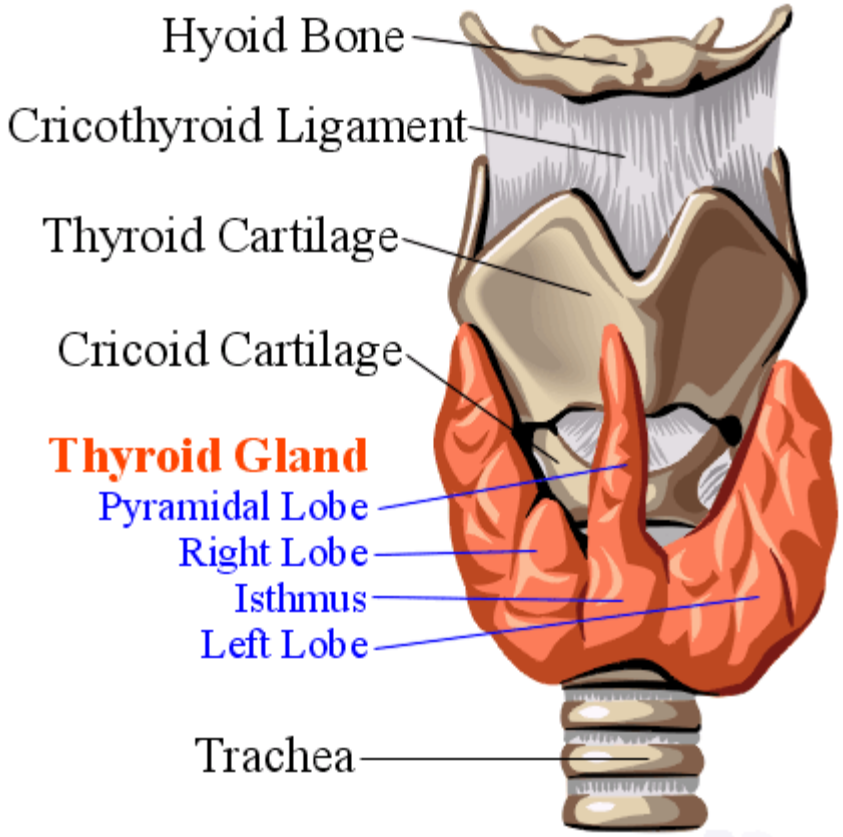


Adapted from Corel Draw 9

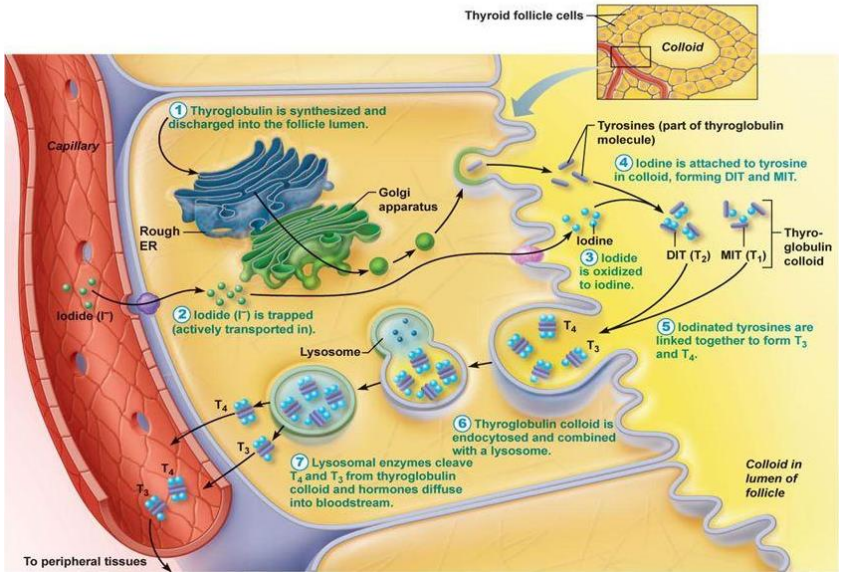
Francesco Lombardo

Andrea Lenzi

IP0TIROIDISMO

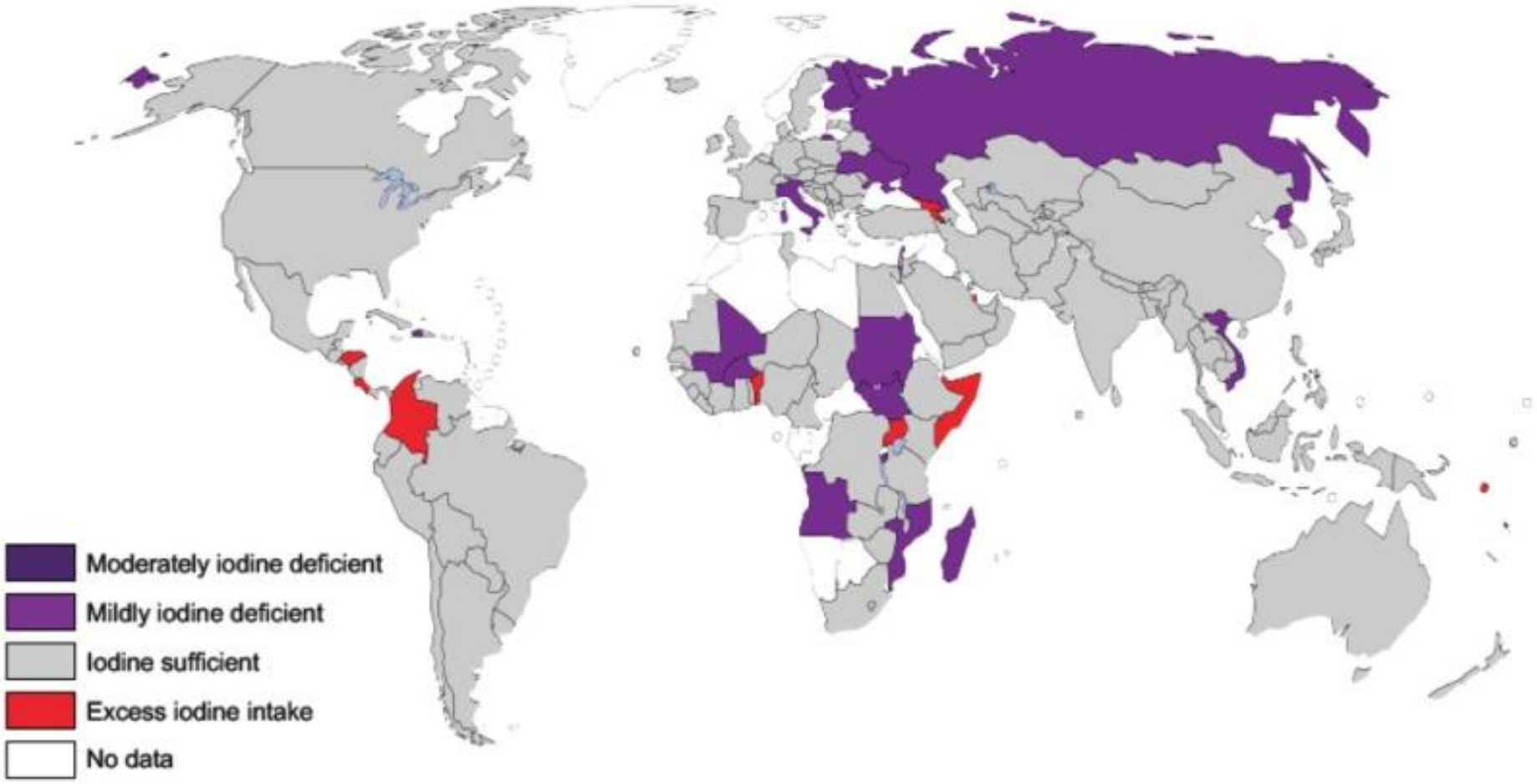
- **In order to attain normal levels of TH synthesis, an adequate supply of iodine is essential.**
- **The recommended minimum intake of iodine is 150 micrograms a day. Intake of less than 50 micrograms a day is associated with goiter. High iodine levels inhibit iodide oxidation and organification. Additionally, iodine excess inhibits TG proteolysis (this is the**

Production of thyroid hormones



Food		Portion	Average iodine/ portion (mcg) (actual iodine content will vary)
Milk and dairy products	Cow's milk	200ml	50-100**
	Organic cow's milk	200ml	30-60**
	Yoghurt	150g	50-100**
	Cheese	40g	15
Fish	Haddock	120g	390
	Cod	120g	230
	Plaice	130	30
	Salmon fillet	100g	14
	Canned tuna	100g	12
Shellfish	Prawns	60g	6
	Scampi	170g	160
Other	Eggs	1 egg (50g)	25
	Meat/Poultry	100g	10
	Nuts	25g	5
	Bread	1 slice (36g)	5
	Fruit and vegetables	1 portion (80g)	3

**Depending on the season, higher value in winter

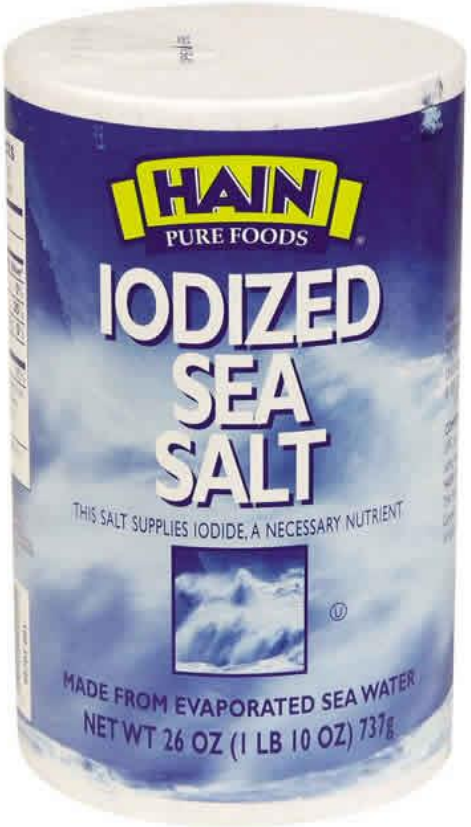

Moderately iodine deficient
Mildly iodine deficient
Iodine sufficient
Excess iodine intake
No data

WHO recommendations

“All food-grade salt, used in household and food processing should be fortified with iodine as a safe and effective strategy for the prevention and control of iodine deficiency disorders in populations living in stable and emergency settings”.

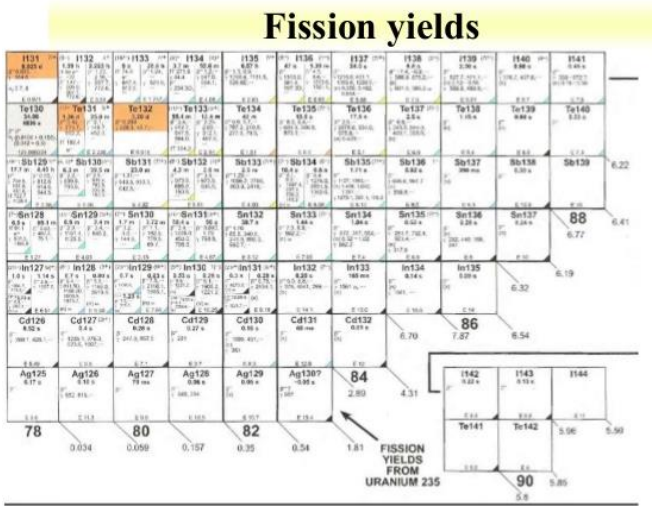
Ma da dove venite dalla Val Brembana!?!

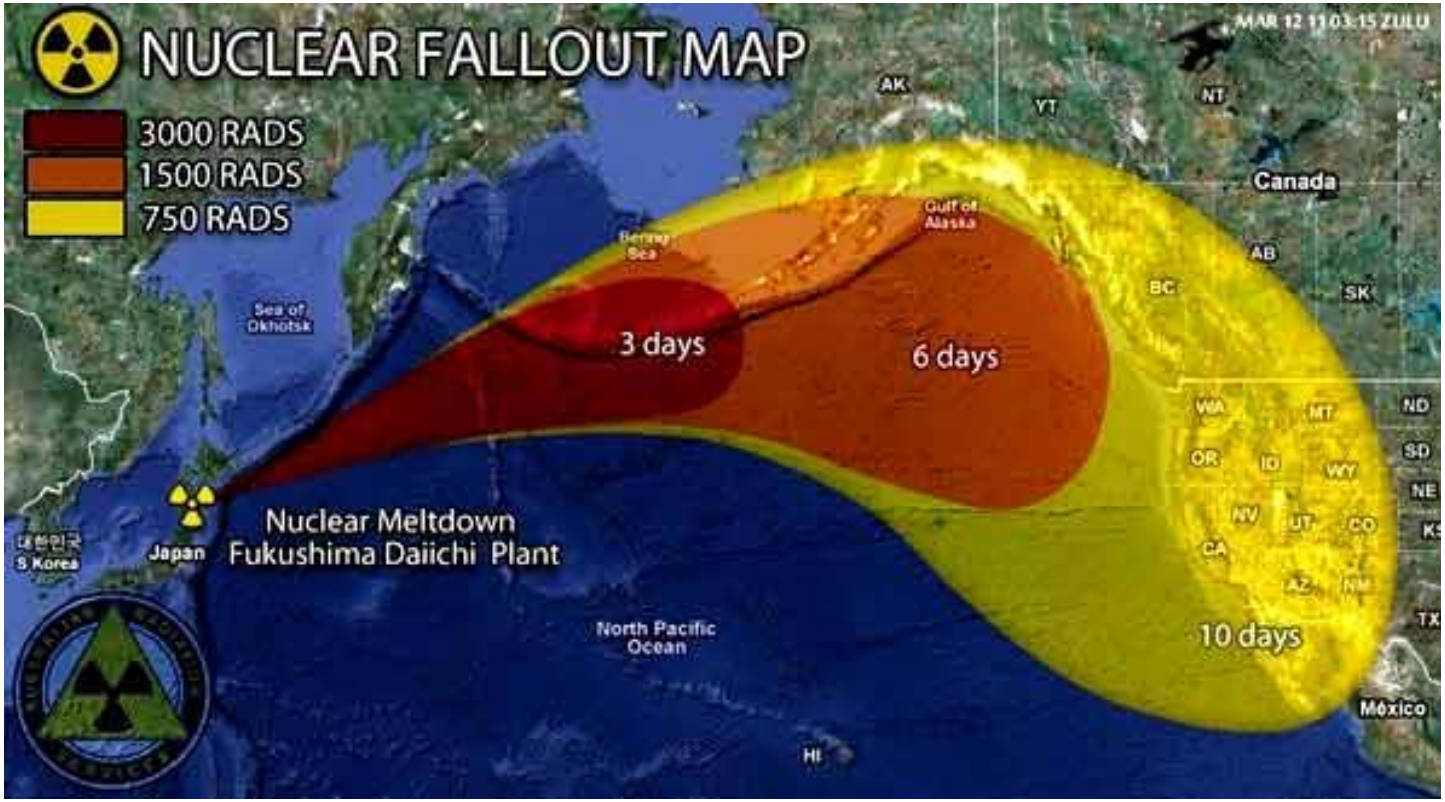
Noio volevan savuar l’indiriss!




Lombardie
Valle Brembana
Bergamo
Milano
Venezia
Italy

The fission of uranium produces large amounts of ^{131}I that may be released into the atmosphere in the course of a nuclear accident; the resultant plume of radioactivity can travel as far as 300 miles.





NATIONAL POST

NEWS

TRENDING Eve Adams | Grammys | Fahmy | Oil prices | Oscars | Target | Leafs | NHL

Post Primer: How iodine tablets help protect against radiation exposure

NP AILEEN DONNELLY | March 14, 2011 2:47 PM ET
More from Aileen Donnelly | @aileendonnelly

Republish
Reprint

SUGGESTED DOSAGE:
2-4 drops in 1/2 oz. of water or as directed by your healthcare provider. Original Nascent Iodine has lower surface tension than other iodine liquids, so the drops are smaller and more precise, requiring 64 drops to equal 1 ml. Use under supervision of qualified health practitioner. Do not exceed recommended dosage unless advised by your healthcare provider.

KEEP OUT OF REACH OF CHILDREN. DO NOT USE IF SAFETY SEAL IS BROKEN.

These statements have not been approved by the FDA. This product is not intended to treat, cure or diagnose any disease.

HEALTH RANGER'S
&
ORIGINAL NASCENT IODINE
HEALTH SUPPLEMENT

1 fl oz (30 ml)

SUPPLEMENT FACTS:
Serving Size: 2 Drops
Servings Per Container: 960

Ingredients	Amt per serving	%DV*
Iodine	506 mcg	337%

Ingredients: Organic (ethyl) alcohol, 2% iodine by weight

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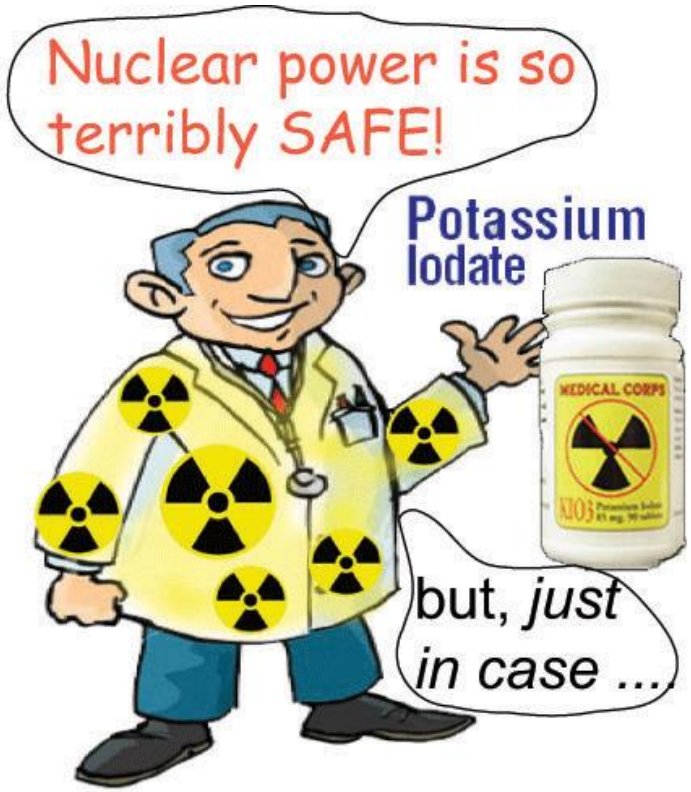
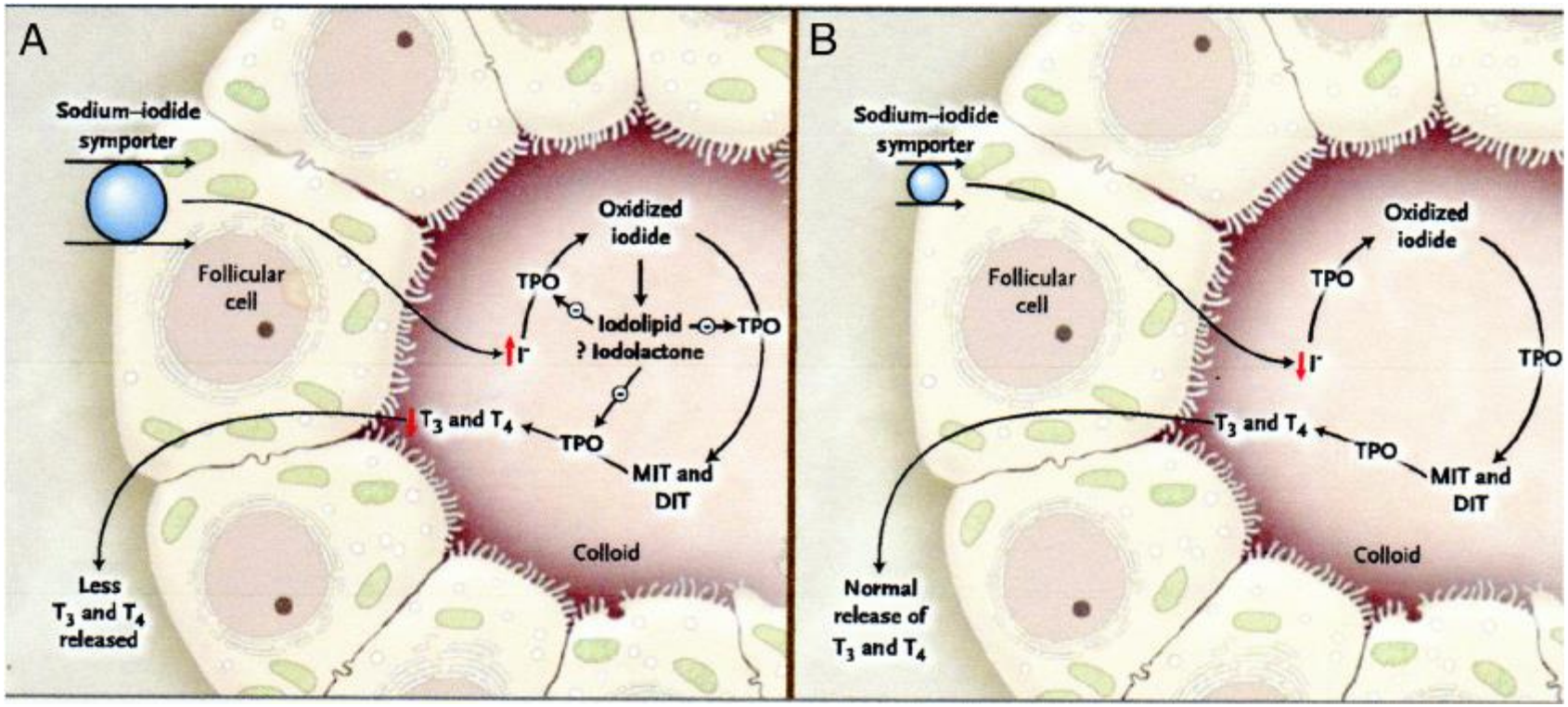


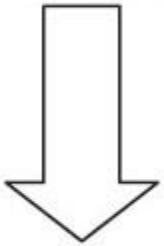
The Wolff-Chaikoff Effect



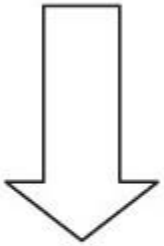
During the first day of iodine exposure, the sodium-iodide symporter transports the excess iodine into the thyroid, resulting in transient inhibition of thyroid peroxidase (TPO) and a decrease in thyroid hormone synthesis.

A dramatic decrease in sodium-iodide symporter expression results in decreased iodine transport and the subsequent resumption of thyroid hormone synthesis.

Non radioactive iodine in potassium iodide preparation will be absorbed by normal thyroid gland cell after intake

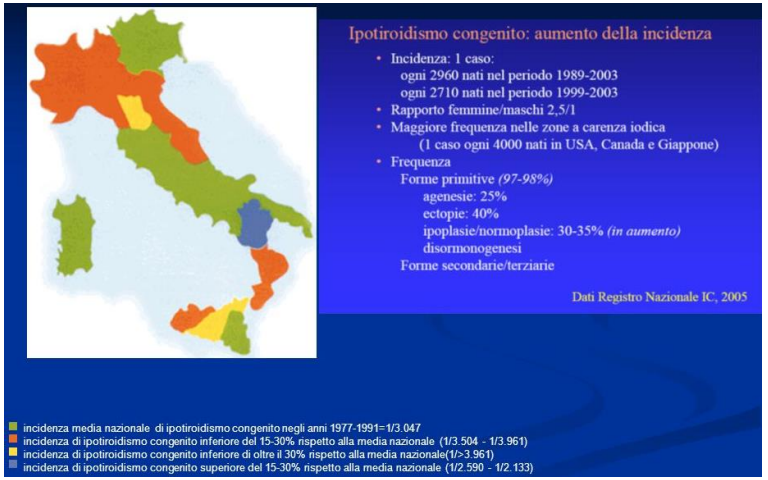


Thyroid gland is saturated with iodine

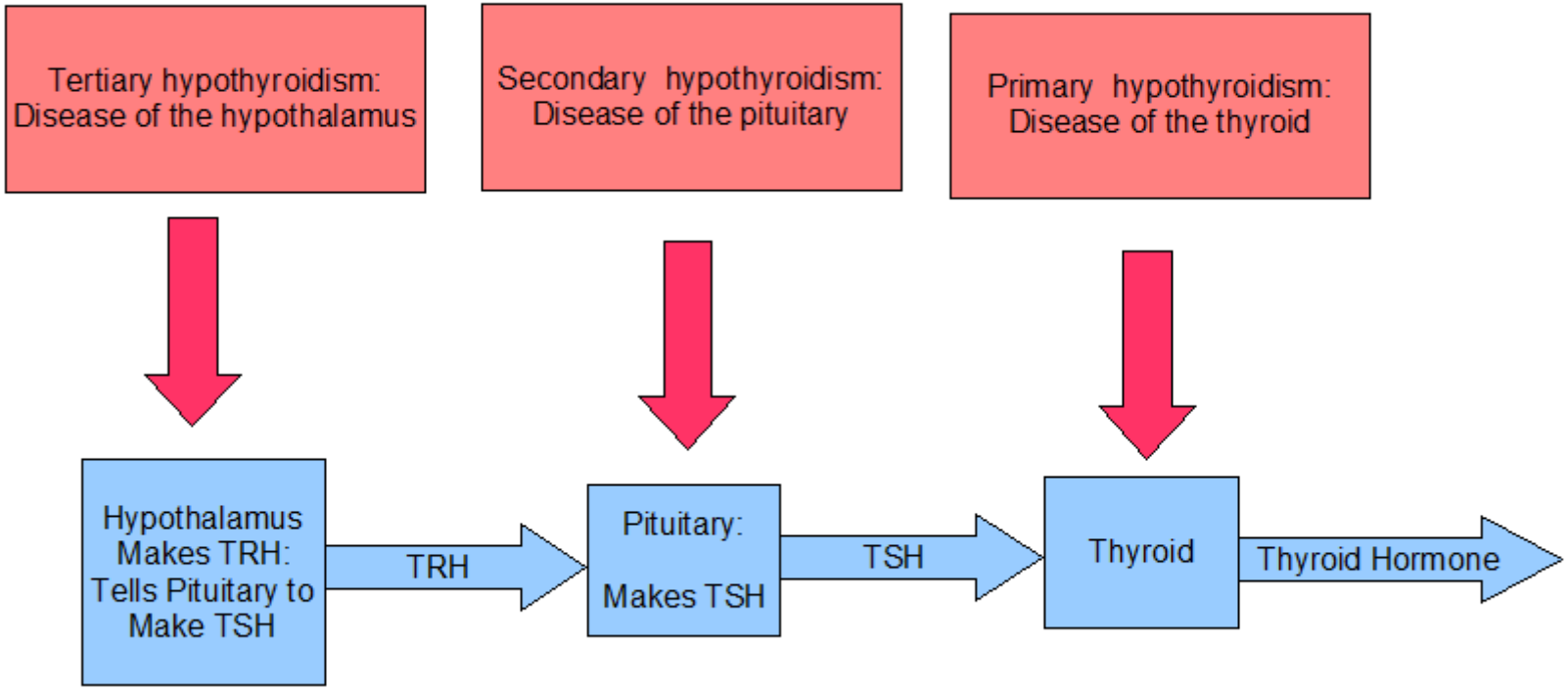


Saturated thyroid gland cannot further uptake the radioactive iodine from nuclear leakage

L'ipotiroidismo è una sindrome caratterizzata dalla riduzione dell'effetto degli ormoni tiroidei nelle cellule bersaglio e, quasi sempre, anche delle concentrazioni degli stessi ormoni nel plasma. In Italia, si stima che l'ipotiroidismo abbia un'incidenza annua di 2 ogni 1000 persone ed una prevalenza nella popolazione generale variabile fra il 2 ed il 7%, con rapporto femmine/maschi di 5:1.



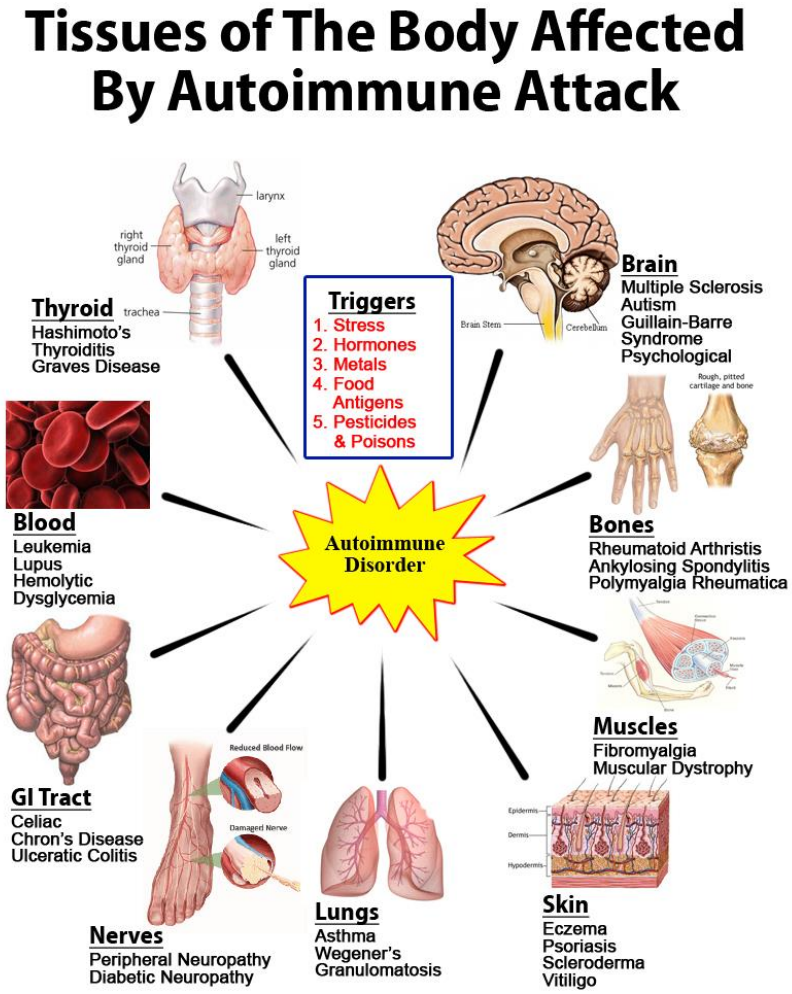
Primary, Secondary and Tertiary Hypothyroidism

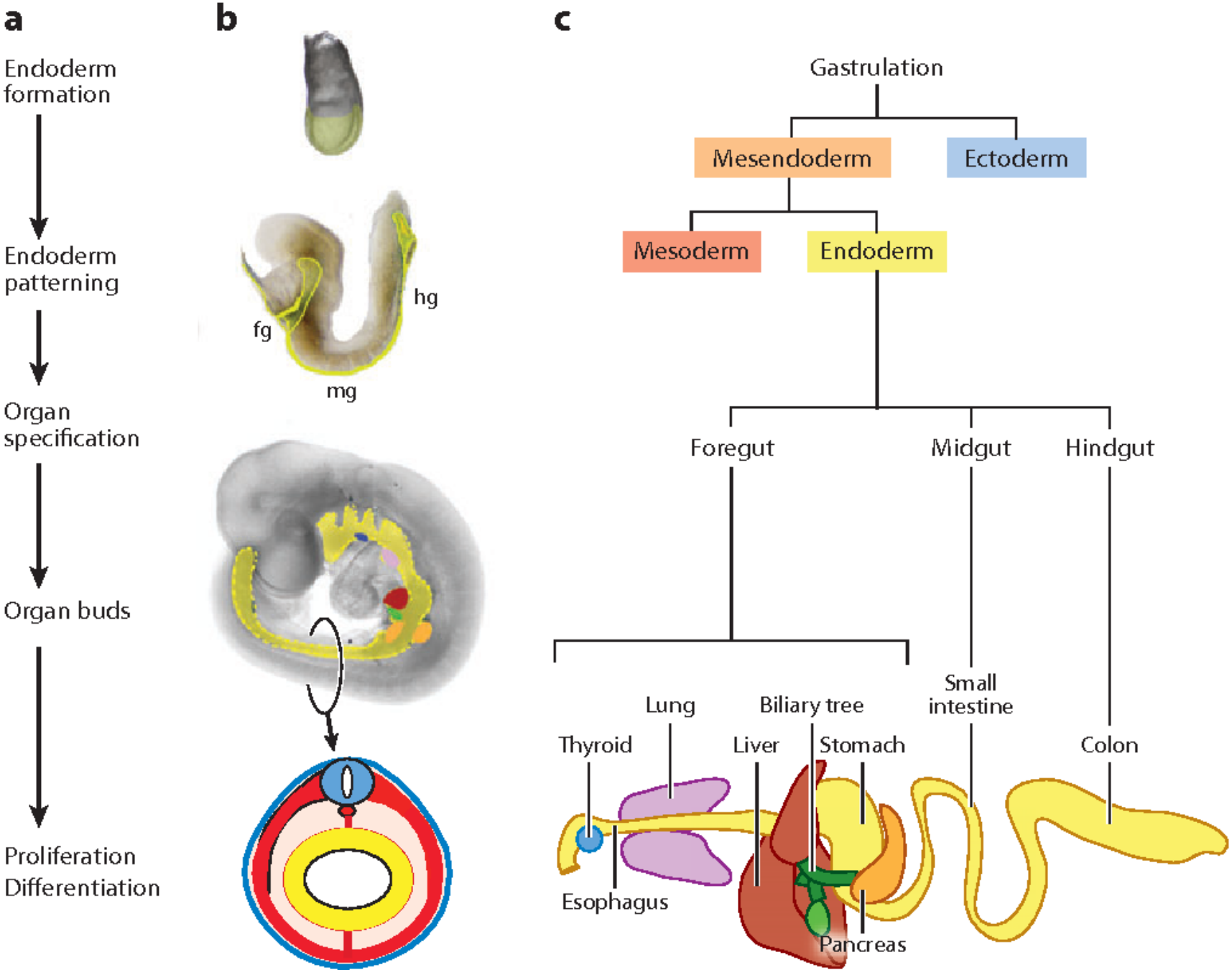


Disorders associated with hypothyroidism

The most common form of thyroid failure has an autoimmune etiology.

There is also an increased frequency of other autoimmune disorders in this population such as type 1 diabetes, pernicious anemia, primary adrenal failure (Addison's disease), myasthenia gravis, celiac disease, rheumatoid arthritis, LES, and rarely thyroid lymphoma.





Classificazione eziologica dell'ipotiroidismo

Primitivo

Congenito

- Agenesia ghiandolare
- Ectopia ghiandolare
- Ipoplasia
- Disormonogenesi
- Forme transitorie

Acquisito

- Da carenza iodica
- Tiroidite cronica autoimmune
- Post chirurgico
- Post terapia radiometabolica
- Fasi ipotiroidee della tiroidite subacuta, postpartum e silente
- Da farmaci (amiodarone, interferone, litio, inibitori di tirosino-chinasi)

Secondario

Da patologia ipofisaria

Terziario

Da patologia ipotalamica

Periferico

Resistenza periferica all'azione degli ormoni tiroidei

QUADRO CLINICO

Segni e sintomi dell'ipotiroidismo

SINTOMI

- Astenia (81%)
- Intolleranza al freddo (64%)
- Ridotta sudorazione (54%)
- Parestesie (52%)
- Stipsi (48%)
- Mialgie, artralgie (47%)
- Depressione (46%)
- Voce rauca (34%)
- Perdita di capelli (30%)
- Sonnolenza (27%)
- Dispnea (27%)
- Disordini ciclo mestruale (iper-polimenorrea) (23%)
- Letargia

SEGNI

- Iporeflessia (77%)
- Cute secca, pallida (76%)
- Edema periorbitale (60%)
- Bradicardia (58%)
- Modesto aumento di peso (54%)
- Ipotermia (50%)
- Gozzo (36%)
- Bradilalia (36%)
- Capelli fini, secchi, fragili (30%)

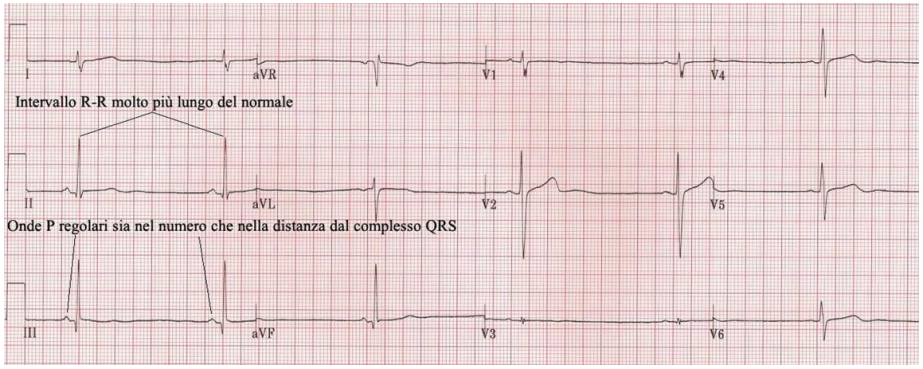
Più rari

- Edema non improntabile (mixedema)
- Macroglossia
- Versamento pericardico
- Rarefazione del 3° esterno del sopracciglio
- Ipertensione arteriosa (particolarmente diastolica)
- Sindrome del tunnel carpale
- Miopatia prossimale

Segni e sintomi dell'ipotiroidismo

A livello cardiovascolare, si verifica riduzione della frequenza cardiaca e della gittata sistolica, e quindi della portata cardiaca, con conseguente ridotta tolleranza all'esercizio fisico, dispnea da sforzo e scompenso cardiaco.

Dal punto di vista elettrocardiografico, si potranno notare bradicardia sinusale, bassi voltaggi, allungamento del tratto QT, onde T invertite o piatte.

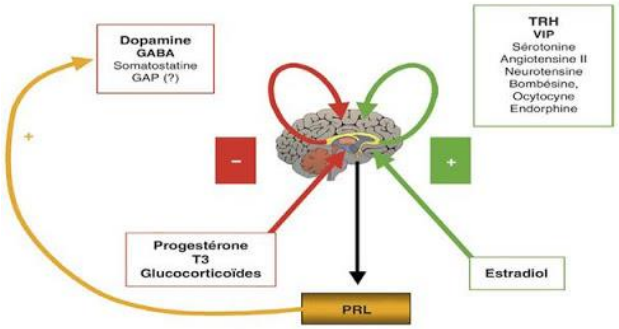


Segni e sintomi dell'ipotiroidismo

L'ipotiroidismo provoca inoltre la disregolazione di altri assi endocrini: l'aumento del TRH stimola anche la produzione di PRL.

Inoltre l'ipotiroidismo riduce la produzione di SHBG.

La combinazione di questi eventi può provocare irregolarità mestruali (amenorrea, oligomenorrea, polimenorrea, menorragia), calo della libido, disfunzione erettile, infertilità.

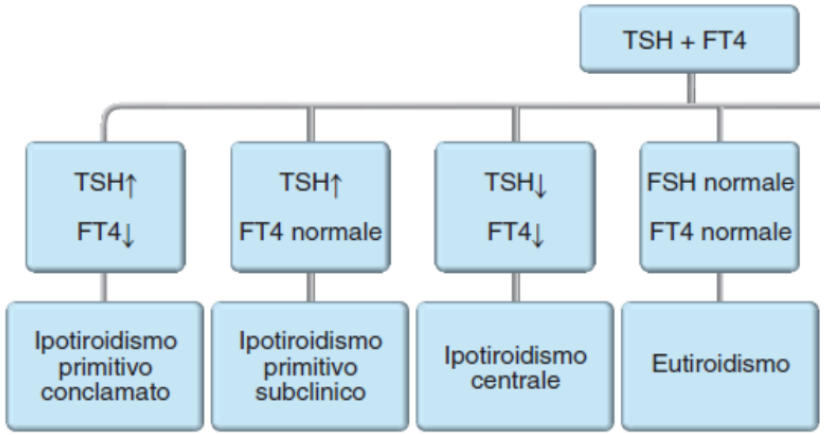


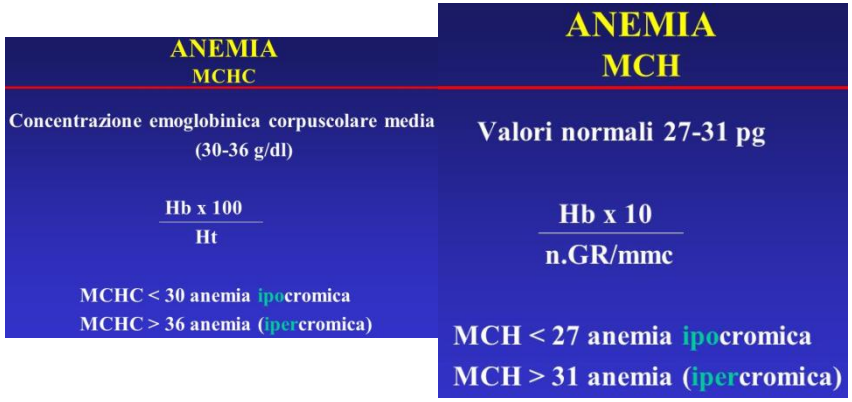
Inquadramento diagnostico

Il dosaggio degli Ab anti-TPO) ed anti-Tg è utile per chiarire l'eziologia autoimmune della sindrome.

Esami di laboratorio di secondo livello sono: il dosaggio dei lipidi ematici (che può dimostrare aumento dei livelli sierici di colesterolo totale, LDL e trigliceridi), delle transaminasi (ALT, AST, γ-GT) e degli enzimi muscolari (CK, mioglobina, LDH) che possono risultare aumentati.

Può inoltre essere presente lieve anemia ipocromica o macrocitica.





Terapia

La terapia si basa sulla somministrazione orale di levotiroxina sodica, il cui dosaggio è variabile in base all'età, al genere e al peso corporeo.

Per migliorarne l'assorbimento, è consigliabile assumerla almeno 4 ore dopo l'ultimo pasto e di mantenere il digiuno per circa un'ora, distanziando i farmaci interferenti (come ad esempio gli inibitori di pompa protonica ed il ferro).

Il dosaggio dovrà poi essere controllato e personalizzato sulla base dei valori circolanti di TSH ed FT4.

ETÀ	L-T4 MCG/KG/DIE
0-6 mesi	10
6-12 mesi	8
1-5 anni	6
5-10 anni	4
10-15 anni	3
>16 anni	1,3-1,6

FORME PARTICOLARI DI IPOTIROIDISMO

Ipotiroidismo subclinico

Si tratta di una condizione asintomatica o meglio paucisintomatica nella quale la funzione tiroidea è solo lievemente ridotta, così che gli ormoni tiroidei circolanti sono ancora compresi nei limiti della norma ma i valori del TSH risultato elevati; infatti il dosaggio TSH è molto più sensibile del dosaggio degli ormoni tiroidei.

Ipotiroidismo subclinico

Questi pazienti devono essere controllati periodicamente per valutare la progressione verso l'ipotiroidismo franco.

Esiste accordo nel trattare i pazienti con livelli di TSH >10 mUI/L, mentre il trattamento di pazienti con valori di TSH più bassi (4-10 mUI/L) è più controverso e deve essere guidato dal giudizio clinico sulla base dell'età, della sintomatologia riportata e dei fattori di rischio del singolo paziente: suggeriscono l'opportunità di intraprendere una terapia la positività degli Ab anti-Tg ed anti-TPO, l'incremento del colesterolo totale e dei trigliceridi, la presenza di disfunzione diastolica.

Ipotiroidismo in gravidanza

Nelle prime settimane di gestazione, l'eutiroidismo è essenziale per garantire lo sviluppo somatico e cerebrale del feto.

La gravidanza è caratterizzata da alterazioni fisiologiche della funzione tiroidea.

Gli estrogeni portano ad un aumento della TBG, che comporta un aumento della concentrazione sia della T3 che della T4 totali, mentre l'azione TSH-simile dell'hCG comporta, soprattutto entro le prime 10-12 settimane, una relativa riduzione del TSH.

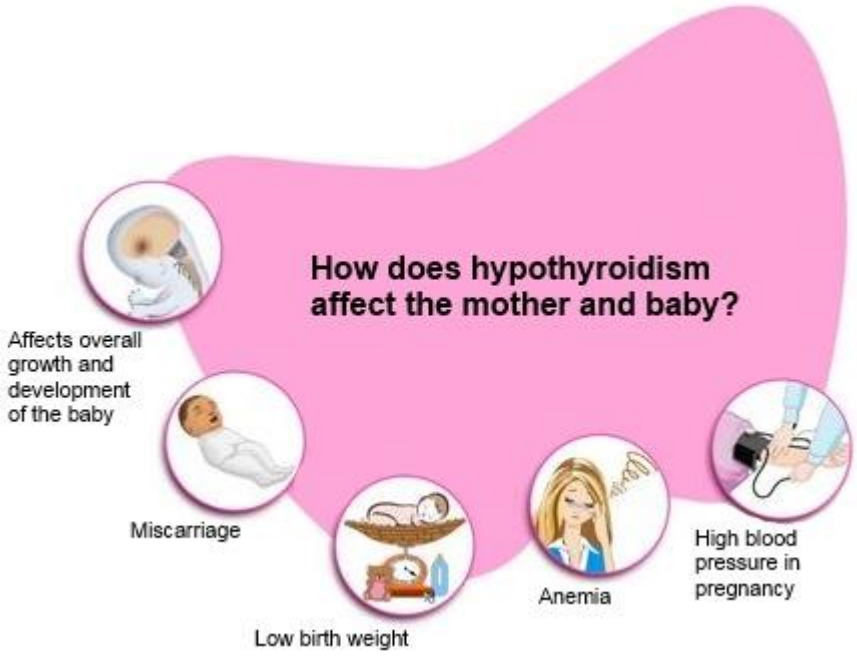
Physiologic changes	Resultant change in thyroid activity
↑ hCG	↑ T_4 ↓TSH
↑ Estrogen	↑ TBG
↑ TBG	↑ Demand for T_4 and T_3 ↑ Total T_4 and T_3
↑ Iodine clearance	↑ Dietary requirement for iodine ↓ TH production in iodine-deficient women ↑ Goiter development in iodine-deficient women

hCG, human chorionic gonadotropin; T_3, tri-iodothyronine; T_4, thyroxine; TBG, thyroxine-binding globulin; TH, thyroid hormone; TSH, thyroid-stimulating hormone.

Ipotiroidismo in gravidanza

Al momento del concepimento è necessario verificare i livelli di ormoni tiroidei, e nelle pazienti con ipotiroidismo, è opportuno attuare una rapida correzione con l'obiettivo di mantenere il TSH <2,5 mUI/L nel primo trimestre e <3 mUI/L nel secondo e terzo trimestre, sempre mantenendo l'FT4 a livelli normali.

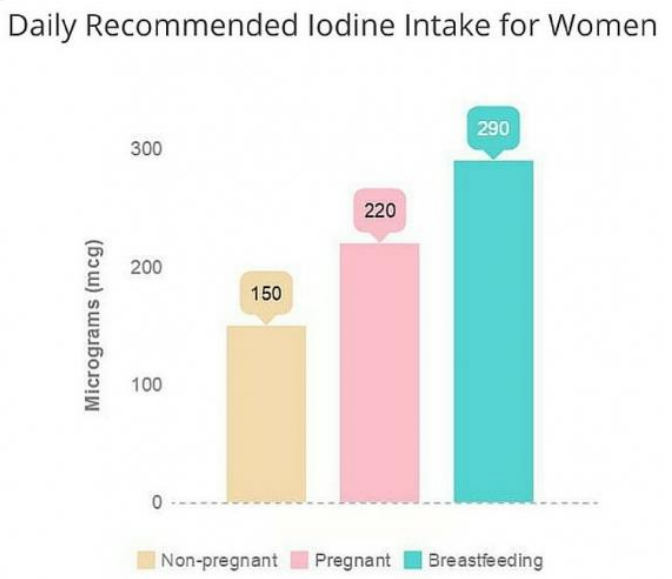
I successivi controlli andrebbero effettuati almeno ogni 2 mesi, al fine di attuare le opportune modifiche posologiche.



Ipotiroidismo in gravidanza

Dopo il parto si può tornare alla posologia pregravidica con nuovo controllo dopo 4-6 settimane, e non ci sono controindicazioni all'allattamento.

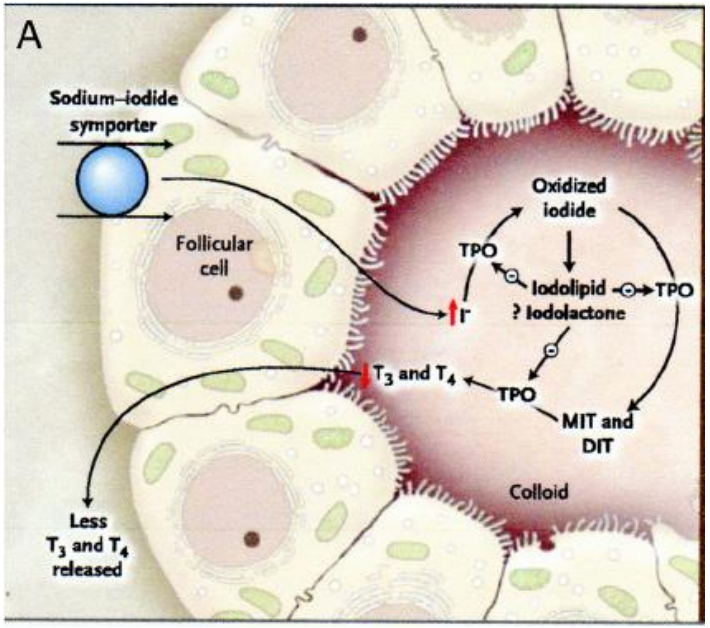
In ogni caso, anche in assenza di tireopatia, in gravidanza e ancora di più durante l'allattamento, è opportuna una supplementazione iodica, poiché in queste situazioni il fabbisogno iodico aumenta fino a 250 µg/die.



Ipotiroidismo da farmaci

I più noti sono:

- **amiodarone** (per il suo elevato contenuto di I, può causare ipotiroidismo sia attraverso l'effetto Wolff-Chaikoff sia provocando una particolare forma di tiroidite),
- **litio** (concentrandosi nei tireociti, interferisce con i loro processi metabolici) e
- **interferone** (può slatentizzare una tiroidite autoimmune o provocare una forma di tiroidite distruttiva),
- **inibitori di tirosino-chinasi** (in grado di interferire con la secrezione del TSH e con il metabolismo periferico degli ormoni tiroidei).

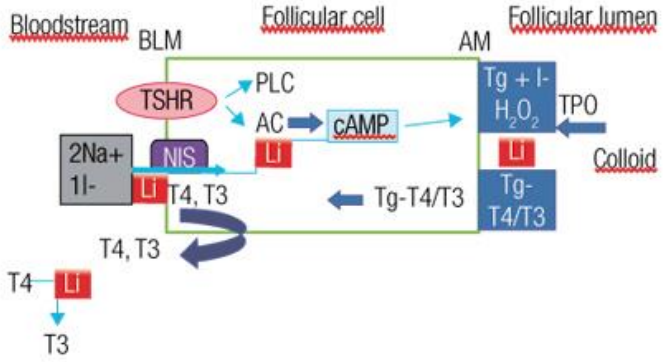


Concurrent conditions of special significance in hypothyroid patients

Lithium

All patients receiving lithium therapy require periodic thyroid evaluation because lithium may induce goiter and hypothyroidism . Occasionally in psychiatric practice, some patients who have depression are treated not only with antidepressants but also with thyroid hormone, even though they have normal thyroid function.

No firm evidence has shown that thyroid hormone treatment alone does anything to alleviate depression in such patients.



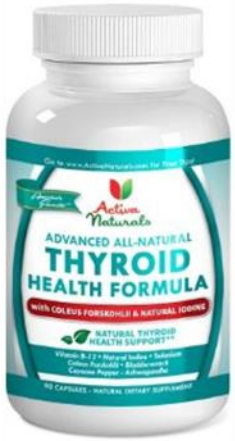
BLM: basolateral membrane; AM: apical membrane; PLC: phospholipase C; AC: adenylate cyclase; cAMP: cyclic adenosine monophosphate; TPO: thyroperoxidase; Tg: thyroglobulin; T4: thyroxine; T3: triiodothyronine; Li: lithium; Na^+: sodium; I^-: iodide; NIS: sodium-iodide symport; TSHR: TSH receptor.

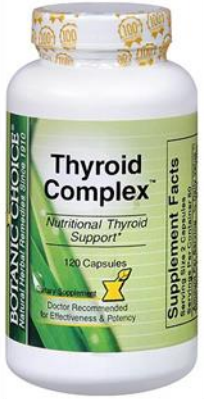
Figure 1. Main points involved in lithium-induced thyroid dysfunction. Adapted from: Williams Textbook of Endocrinology. 11th edition. 2008 (34).

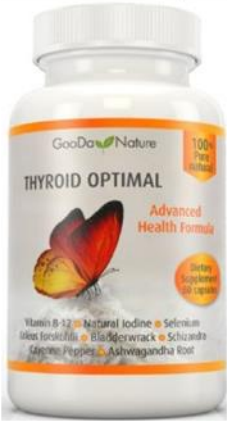

THYROID
MEDICATIONS

Is there a role for the use of dietary supplementation, nutraceuticals, and over-the-counter products in either hypothyroid or euthyroid individuals?

- **We recommend against the use of dietary supplements, nutraceuticals, or other over-the-counter products either in euthyroid individuals or as a means of treating hypothyroidism.**
- **We particularly caution against the use of pharmacologic doses of iodine because of the risk of thyrotoxicosis and hypothyroidism in those with intact thyroid glands susceptible to becoming further dysregulated because of underlying thyroid pathology.**
- **The majority of dietary supplements (DS) fail to meet a level of scientific substantiation deemed necessary for the treatment of disease. This is the case for over-the-counter products marketed for "thyroid support" or as a "thyroid supplement" or to promote "thyroid**



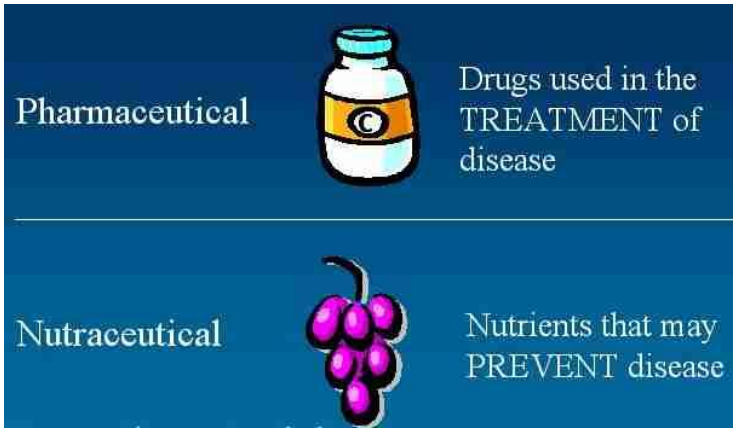




Is there a role for the use of dietary supplementation, nutraceuticals, and over-the-counter products in either hypothyroid or euthyroid individuals?

Nutraceuticals are dietary supplements that "contain a concentrated form of a presumed bioactive substance originally derived from a food, but now present in a non-food matrix, and used to enhance health in dosages exceeding those obtainable from normal foods".

Use of such products, including vitamin preparations and herbal supplements, is common. Approximately 20% of the subset of the hypothyroid population who are being treated for thyroid cancer use such supplements.



KELP

Kelp is a type of seaweed, or algae, commonly eaten in Asian countries, such as Japan and China. Kelp is found mainly in kelp forests within shallow bodies of saltwater and can grow up to half a meter a day, ultimately reaching heights of 30 to 80 meters.

Kelp is considered a super-food because of all the nutrients it contains.

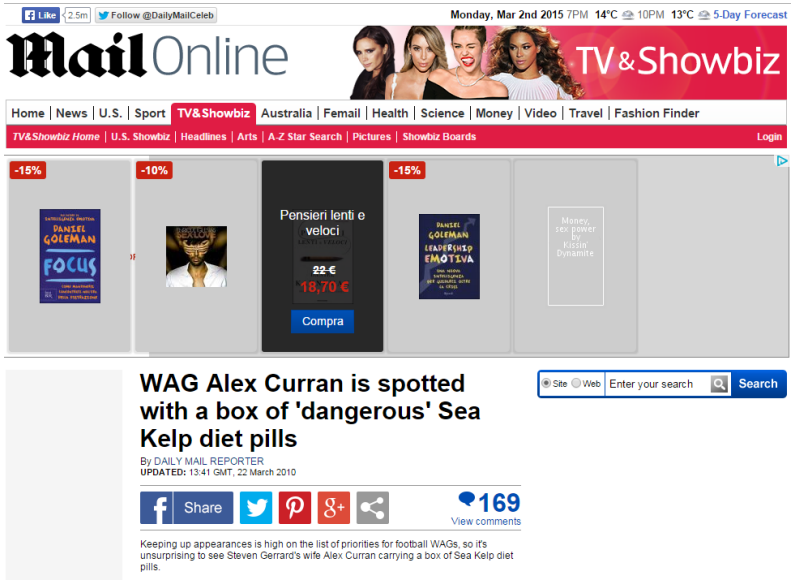
Eating large amounts of it can cause side effects.

Excess iodine intake and hypothyroidism

- Iodine is used as a pharmaceutical in the management of hyperthyroidism and thyroid cancer (as RAI).
- Kelp supplements contain at least 150-250 µg of iodine per capsule compared with the recommended daily intake of iodine of 150 µg for adults who are not pregnant or nursing.
- In euthyroid patients, especially those with chronic thyroiditis, substantial kelp use may be associated with significant increases in TSH levels. No clinical data exist to support the preferential use of stable iodine, kelp, or other iodine-containing functional foods in the management of hypothyroidism in iodine-sufficient regions unless iodine deficiency is strongly suspected and confirmed

Excess iodine intake and hypothyroidism

- **Adverse metabolic effects of iodine supplementation are primarily reported in patients with organification defects (e.g., Hashimoto's thyroiditis) in which severe hypothyroidism ensues and is referred to as "iodide myxedema".**
- **Even though pregnant women may be iodine deficient and require supplementation to achieve a total iodine intake of 200-300 µg/d, ingesting kelp or other seaweed-based products is not recommended owing to the variability in iodine content.**



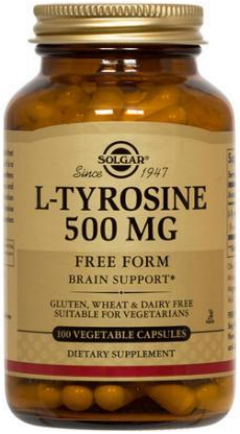
- It is thought the tablets can be used to aid weight loss, but experts have warned against using them because of the lack of research into their long-term effects.
- "People mistakenly think that because these are natural tablets they must be harmless, but used in the wrong way they can be very dangerous".

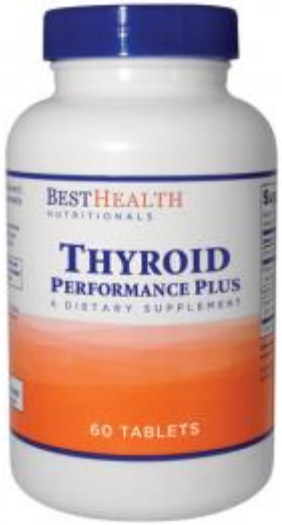
3,5,3´-Triiodothyroacetic acid

- Another DS/N used for thyroid health is 3,5,3´-triiodothyroacetic acid (TRIAC; tiratricol), an active metabolite of T3, which has been sold over the counter for weight loss.
- TRIAC appears to have enhanced hepatic and skeletal thyromimetic effects compared with L-T4 . The FDA scrutinized its use because of its lack of proven benefit as well as thyrotoxic and hypothyroid side effects. It is difficult to titrate or monitor clinically and biochemically. Its role in the treatment of hypothyroidism in syndromes of generalized resistance to thyroid hormone, particularly when L-T4 alone appears to be inadequate, remains uncertain .
- There are no data supporting its use in lieu of synthetic L-thyroxine in the treatment of

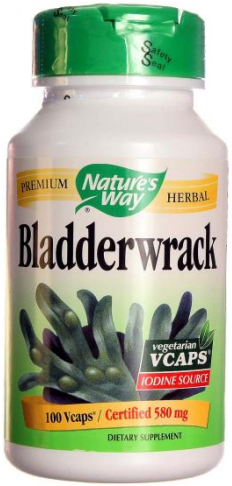
Thyroid-enhancing preparations

- **L-tyrosine has been touted as a treatment for hypothyroidism by virtue of its role in thyroid hormone synthesis. There are no studies demonstrating that L-tyrosine has thyromimetic properties.**
- **B vitamins, garlic, ginger, gingko, licorice, magnesium, manganese, meadowsweet, oats, pineapple, potassium, saw palmetto, and valerian are included in various commercially available "thyroid-enhancing preparations."**
- **There are no studies demonstrating any thyromimetic properties of any of these DS/N.**





Thyromimetic preparations



Some DS/N with thyromimetic properties that have been studied **but are of unproven clinical benefit** include Asian ginseng , bladderwrack, capsaicin, echinacea, and forskolin.

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Thyroxine and Triiodothyronine Content in Commercially Available Thyroid Health Supplements

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AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND THE AMERICAN THYROID ASSOCIATION

RECOMMENDATION 34 - Patients taking DS and N for hypothyroidism should be advised that commercially available thyroid-enhancing products are not a remedy for hypothyroidism and should be counseled about the potential side effects.

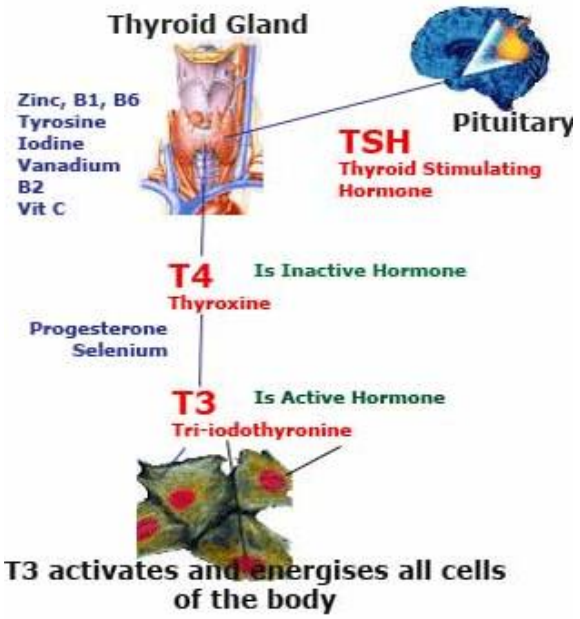
TABLE 1. MEASURED THYROXINE AND THYRONINE IN OVER-THE-COUNTER THYROID SUPPLEMENTS

Sample ID no.	*L-tyrosine*[a] *(mg)*	*Iodine*[a] *(μg)*	*T4 (μg/tab)*[b]	*T3 (μg/tab)*[b]	*Recommended daily dose*	*Total daily dose T4 (μg/day)*[c]	*Total daily dose T3 (μg/day)*[c]
1	150	150	Undetectable	2.73±0.38	1 capsule daily	—	2.73
2	300	150	5.77±1.07	1.83±0.68	3 capsules daily	17.30	5.50
3	700	240	22.90±1.83	4.13±0.40	4 capsules daily	91.60	16.53
4	500	100	Undetectable	8.03±0.23	2 capsules 1–2×daily	—	32.13
5	1000	225	<0.5	5.00±1.01	2 capsules 2×daily	<1.0	20.00
6	—	—	Undetectable	3.67±0.31	1 capsule daily	—	3.67
7	—	—	Undetectable	Undetectable	1 tablet daily	—	—
8	—	—	Undetectable	2.30±0.52	1 capsule daily	—	2.30
9	200	—	8.57±0.12	25.40±0.53	1 capsule daily	8.57	25.40
10	—	—	9.40±1.27	1.27±0.12	>1 tablet daily	9.40	1.27

[a]As provided on the label.
[b]Mean±SD.
[c]Calculated maximum/total daily dose (mean) per recommended daily intake dose.
ID, identification; T3, triiodothyronine; T4, thyroxine.

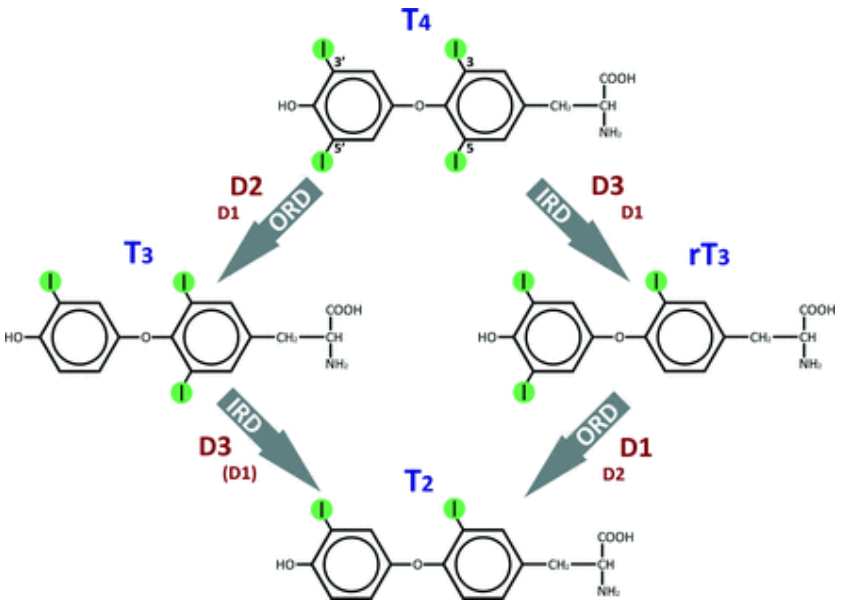
Selenium

- Selenium is an essential dietary mineral that is part of various selenoenzymes. These compounds are in many antioxidant, oxidation-reduction, and thyroid hormone deiodination pathways.
- It is not surprising that by virtue of these biochemical effects, selenium has been investigated as a modulator of autoimmune thyroid disease and thyroid hormone economy. Selenium has notable theoretical potential for salutary effects on hypothyroidism and thyroid autoimmunity including Graves' eye disease, both as a preventive measure and as a treatment.
- However, there are simply not enough outcome data to suggest a role at the present time for routine



Is levothyroxine monotherapy considered to be the standard of care for hypothyroidism?

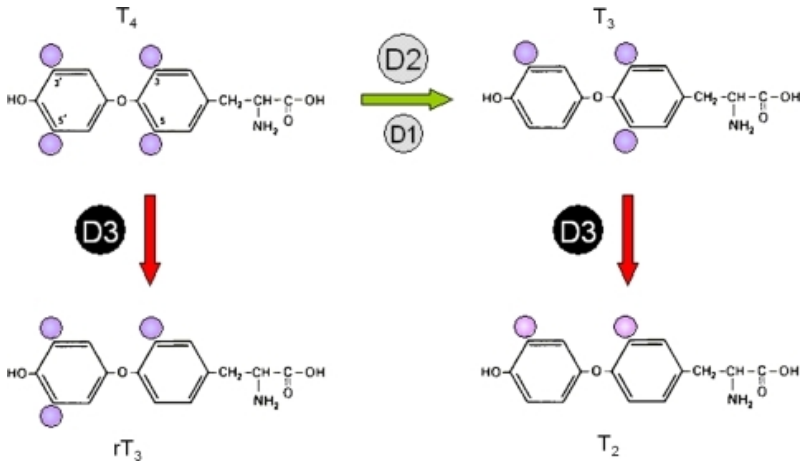
- **The rationale for the therapeutic use of LT4 in the treatment of hypothyroidism lies in the peripheral conversion of the exogenously administered pro-hormone thyroxine (T4) into its active metabolite T3.**
- **This activating conversion is accomplished by two enzymes, the type 1 (D1) and type 2 (D2) deiodinases.**
- **A third deiodinase, type 3 deiodinase (D3) participates in the clearance of both serum T4 and T3.**



T4 is a pro-hormone

Approximately 85 µg of T4 is secreted by the thyroid gland daily. Of the total daily T3 production of about 33 µg in normal man, approximately 80% (about 26 µg) arises from peripheral conversion from T4, and only about 20% (approximately 6.5 µg) derives from direct thyroidal secretion.

It is now well established that while T4 is the major secretory product of the thyroid gland, thyroid hormone action in peripheral tissues is due to the effects of T3 binding to its nuclear receptor, defining T4 as a pro-hormone for T3.

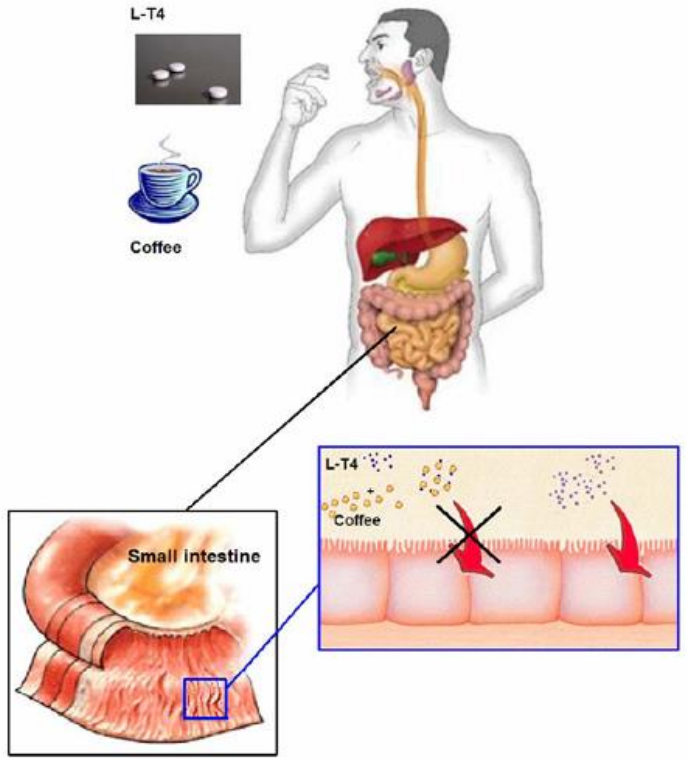


Absorption of LT4 occurs in the **jejunum** and **ileum**. **An acidic pH** in the stomach, as occurs during fasting conditions, appears to be important for subsequent intestinal absorption. The absorption of an orally administered dose of LT4 is about 70%–80% under optimum fasting conditions. With such therapy, there will be a transient peak in serum T4 and fT4 levels of about 15% magnitude about 4 hours after LT4 administration.

Steady-state levels of T4 and TSH are generally achieved in **6 weeks** after initiation of therapy.

Table 1 Main gastrointestinal disorders that interfere with levothyroxine absorption

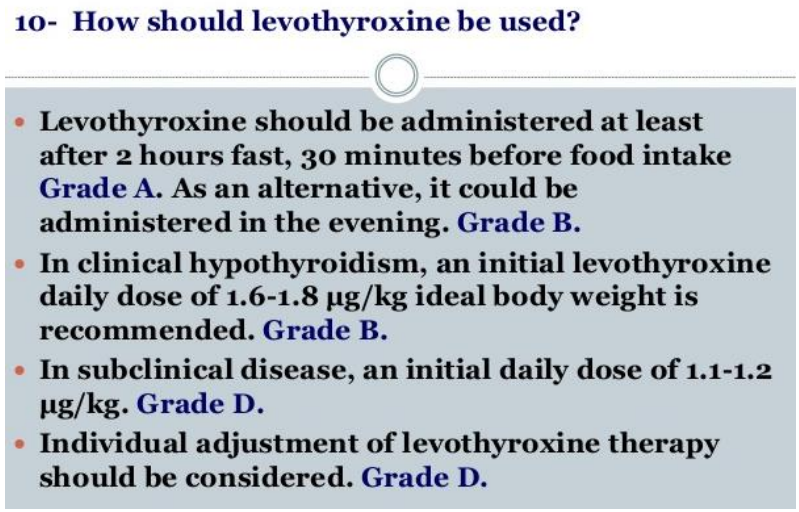
Gastrointestinal disorders	Mechanism
Atrophic gastritis	Hypochlorhydria
Helicobacter pylori infection	Ammonia production increased gastric pH
Celiac disease	Inflammation; intestinal villous atrophy (enterocytes)
Lactose intolerance	Inflammation
Bowel resection	Short bowel syndrome



How should levothyroxine administration be timed with respect to meals and beverages in order to maintain maximum, consistent absorption?

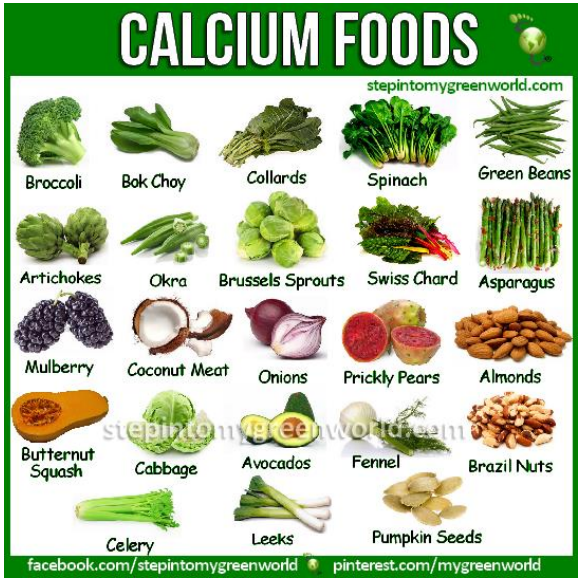
Although a fasting regimen may promote absorption, it may have the disadvantage of being maximally inconvenient for patients. Thus, a patient's schedule and preference should be taken into account and if consumption of LT4 1 hour before breakfast is not feasible, a bedtime regimen may be the next best choice.

In order to maintain a stable serum TSH, it would be important to consume a breakfast with similar daily food choices and avoid foods that are most noted for interfering with LT4 absorption.



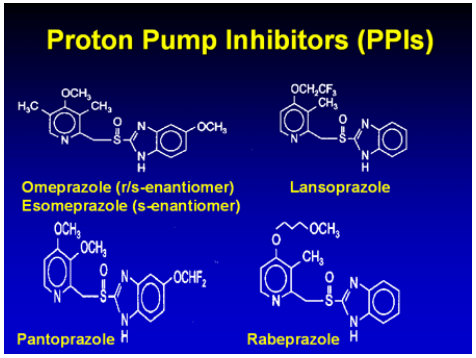
Thyroid hormones levels can decrease if you take your medication with foods or foods that contain soybean flour, cotton seed meal, walnuts, dietary fiber, calcium or calcium fortified juices.

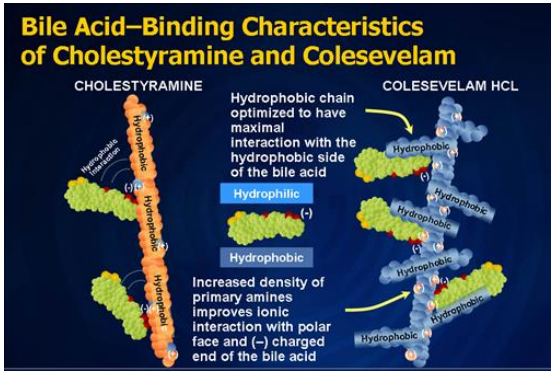
These foods should be avoided within several hours of taking LT4.

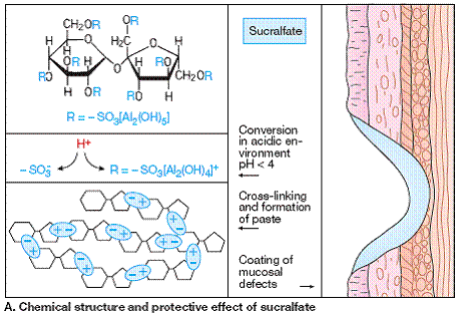


What medications may alter a patient's levothyroxine requirement by affecting either metabolism or binding to transport proteins?

- **The list of medications that can alter the absorption of LT4 is extensive and includes calcium carbonate, PPIs, bile acid sequestrants (cholestyramine and colesevelam), phosphate binders, ferrous sulfate, aluminum-containing antacids and sucralfate.**
- **Although the impact of multivitamins on LT4 absorption does not appear to have been studied, their calcium and ferrous salt content would be expected to result in impaired absorption. Based on this supposition they are included in lists of drugs potentially impairing LT4 absorption.**
- **Only chronic oral therapy is associated with decreased LT4 absorption.**







A. Chemical structure and protective effect of sucralfate

What medications may alter a patient's levothyroxine requirement by affecting either metabolism or binding to transport proteins?

Table 2. Management of Interactions With Levothyroxine

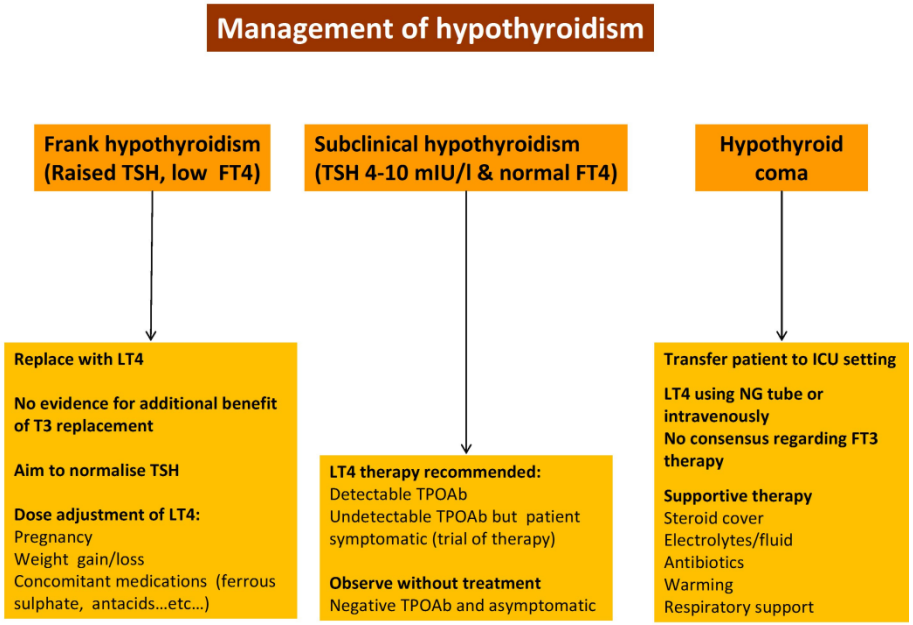
Agent	Reported Increase in TSH Level (reference range, 0.1 - 5 mIU/L)[18]	Recommended Timing and Spacing
Calcium carbonate[1,4,6,7,9]	7.8 - 41.4 mIU/L	3 - 4 h
Iron supplements[10-12]	5.4 - 243 mIU/L	≥ 2 h; give levothyroxine first
Chromium[16]	N/A[a]; 83% of baseline levothyroxine absorption	≥ 4 h
Aluminum-containing and magnesium-containing antacids[13-15]	7.2 - 64.3 mIU/L	3 - 4 h
Sucralfate[17]	30.5 mIU/L	≥ 8 h

TSH, thyroid-stimulating hormone; [a] TSH level not reported.

Although there are preliminary small studies suggesting that LT4 dissolved in glycerin and supplied in gelatin capsules may be better absorbed than standard LT4 in selected circumstances such as concomitant use of proton pump inhibitors or concomitant coffee consumption, the present lack of controlled long-term outcome studies does not support a recommendation for the use of such preparations in these circumstances. Switch to a gel capsule might be considered in the rare case of putative allergies to excipients.

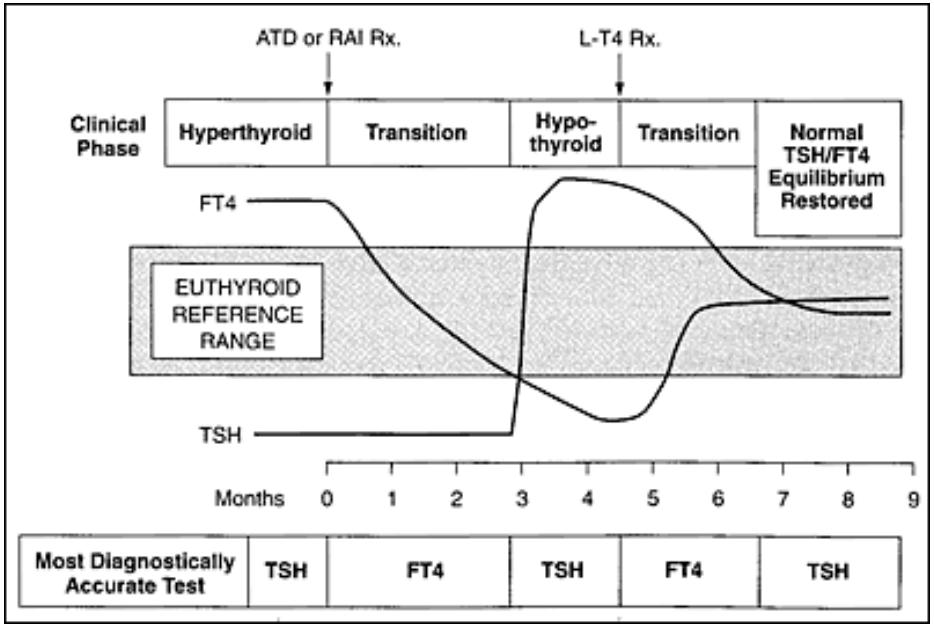
The goal of LT4 replacement in primary HT are to achieve a state of euthyroidism and normalization of the circulating levels of TSH and thyroid hormones.

A state of euthyroidism is defined as the normalization of indices of thyroid hormone action and the absence or the regression of symptoms and clinical signs associated with HT. The lack of specificity of hypothyroid symptoms and signs and, particularly in case of autoimmune thyroid disease (AITD), the slow development of the pathologic state, renders difficult the assessment of the adequacy of the replacement therapy on a purely clinical basis.



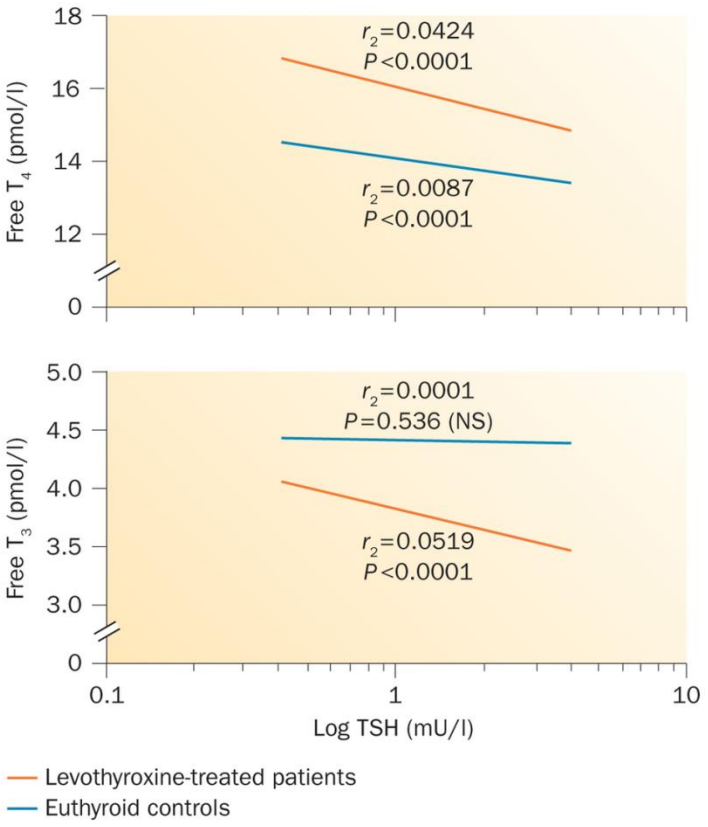
What are the clinical and biochemical goals for levothyroxine replacement in primary hypothyroidism?

TSH is the most reliable marker of adequacy of replacement treatment, and a value within the reference range (0.4–4.0mIU/L) should be considered the therapeutic target. Although no RCTs are currently available, a recent meta-analysis showed that significantly increased risk of CV mortality and morbidity was primarily observed in individuals with TSH levels > 10 mIU/L, with potential effects of TSH values > 7mIU/L



In some cases, LT4 alone may fail to restore the T3 levels to a value within the reference range in patients who have undergone total thyroidectomy and thus are devoid of residual endogenous production of thyroid hormone. In euthyroid patients undergoing thyroidectomy and not requiring suppressive therapy, if T3 levels are chosen as one of the therapeutic targets, it is reasonable to titrate the therapy to achieve circulating levels of T3 similar to the pre-surgery values while maintaining the TSH value within the range of normality.

Levels of FT4 above the reference range are often observed during replacement therapy with LT4; no evidence yet exists indicating that this condition is associated with adverse events or poor outcome.

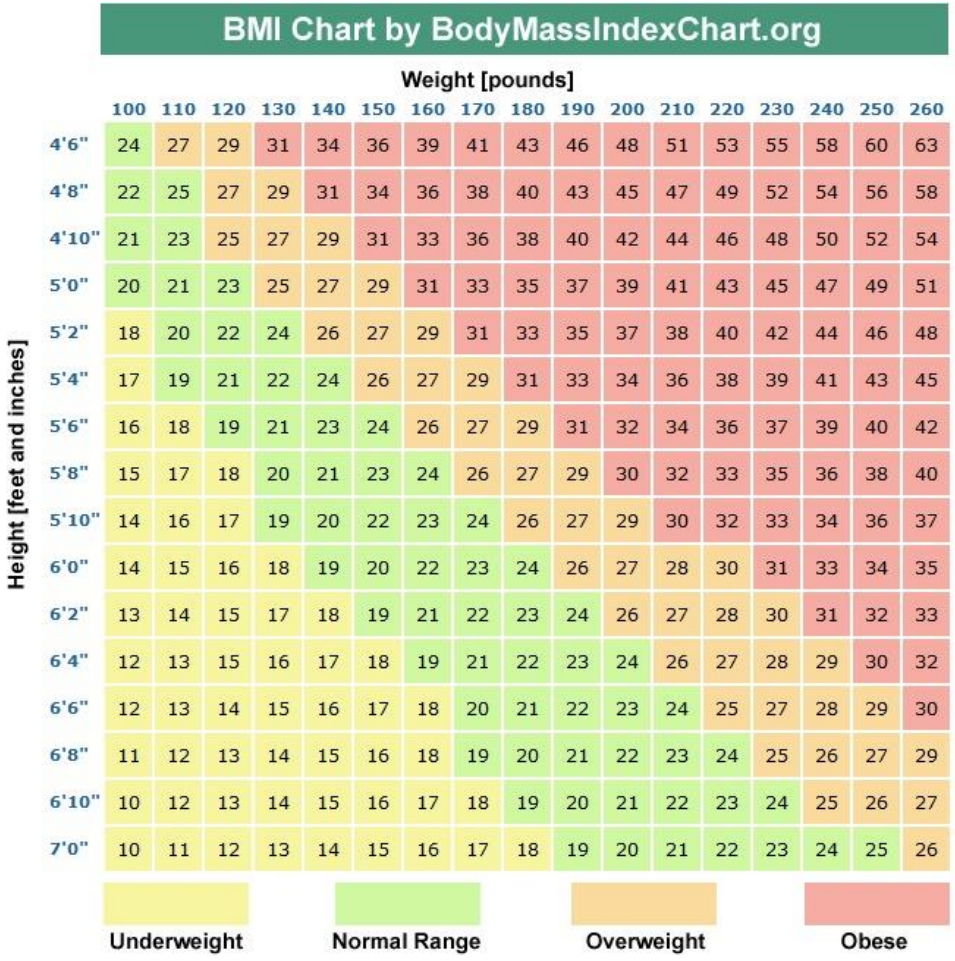


Is there a clinical rationale for prescribing brand-name levothyroxine preparations in preference to generic levothyroxine?

- **Prescription of brand name levothyroxine, or alternatively maintenance of the same generic preparation (i.e., maintenance of an identifiable formulation of levothyroxine), is advised.**
- **Switches between levothyroxine products could potentially result in variations in the administered dose and should generally be avoided for that reason.**

What factors determine the LT4 dose required by a hypothyroid patient for reaching the appropriate serum TSH goal?

When deciding on a starting dose of LT4 , the patient's weight, BMI, pregnancy status, etiology of hypothyroidism, degree of TSH elevation, age, and general clinical context, including the presence of cardiac disease, should all be considered.



Height	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	250	260
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4'8"	22	25	27	29	31	34	36	38	40	43	45	47	49	52	54	56	58
4'10"	21	23	25	27	29	31	33	36	38	40	42	44	46	48	50	52	54
5'0"	20	21	23	25	27	29	31	33	35	37	39	41	43	45	47	49	51
5'2"	18	20	22	24	26	27	29	31	33	35	37	38	40	42	44	46	48
5'4"	17	19	21	22	24	26	27	29	31	33	34	36	38	39	41	43	45
5'6"	16	18	19	21	23	24	26	27	29	31	32	34	36	37	39	40	42
5'8"	15	17	18	20	21	23	24	26	27	29	30	32	33	35	36	38	40
5'10"	14	16	17	19	20	22	23	24	26	27	29	30	32	33	34	36	37
6'0"	14	15	16	18	19	20	22	23	24	26	27	28	30	31	33	34	35
6'2"	13	14	15	17	18	19	21	22	23	24	26	27	28	30	31	32	33
6'4"	12	13	15	16	17	18	19	21	22	23	24	26	27	28	29	30	32
6'6"	12	13	14	15	16	17	18	20	21	22	23	24	25	27	28	29	30
6'8"	11	12	13	14	15	16	18	19	20	21	22	23	24	25	26	27	29
6'10"	10	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
7'0"	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26

What is the best approach to initiating and adjusting levothyroxine therapy?

Thyroid hormone therapy should be initiated as an initial full replacement or as partial replacement with gradual increments in the dose titrated upward using TSH as the goal.

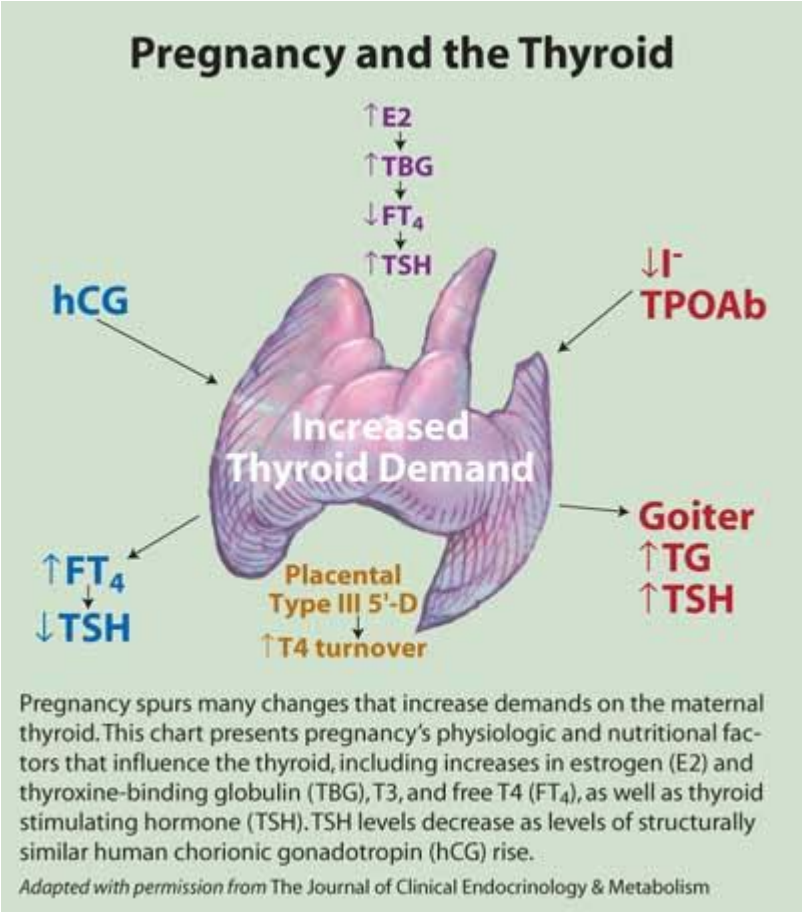
Dose adjustments should be made when there are large changes in body weight, with aging (“start low and go slow”) , and with pregnancy, with TSH assessment 4–6 weeks after any dosage change.

Initiation of levothyroxine therapy
- Healthy patients < 65 years old
  - Full daily replacement dose (1.6 μg/kg ideal body weight)
    - Women: 75 to 100 μg/d
    - Men: 100 to 150 μg/d
- Patients ≥ 65 years old or with a history of cardiac disease
  - Begin with 25 μg/d
  - Increase dose by 25-μg increments at 8-week intervals until serum thyroid-stimulating hormone concentration falls to normal
  - If cardiac symptoms develop or worsen, evaluate cardiac disease and modify levothyroxine therapy (*see* text).

* For monitoring levothyroxine therapy in patients with primary hypothyroidism, measurement of serum thyroid-stimulating hormone is adequate, and concentrations should be maintained between 0.5 and 3.0 mU/L. For monitoring therapy in patients with central hypothyroidism, measurement of the serum free thyroxine index is appropriate, and it should be maintained in the upper half of the normal range.

How should levothyroxine therapy be managed in pregnant women with hypothyroidism?

- **Women with overt hypothyroidism should receive LT4 replacement therapy with the dose titrated to achieve a TSH concentration within the trimester specific reference range. Serial serum TSH should be assessed every 4 weeks during the first half of pregnancy in order to adjust LT4 dosing to maintain TSH within the trimester specific range. TSH should also be reassessed during the second half of pregnancy.**
- **For women already taking LT4, two additional doses per week of the current LT4 dose, given as one extra dose twice weekly with several days separation, may be started as soon as pregnancy is confirmed.**



Pregnancy spurs many changes that increase demands on the maternal thyroid. This chart presents pregnancy's physiologic and nutritional factors that influence the thyroid, including increases in estrogen (E2) and thyroxine-binding globulin (TBG), T3, and free T4 (FT_4), as well as thyroid stimulating hormone (TSH). TSH levels decrease as levels of structurally similar human chorionic gonadotropin (hCG) rise.

Adapted with permission from The Journal of Clinical Endocrinology & Metabolism

Is there a role for the use of levothyroxine to treat euthyroid patients with depression?

We recommend against the routine use of LT4 for the treatment of euthyroid individuals with depression due to a paucity of controlled data examining treatment efficacy in this setting.

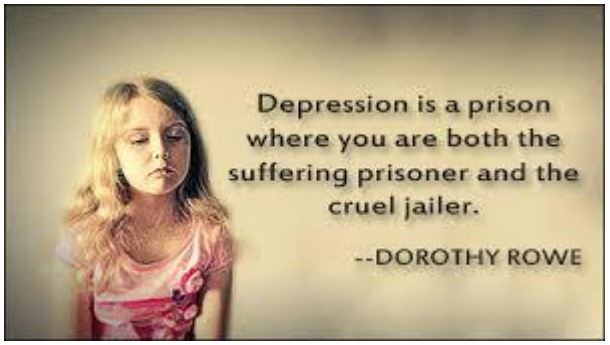
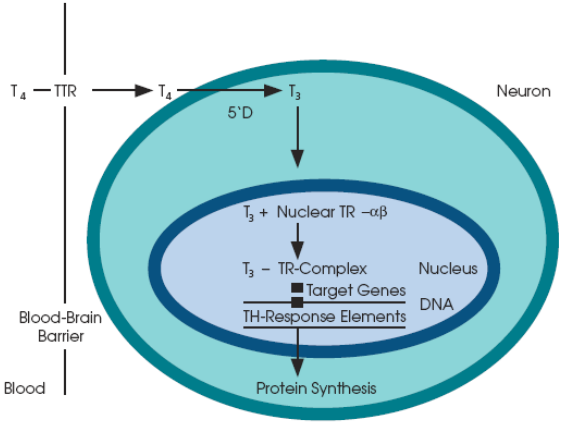


Figure 2
Thyroid Hormone Metabolism in the Brain

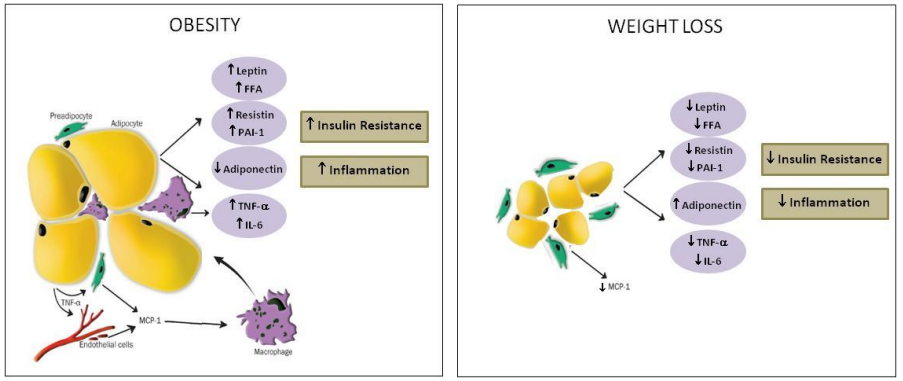


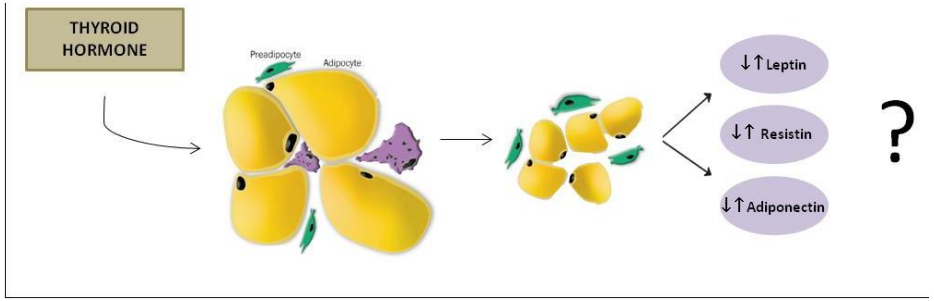
T_4=thyroxine; TTR=transthyretin; 5´D=deiodinase; T_3=triiodothyronine; TR=thyroid hormone receptor; TH=thyroid hormone.

Pfennig A, Frye MA, Köberle U, Bauer M. *Primary Psychiatry.* Vol 11, No 10. 2004.

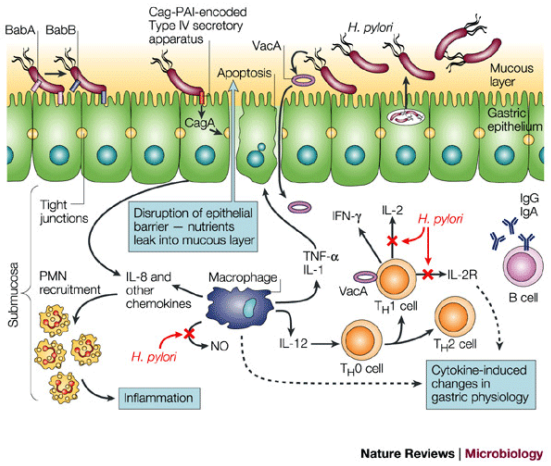
Is there a role for the use of levothyroxine to treat euthyroid patients with obesity?

- We recommend against the treatment of obesity with LT4 in euthyroid individuals due to a lack of treatment efficacy for this condition.
- Although hypothyroidism is often perceived to be a cause of obesity by the public, most of the weight gain (and weight loss with therapy) in TH deficiency states is due to fluid retention.
- There is no significant loss of fat mass, even after therapy of severe hypothyroidism, despite increases in resting energy expenditure.





Are there gastrointestinal conditions that should be considered when a patient's levothyroxine dose is much higher than expected?



- **In patients in whom LT4 dose requirements are much higher than expected, evaluation for GI disorders such as Helicobacter pylori–related gastritis, atrophic gastritis, or celiac disease should be considered.**
- **Furthermore, if such disorders are detected and effectively treated, re-evaluation of thyroid function and LT4 dosage is recommended.**