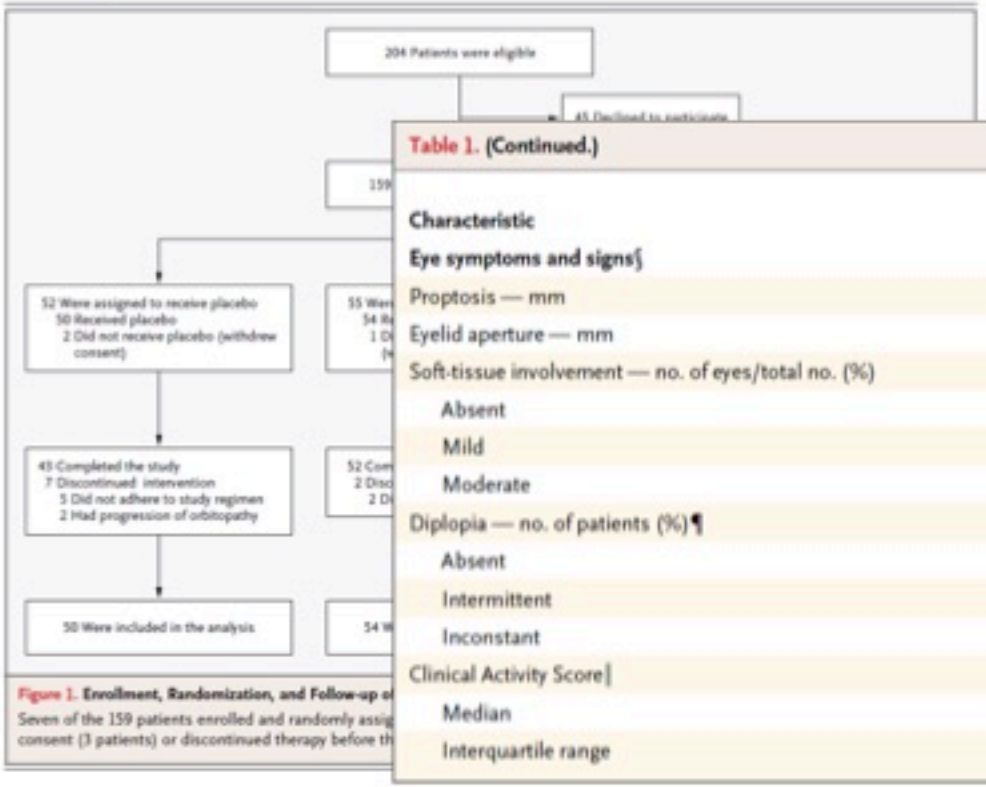


Figure 1. **Enrollment, Randomization, and Follow-up o**

Seven of the 159 patients enrolled and randomly assig consent (3 patients) or discontinued therapy before th

Table 1. (Continued.)

Characteristic	Selenium (N = 54)	Placebo (N = 50)	Pentoxifylline (N = 48)
Eye symptoms and signs§			
Proptosis — mm	19.7±2.7	19.8±2.3	20.0±2.5
Eyelid aperture — mm	11.5±1.9	11.3±1.7	11.6±2.1
Soft-tissue involvement — no. of eyes/total no. (%)			
Absent	5/108 (5)	5/100 (5)	0
Mild	64/108 (59)	65/100 (65)	52/96 (54)
Moderate	39/108 (36)	30/100 (30)	44/96 (46)
Diplopia — no. of patients (%)¶			
Absent	43 (80)	44 (88)	43 (90)
Intermittent	6 (11)	3 (6)	2 (4)
Inconstant	5 (9)	3 (6)	3 (6)
Clinical Activity Score‖			
Median	3.5	3.0	3.0
Interquartile range	3.0–4.0	2.0–4.0	2.0–5.0

Table 1. Baseline Characteristics of the Patients.*

Characteristic	Selenium (N = 54)	Placebo (N = 50)	Pentoxifylline (N = 48)
Demographic and clinical characteristics			
	43.0±11.0	44.6±10.7	43.7±12.4
	48 (89)	41 (82)	37 (77)
	52 (96)	50 (100)	48 (100)
	1 (2)	0	0
	1 (2)	0	0
	51 (94)	43 (86)	46 (96)
	2 (4)	3 (6)	2 (4)
	1 (2)	4 (8)	0
	4 (7)	4 (8)	6 (12)
	4 (7)	9 (18)	6 (12)
	41 (76)	34 (68)	35 (73)
	9 (17)	9 (18)	11 (23)
	4 (7)	7 (14)	2 (4)
	7.7±5.8	6.1±4.6	6.0±4.6
	23 (43)	25 (50)	17 (35)
	0.6	0.7	1.1
	0.5–2.1	0.5–2.0	0.5–2.2
	6.8	4.3	4.4
	3.5–23.0	2.0–15.0	1.3–11.0
Positive for thyrotropin-receptor autoantibodies — no. of patients/total no. (%)	32/47 (68)	30/41 (73)	27/41 (66)
Positive for thyroid peroxidase autoantibodies — no. of patients/total no. (%)	32/47 (68)	27/41 (66)	26/41 (63)

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Selenium and the Course of Mild Graves' Orbitopathy

Claudio Marcocci, M.D., George J. Kahaly, M.D., Gerasimos E. Krassas, M.D., Luigi Bartalena, M.D., Mark Prummel, M.D.,* Matthias Stahl, M.D., Maria Antonietta Altea, M.D., Marco Nardi, M.D., Susanne Pitz, M.D., Kostas Boboridis, M.D., Paolo Sivelli, M.D., George von Arx, M.D., Maarten P. Mourits, M.D., Lelio Baldeschi, M.D., Walter Bencivelli, Ph.D., and Wilmar Wiersinga, M.D., for the European Group on Graves' Orbitopathy

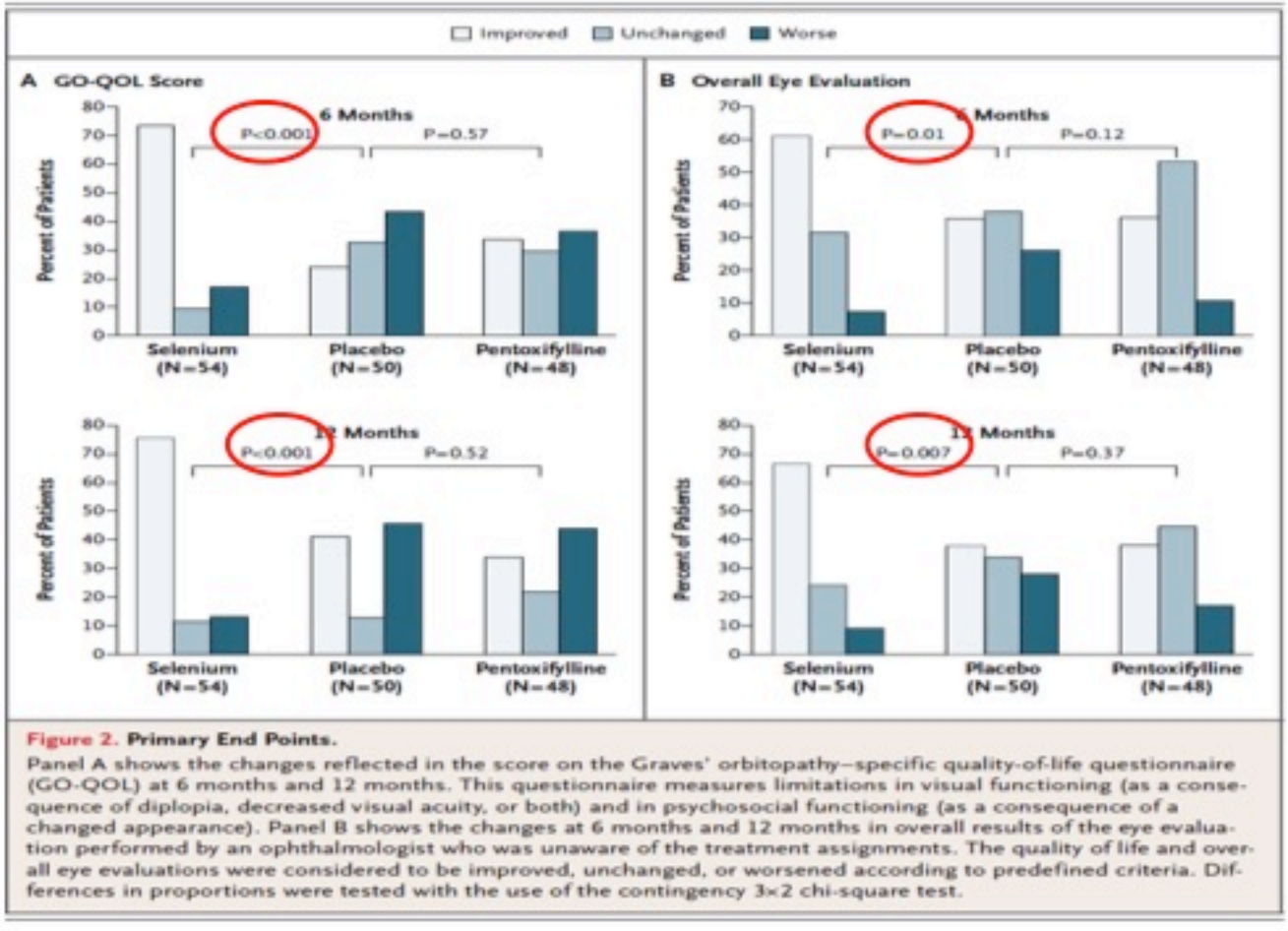


Figure 2. Primary End Points.
Panel A shows the changes reflected in the score on the Graves' orbitopathy–specific quality-of-life questionnaire (GO-QOL) at 6 months and 12 months. This questionnaire measures limitations in visual functioning (as a consequence of diplopia, decreased visual acuity, or both) and in psychosocial functioning (as a consequence of a changed appearance). Panel B shows the changes at 6 months and 12 months in overall results of the eye evaluation performed by an ophthalmologist who was unaware of the treatment assignments. The quality of life and overall eye evaluations were considered to be improved, unchanged, or worsened according to predefined criteria. Differences in proportions were tested with the use of the contingency 3×2 chi-square test.

ORBITOPATIA BASEDOWIANA
CAS (Clinical Activity Score)
Assegna un punto per ogni elemento positivo:
(punteggio max = 7; significativo se > 3)

- ✓ dolore retrobulbare spontaneo
- ✓ dolore con il movimento oculare
- ✓ eritema palpebrale
- ✓ iniezione congiuntivale
- ✓ chemosi (edema congiuntivale)
- ✓ rigonfiamento caruncola
- ✓ edema palpebrale

Score diplopia
0. Assente
1. intermittente (in posizione primaria se stanco o al risveglio)
2. incostante (agli estremi di lateralità)
3. costante

Review Article

The Evolving Role of Selenium in the Treatment of Graves' Disease and Ophthalmopathy

Leonidas H. Duntas

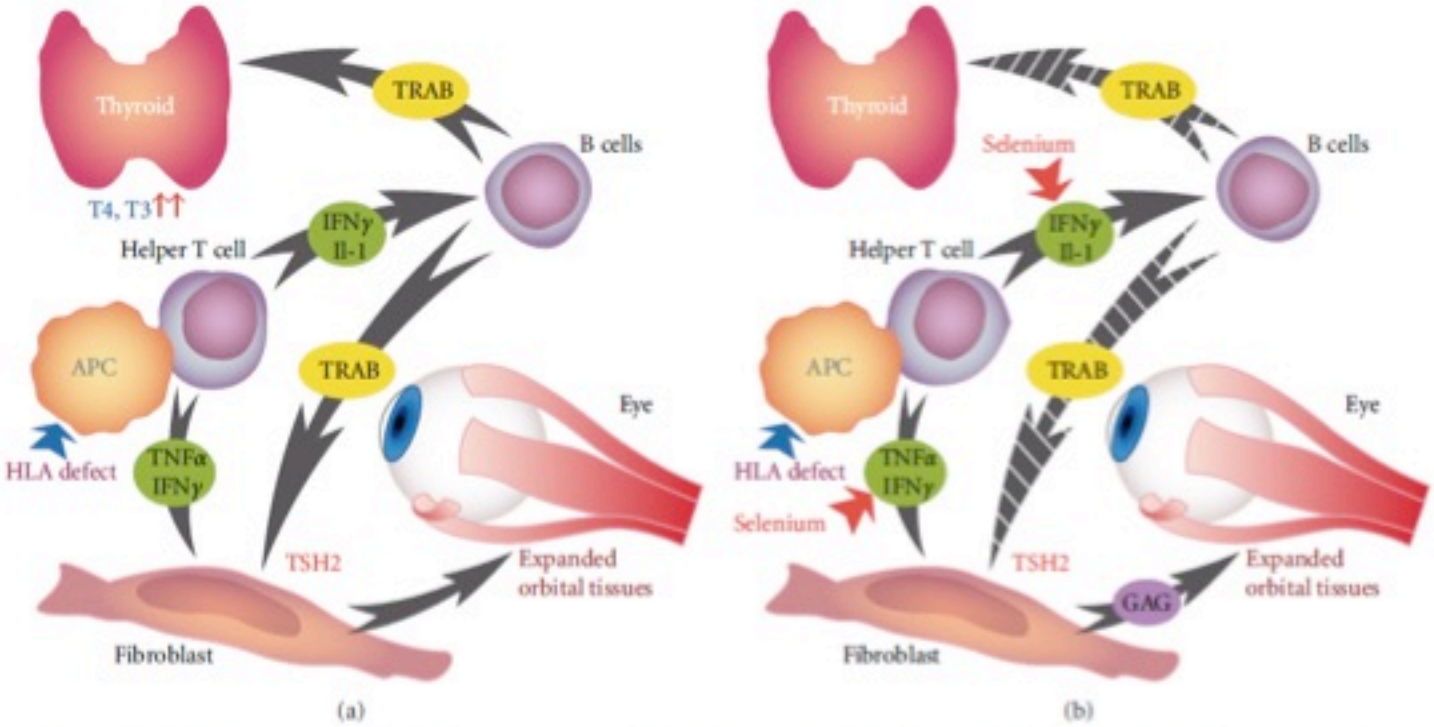


FIGURE 1: (a) Schematic presentation of the cascade of events in the pathogenesis of Graves' ophthalmopathy. Secretion of cytokines, such as IFN-γ and IL-2, by activated helper cells result in activation of B cells and secretion of TSH receptor antibodies. These bind to the TSH receptor in the orbital fibroblast and on the thyroid follicular cells, thereby, extending muscle enlargement resulting in oedema. (b) Selenium by suppressing cytokines production considerably attenuates the inflammation leading to alleviation of symptoms and signs. Abbreviations: HLA: human leukocyte antigen; APC: antigen presenting cell; IFN-γ: interferon-γ; IL-1: interleukin-1; TRAB: TSH-receptor antibodies; GAG: glycosaminoglycans.

Journal of Thyroid Research 2012

….MOLTI PUNTI ANCORA DA DEFINIRE….

✓Necessità di identificare un marcatore espressione del pool di selenio nell'organismo e/o nella tiroide

✓La concentrazione plasmatica di selenio non riflette quella intratiroidea: dosaggio dei livelli plasmatici di selenio non raccomandato nella pratica clinica (utilità Selenoproteina P??)

La supplementazione del micronutriente in individui non affetti da deficit di Selenio può essere dannoso!? (Rischio DM T2) Stranges …et al Annals of Internal Medicine 2007

CATALYST TRIAL

✓Quale composto utilizzare (Seleniometionina,sodio selenite)

✓Timing, dosi e durata del trattamento

✓Tipologia di paziente: familiari "sani" di soggetti con tireopatia autoimmune o portatori di anticorpi antitiroide ad alto titolo, gravide con positività anticorpale, ipotiroidismo subclinico??;

✓Rapporto costo-beneficio di tale terapia (la progressione della TCA è inevitabile; la tiroxina è ben tollerata ed a basso costo quando subentra l'ipotiroidismo; nel Graves' forse qualche spazio in più…)

Nutraceutici e tiroide

Iodio

Selenio

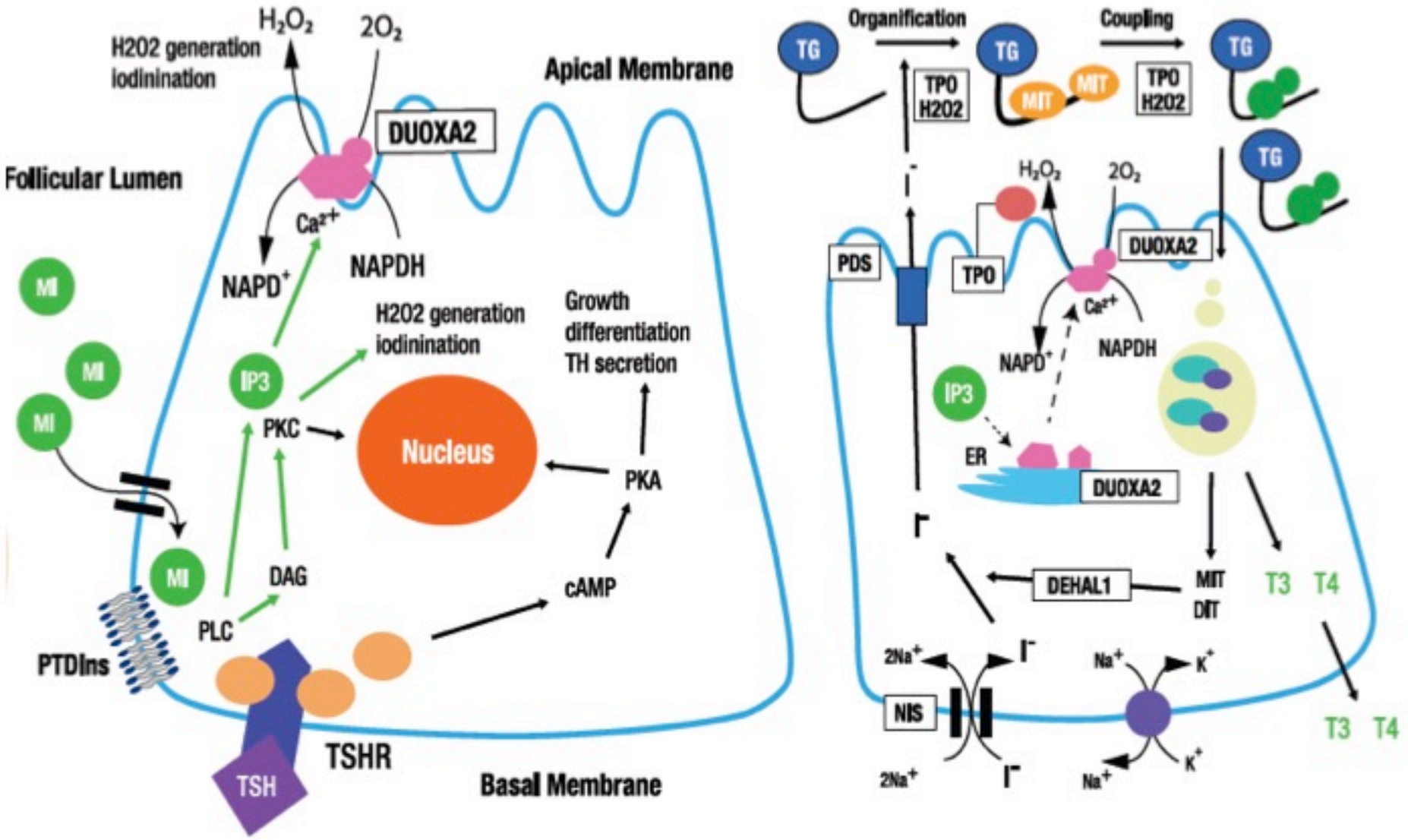
Selenio+Inositolo

Interferenti funzione ghiandolare

Mio-Inositolo come secondo messaggero

Insulina
FSH
TSH

Riduce livelli di insulina
Riduce i livelli di FSH
Riduce i livelli di TSH


H202 generation
iodination
H_2O_2
$2O_2$
Apical Membrane
DUOXA2
Follicular Lumen
Ca^{2+}
$NAPD^+$
NAPDH
MI
MI
MI
MI
IP3
PKC
H202 generation
iodination
Growth
differentiation
TH secretion
Nucleus
PKA
cAMP
DAG
PLC
PTDIns
TSHR
TSH
Basal Membrane
Organification
Coupling
TG
TG
TG
TG
TPO
H202
MIT
MIT
TPO
H202
H_2O_2
$2O_2$
PDS
TPO
DUOXA2
Ca^{2+}
$NAPD^+$
NAPDH
IP3
ER
DUOXA2
I^-
DEHAL1
MIT
DIT
T3
T4
$2Na^+$
I^-
NIS
$2Na^+$
I^-
Na^+
K^+
Na^+
K^+
T3
T4

The FASEB Journal • Research Communication

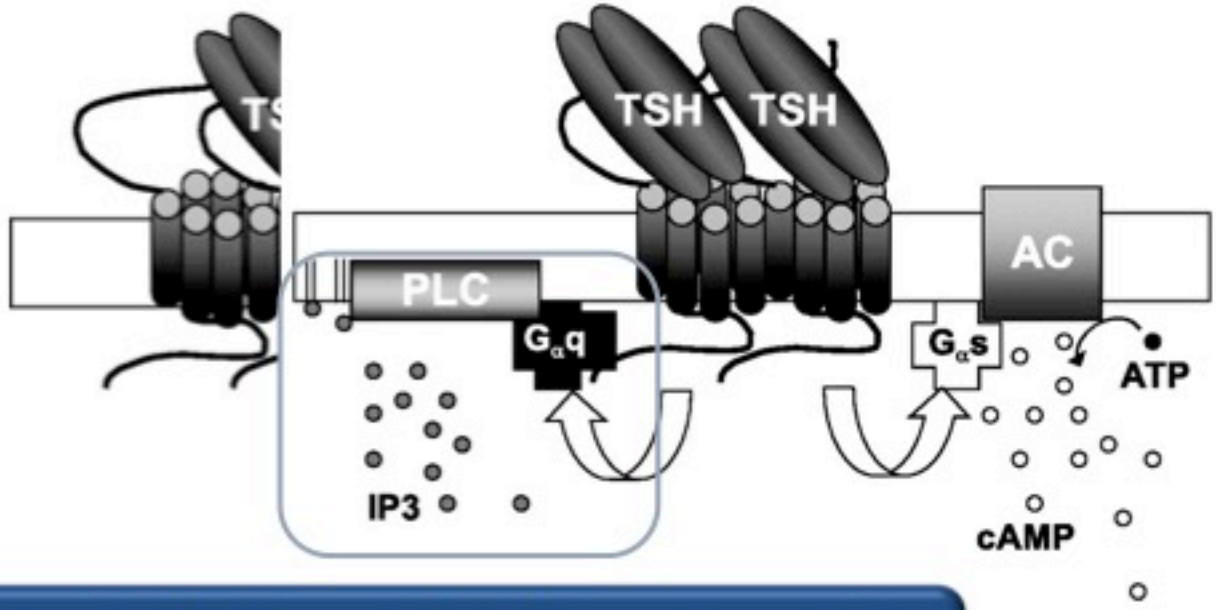
Occupancy of both sites on the thyrotropin (TSH) receptor dimer is necessary for phosphoinositide signaling

Vol. 25 October 2011

D. Allen, Susanne Neumann, and Marvin C. Gershengorn[1]

Clinical Endocrinology Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland, USA

TSH signalling



Il TSHR attiva la produzione di cAMP quando il TSH lega ad un solo dei due siti disponibili

Il TSHR attiva sia la produzione di cAMP che di IP3 quando il TSH si lega ad entrambi I siti disponibili.

Pertanto, è stata verificata l'utilità di un impiego combinato di selenio (83 µg/die) e myo-inositolo (600 mg/die) per 6 mesi, nel trattamento dell'ipotiroidismo sub-clinico in pazienti con tiroidite di Hashimoto.

Hindawi Publishing Corporation
Journal of Thyroid Research
Volume 2013, Article ID 424163, 5 pages
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Research Article

Combined Treatment with Myo-Inositol and Selenium Ensures Euthyroidism in Subclinical Hypothyroidism Patients with Autoimmune Thyroiditis

Maurizio Nordio[1] and Raffaella Pajalich[2]

[1] *University of Rome "Sapienza", Institute of Gynecology and Obstetrics, Viale del Policlinico, 00155 Rome, Italy*
[2] *Ars Medica spa, Via Ferrero di Cambiano Cesare 29, 00191 Rome, Italy*

Correspondence should be addressed to Maurizio Nordio; maurizionordio1@gmail.com

Riduzione del TSH e degli anticorpi anti-tiroide dopo terapia combinata

	MI-SEL pre	Mi-SEL post	SEL pre	SEL post	P value
Age	37,95±2,16		38,03± 1,63		NS
TSH	4,43±0,89	3,1±0,6*	4,33±0,91	4,4±0,8**	<0.01* NS**
AbTg	1019,7±374,2	533,9±258,4*	1080,8±485,1	670,1±300,8#	<0,01* <0,01#
AbTPO	913,9±543,9	516,1±315,4*	905,6±401,6	522,6±236,8#	<0,01* <0,01#

SELENIOMETHIONINE GROUP
TPOAb decreased of 42%
TgAb decreased of 38%
TSH decreased of -

COMBINED TREATMENT GROUP
TPOAb decreased of 44%
TgAb decreased of 48%
TSH decreased of 31%

GYNECOLOGICAL ENDOCRINOLOGY

http://informahealthcare.com/gye
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 DOI: 10.3109/09513590.2013.829445

informa healthcare

THYROID AND PCO

Alterations in thyroid function among the different polycystic ovary syndrome phenotypes

Table 1. Clinical, hormonal and metabolic profiles of the PCOS and control groups.

	Controls ($n=155$)	PCOS ($n=151$)	p Value
Age	36.7 (6.5)	32.2 (6.5)	<0.001
Weight (kg)	62.7 (21.5)	69.3 (19.3)	<0.001
Height (cm)	160.1 (22.8)	162.9 (17.8)	0.225
BMI (kg/m^2)	21.9 (3.2)	24.9 (5.9)	<0.001
FSH (mU/ml)	9.2 (5.8)	6.35 (1.9)	<0.001
LH (mU/ml)	6.2 (5.41)	7.8 (7.1)	<0.05
LH/FSH	0.8 (0.2)	1.2 (0.9)	<0.001
Testosterone (ng/ml)	0.6 (0.7)	2.4 (5.5)	0.180
Estradiol (pg/ml)	77.6 (73.8)	54.1 (58.6)	<0.001
Fasting glucose (mg/dl)	85.4 (8.5)	86.3 (10.4)	0.375
Fasting insulin (μUI/ml)	6.3 (2.2)	10.2 (7.0)	<0.001
HOMA	1.3 (0.5)	2.3 (2.3)	<0.001
TSH (μU/ml)	1.82 (1.10)	2.17 (1.19)	<0.009
fT3 (pg/ml)	3.34 (0.83)	3.43 (1.34)	0.464
fT4 (pg/ml)	8.81 (3.74)	8.51 (3.31)	0.464

Table 2. The distribution of subclinical hypothyroidism (TSH > 2.5) in controls and PCOS.

Group	No subclinical Hypothyroidism TSH < 2.5	Subclinical hypothyroidism TSH > 2.5	Total
Control (n)	119	36	155
PCOS (n)	100	51	151
Total (n)	219	87	306

Table 3. Values of TSH before and after six months of treatment with insulin sensitizers (metformin, or inositol + metformin).

Treatment	TSH levels before treatment	TSH levels after 6 months of treatment	p Value
Metformin + Inositol ($n=34$)	4.00 (1.98)	2.35 (1.65)	0.004
Metformin ($n=38$)	3.54 (0.75)	2.35 (0.38)	0.06

Morgante et al 2013

JAMA®
The Journal of the American Medical Association

Subclinical Hypothyroidism and the Risk of Coronary Heart Disease and Mortality

Nicolas Rodondi, MD, MAS
Wendy P. J. den Elzen, MSc
Douglas C. Bauer, MD
Anne R. Cappola, MD, ScM
Salman Razvi, MD, FRCP
John P. Walsh, MBBS, FRACP, PhD
Bjørn O. Åsvold, MD, PhD
Giorgio Iervasi, MD
Misa Imaizumi, MD, PhD
Tinh-Hai Collet, MD
Alexandra Bremner, PhD
Patrick Maisonneuve, Ing
José A. Sgarbi, MD

Context Data regarding the association between subclinical hypothyroidism and cardiovascular disease outcomes are conflicting among large prospective cohort studies. This might reflect differences in participants' age, sex, thyroid-stimulating hormone (TSH) levels, or preexisting cardiovascular disease.

Objective To assess the risks of coronary heart disease (CHD) and total mortality for adults with subclinical hypothyroidism.

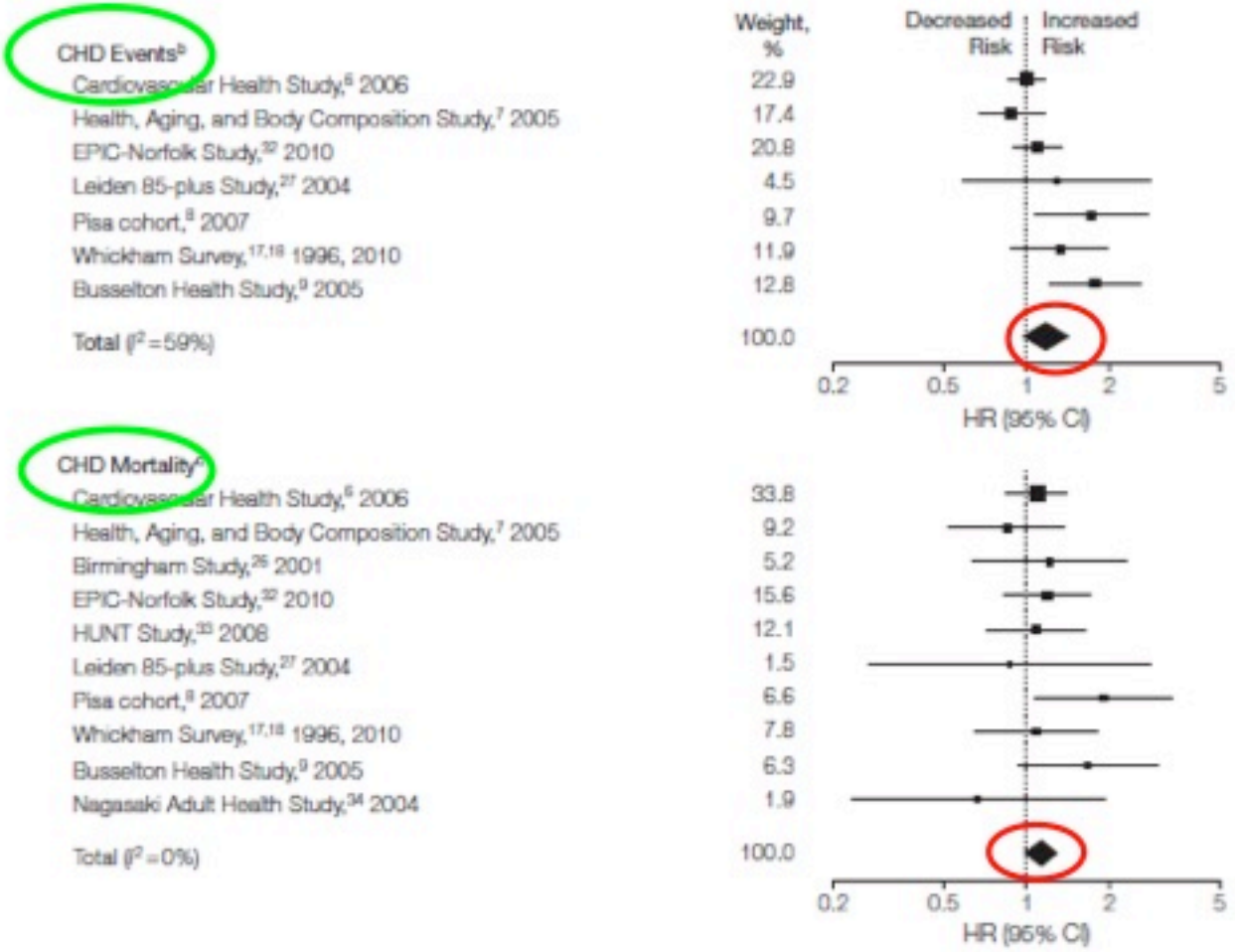
Data Sources and Study Selection The databases of MEDLINE and EMBASE (1950 to May 31, 2010) were searched without language restrictions for prospective cohort studies with baseline thyroid function and subsequent CHD events, CHD mortality, and total mortality. The reference lists of retrieved articles also were searched.

Data Extraction Individual data on 55 287 participants with 542 494 person-years of follow-up between 1972 and 2007 were supplied from 11 prospective cohorts in the United States, Europe, Australia, Brazil, and Japan. The risk of CHD events was examined in 25 977 participants from 7 cohorts with available data. Euthyroidism was defined as a TSH level of 0.50 to 4.49 mIU/L. Subclinical hypothyroidism was defined as a TSH level of 4.5 to 19.9 mIU/L with normal thyroxine concentrations.

Conclusions Subclinical hypothyroidism is associated with an increased risk of CHD events and CHD mortality in those with higher TSH levels, particularly in those with a TSH concentration of 10 mIU/L or greater.

JAMA. 2010;304(12):1365-1374

Figure 1. Subclinical Hypothyroidism vs Euthyroidism for Coronary Heart Disease (CHD) Events, CHD Mortality, and Total Mortality[a]



Nutraceutici e tiroide

Iodio

Selenio

Selenio+Inositolo

Interferenti funzione ghiandolare

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SPECIAL ARTICLE

Guidelines for the Treatment of Hypothyroidism

Prepared by the American Thyroid Association
Task Force on Thyroid Hormone Replacement

Jacqueline Jonklaas,[1*†] Antonio C. Bianco,[2*‡] Andrew J. Bauer,[3†] Kenneth D. Burman,[4†]
Anne R. Cappola,[5†] Francesco S. Celi,[6‡] David S. Cooper,[7†] Brian W. Kim,[8‡] Robin P. Peeters,[9‡]
M. Sara Rosenthal,[3†] and Anna M. Sawka[10†]

can have significant clinical consequences. Excess iodine may precipitate thyroid dysfunction, particularly in patients with underlying thyroid autonomy, Hashimoto's thyroiditis, or multinodular thyroid glands. Large amounts of iodine doses, with the possibility of causing adverse effects. However, there is little evidence that iodine supplementation in pharmacologic amounts can beneficially improve thyroid function in euthyroid individuals. As a result, the AACE guidelines note that "No data support the role of iodine in enhancing thyroid function (patient advised to discontinue use)."

Tyrosine is an amino acid that that forms the basis for synthesis of T_4 and T_3, and it has been speculated that giving tyrosine supplementation to euthyroid individuals would improve thyroid gland function. Nonetheless, as noted in the AACE guidelines "No published data, however, support the claim that ingestion of tyrosine increases the production of TH (patient advised to discontinue use)." Commercially

sial area. TRIAC is a naturally occurring metabolite of LT_4 that has significant metabolic action. It can bind to the T_3 receptor and it can decrease TSH secretion. It may have a role in managing cases of resistance to TH (573). However, TRIAC administration in pharmacologic doses can cause toxicity like that caused by TH (574–578). Although TRIAC

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nr. 16 - aprile 2016

TERAPIA DELL'IPOTIROIDISMO: NESSUN RUOLO DEGLI ESTRATTI TIROIDEI

Responsabile Editoriale
Renato Cozzi

Partendo dal presupposto che la tiroide produce fisiologicamente sia T_4 che T_3 e dall'osservazione che in una minoranza di pazienti l'eutiroidismo biochimico non corrisponde a un completo benessere clinico, molti siti *web*, privi di autorevolezza scientifica, pubblicizzano o sostengono ancora oggi la terapia di combinazione con LT_4 + LT_3 sotto forma di estratti tiroidei di derivazione animale. La spiegazione a sostegno di questa preferenza sarebbe una presunta superiorità delle molecole "naturali" rispetto a quelle sintetiche.

Nelle ore successive all'assunzione di estratti tiroidei è ben documentato in letteratura l'**aumento sovra-fisiologico dei livelli ematici di T_3**, con aumento relativamente minore di T_4, e conseguente incremento del **rischio di tireotossicosi**. Tali preparazioni possono contenere inoltre anche piccole quantità di **altri costituenti**, come rT_3, T_2, tireoglobulina e calcitonina, e **sfuggono ai rigorosi controlli** di qualità delle autorità regolatorie. Ne deriva che il supposto rapporto ottimale tra T_4 e T_3 è tutt'altro che dimostrato, essendo in realtà di gran lunga minore di quello fisiologicamente presente nell'uomo, che è di circa 15:1.

Anche i supplementi dietetici e nutraceutici, commercializzati come prodotti di "supporto" per la funzione tiroidea, **non dovrebbero essere utilizzati**, perché privi di fondamento scientifico e soprattutto, in qualche caso, adulterati con quantità anche significative di ormoni tiroidei di origine sintetica o animale (anche più di 90 µg di T_4 e 10 µg di T_3 al giorno alle dosi raccomandate dai produttori, come segnalato in letteratura).

Le preparazioni galeniche magistrali a scopo dimagrante contenenti ormoni tiroidei sono altresì **vietate**, perché, non essendo soggette a controlli né sperimentazioni condotte con rigore scientifico, possono risultare dannose e talvolta, come osservato direttamente anche nella nostra pratica clinica, a rischio di vita per l'impiego di dosi sovra-massimali di tiroxina.

Thyroxine and triiodothyronine content in commercially available thyroid health supplements.

Abstract

BACKGROUND:

As defined by the Dietary Supplement Health and Education Act 1997, such substances as herbs and dietary supplements fall under general Food and Drug Administration supervision but have not been closely regulated to date. We examined the thyroid hormone content in readily available dietary health supplements marketed for "thyroid support."

METHODS:

Ten commercially available thyroid dietary supplements were purchased. Thyroid supplements were dissolved in 10 mL of acetonitrile and water with 0.1% trifloroacetic acid and analyzed using high-performance liquid chromatography for the presence of both thyroxine (T4) and triiodothyronine (T3) using levothyroxine and liothyronine as a positive controls and standards.

RESULTS:

The amount of T4 and T3 was measured separately for each supplement sample. Nine out of 10 supplements revealed a detectable amount of T3 (1.3-25.4 μg/tablet) and 5 of 10 contained T4 (5.77-22.9 μg/tablet). Taken at the recommended dose, 5 supplements delivered T3 quantities of greater than 10 μg/day, and 4 delivered T4 quantities ranging from 8.57 to 91.6 μg/day.

CONCLUSIONS:

The majority of dietary thyroid supplements studied contained clinically relevant amounts of T4 and T3, some of which exceeded common treatment doses for hypothyroidism. These amounts of thyroid hormone, found in easily accessible dietary supplements, potentially expose patients to the risk of alterations in thyroid levels even to the point of developing iatrogenic thyrotoxicosis. The current study results emphasize the importance of patient and provider education regarding the use of dietary supplements and highlight the need for greater regulation of these products, which hold potential danger to public health.

Kang GY et al Thyroid 2013

Grazie per l'attenzione