

In the name of god

Hypothyroidism *in special groups*

Cardiac disease:

- Thyroid hormone therapy (inotropic and chronotropic effects on the heart), is a potential cause of angina in patients with severe CAD.
- starting with low doses of L-T4 in this patient, and building the dose up slowly.
- monitoring for the development of angina or other cardiac symptoms such as tachyarrhythmias.
- With the current use of **beta adrenergic blocking** drugs, most patients with CAD can be fully replaced with L-T4 without difficulty.
- If patients are unable to tolerate the full L-T4 dose required to normalize the serum TSH, **additional measures (medical or surgical)** to treat the **CAD** would be indicated.
- Patients with known CAD should always be started on a **low L-T4 dose (12.5-25 mcg/day)**, with gradual increases based on symptoms and serum TSH levels.

Renal and liver disease:

- **no adjustments** in L-T₄ dosing are required in cases of **cirrhosis** or **renal failure**.
- **Nephrotic syndrome** (large urinary protein losses e.g TBG, transthyretine & albumin), can be a cause of **increased L-T₄ requirements**

GI disorders:

- In patients in whom **levothyroxine dose requirements are much higher than expected**, evaluation for GI disorders such as *H. pylori*–related gastritis, atrophic gastritis, or celiac(possibly mediated through an impact on gastric acidity)should be considered.
- Furthermore, if such disorders are **effectively treated**, re-evaluation of thyroid function and levothyroxine dosage is recommended.

co-existent psychosocial, behavioral, and mental health conditions (such as addiction, somatization disorder, and depression)

- The **treatment goals** of hypothyroidism in this patient **as for the general population**
- *patients with somatization disorders, who have been treated for hypothyroidism, may persistently complain of a range of symptoms associated with hypothyroidism despite normal laboratory testing*
- *Referral to a mental health professional should be considered if the severity of the symptoms is not sufficiently explained by the severity of the biochemically-confirmed thyroid dysfunction or another medical condition, or if the mental health condition is impairing effective management of levothyroxine replacement therapy*



HYPOTHYROIDISM IN THE OLDER PATIENT

- Hypothyroidism is very common in patients over 60 years of age and steadily increases with age.
- Up to 1 in 4 patients in nursing homes may have undiagnosed hypothyroidism.
- There are observational data showing **decreased mortality** rates and improved measures of well being in elderly persons with **TSH levels that are above the traditional reference range** (i.e., 0.5-4.5 mIU/L) for the general population.
- there are also observational data showing that **higher FT4 concentrations** are **associated with mortality** in the elderly.
- some data suggest that that **subclinical hypothyroidism** may be associated with **increased mortality**, possibly limited to those with cardiac disease such as congestive heart failure.

HYPOTHYROIDISM IN THE OLDER PATIENT

- **Symptoms** of hypothyroidism are very **non-specific** in all patients, even more so in the **older patient**, the **frequency of multiple symptoms decreases in the older patient**. For example, **memory loss** or a **decrease in cognitive functioning**, often attributed to advancing age, may be the **only symptoms** of hypothyroidism present.
- Symptoms and signs of hypothyroidism may include weight gain, sleepiness, dry skin, and constipation, but lack of these symptoms does not rule out the diagnosis. To make this **diagnosis in the elderly patient**, a doctor often needs a high **index of suspicion**.
- **Clues** to the possibility of hypothyroidism include a positive **family history** of thyroid disease, **past treatment for hyperthyroidism**, or a **history of extensive surgery and/or radiotherapy to the neck**.

HYPOTHYROIDISM IN THE OLDER PATIENT

- A decision to treat the patient with a new diagnosis of hypothyroidism will rest on several factors, including whether the patient is symptomatic from hypothyroidism, or just has an elevated TSH level.
- In the case of the latter finding, many doctors will repeat the test in 3-4 months and elect to begin thyroid hormone replacement when the TSH level stays above the normal range.
- The presence or absence, and severity, of thyroid-related symptoms and co-existing diseases such as coronary artery disease or heart failure will determine the dose of thyroid hormone replacement that is given.

HYPOTHYROIDISM IN THE OLDER PATIENT

- In particular, treatment of the **older** hypothyroid patient must take into account that full **thyroid hormone replacement need not take place rapidly**. Rather, hormone treatment is usually begun **slowly** with **a partial daily dose**, in order to allow the heart and central nervous system to adjust to increasing levels of thyroid hormone.
- The patient and family members **must be aware** of a possible increase in angina, shortness of breath, confusion and change in sleep habits, and notify the prescribing physician if these occur.
- In patients who experience increased angina pectoris, symptoms of congestive heart failure, or mental changes such as confusion will need to have their dose of L-T4 **decreased**, then more gradually increased over several months' time.

HYPOTHYROIDISM IN THE OLDER PATIENT

- In **elderly** persons (> 65-70 years) who are **without known heart disease** or **without major risk factors for heart disease** with no evidence of **stroke** or **dementia** , L-T4 therapy **can** be initiated at the **full dose**, *although* the method of ***starting with a low dose*** and increasing it slowly is ***still preferred*** by some experts
- Treatment may therefore begin with L-T4 in a dose of **25 to 50** micrograms daily, and the dose **increased** in steps **every 4-6 weeks** until the laboratory tests show a gradual return of blood thyroid hormone and **TSH** levels to the **normal range**.
- The final L-T4 dose that normalizes the serum TSH is generally lower in the elderly(caused by decreases in lean body mass).
- The **elderly** are **more susceptible** to the **adverse effects** of thyroid hormone excess, especially atrial fibrillation , and osteoporotic fractures.
- the target serum TSH should likely be raised in older persons, especially the oldest old (patients >80 years), **target serum TSH to 4-6 mIU/L in persons greater than age 70-80 years**



infants with overt hypothyroidism

- **Thyroid dysgenesis** is the most common etiology of CH, affecting approximately 1:2000 to 1:4000 newborns
- while the controversy remains in starting doses, there is reasonable agreement that the severity of the CH at the time of diagnosis (the maximum TSH level), and the length of time to achieve normal thyroid function (TSH and T₄), may ultimately have a greater impact on neurocognitive outcome than the initial starting dose
- In addition to the **degree of TSH elevation**, a **distal femur plain radiograph** may also help determine the **severity** of the hypothyroidism with a bony nucleus diameter <3mm
- The addition of L-T₃ to L-T₄ has not been adequately studied to determine risk or benefit, but in a subgroup of patients with persistent elevations in TSH despite T₄ levels in the mid to upper part of the reference range, the addition of L-T₃ may result in normalization of TSH
- **LT-4 replacement** at a dose of **10-15 mcg/kg/day** should be initiated once newborn **screening** is **positive**, pending the results of confirmatory testing
- **Higher doses** may be required for infants with **severe congenital hypo**
- **standard or low dose** therapy is defined by a range of **5 to 10 mcg/kg/day**, while **high dose** regimens is defined as a range of **10-15 mcg/kg/day**

infants with overt hypothyroidism

- The **aim** of therapy is to maintain the serum **T4** in the **mid- to upper half of the pediatric reference range** and the serum **TSH** in the **mid- to lower half of the pediatric reference range** (optimally between 0.5 to 2.0 mIU/L)
- The target should be to **normalize** serum **thyroxine** approximately **2-4 weeks** after **initiation** of therapy
- Once the proper dose is identified, surveillance testing with a serum **TSH and thyroxine** should be performed **every 1 to 2 months** during the **first year of life** with decreasing frequency as the child ages/ Linear growth and development should be followed closely.
- For patients with **mild CH** and **no change** in the **L-T4 dose over the first 3 years of life**, a **trial off L-T4 therapy** is reasonable in an effort to determine if the patient has transient or permanent CH
- **Permanent** CH is established if the **TSH rises** and the **T4 decreases** on repeat testing 4 to 6 weeks after stopping L-T4 therapy
- **L-T4** should be administered **during the same time of day, crushed** and **mixed** with **water, non-soy formula** or **breast milk** and administered via a spoon
- Older children may **chew** or **swallow** the pill
- Soy, iron, calcium and infant colic drops (simethicone) can decrease the absorption of L-T4



children with overt hypothyroidism

- **Autoimmune thyroiditis** is the most common cause of acquired hypothyroidism, is more common in **females** compared to males, and the incidence increases during adolescence.
- **Linear growth failure** and concomitant **bone age delay** are the most common clinical signs.
- The **management** of hypothyroidism in children is **similar to adults**

children with overt hypothyroidism

- The L-T4 dose for patients 1 to 3 years of age is 4 to 6 mcg/kg/day, for patients 3 to 10 years the L-T4 dose is 3 to 5 mcg/kg/day, and for patients 10 to 16 years the L-T4 dose is 2 to 4 mcg/kg/day L-T4
- As the child advances through the pediatric age into adulthood thyroid hormone replacement doses decrease, with newborns typically requiring 10 mcg/kg/day, one year old children 4-6 mcg/kg/day, adolescents 2-4 mcg/kg/day, with transition to the average adult dose of 1.6 mcg/kg/day

children with subclinical hypothyroidism

- The majority of pediatric patients with SCH will not progress to Overt-H.
- The presence of anti-thyroid antibodies may help identifying a subpopulation at increased risk of progression to OH.
- there are no data showing short-term or long-term negative consequences associated with untreated SCH in the pediatric population, including no adverse effect on linear growth and no increase in cardiovascular risk, behavioral disorders, or problems with cognition.
- In children with subclinical hypothyroidism, due to the low risks of L-T₄ replacement therapy, many clinicians still consider it reasonable to initiate treatment to avoid any potential risk of negative impact on growth and development

children with subclinical hypothyroidism

- Treatment is generally **not recommended** when the TSH is **5-10** mIU/L.
- For patients with SCH and a **TSH > 10** mIU/L with **signs** and **symptoms** consistent with primary thyroid disease and/or **risk factors associated with progression**, L-T₄ replacement may be reasonable.
- For patients with SCH and concern over **linear growth**, the presence of a **goiter** on exam, or evidence of **autoimmune** disease (including TPO-Ab positivity and/or an associated autoimmune disorder such as celiac disease or diabetes), initiation of **L-T₄ should be strongly considered** secondary to potential benefit and an increased risk of progression
- patients with SCH and an **increased total cholesterol** with elevated **LDL** fraction may also benefit from initiation of therapy
- L-T₄ should also be considered in pediatric patients with a **history of exposure to radiation** for the treatment of a **benign condition** or **non-thyroid malignancy** due to an increased risk for progression from SCH to OH



individuals who have elevated serum TSH values due to non-adherence

- If patients experience **unexpected fluctuations** in their serum **TSH**, or **persistently elevated TSH** concentrations **despite** the prescription of **large doses of L-T4**, factors affecting L-T4 *formulation, absorption, and metabolism* can be investigated as potential culprits. Loss of potency due to use of L-T4 that is beyond its *expiry date*, or use of pills that have deteriorated due to *environmental causes* such as excessive *heat* or *moisture* are other considerations.
- If, such **factors do not appear** to be responsible, variable adherence or **non-adherence** to L-T4 therapy should be considered.

individuals who have elevated serum TSH values due to non-adherence

- **Absorption testing** can be conducted by administering a specific oral dose of L-T₄ (L-T₄ of 600 mcg to 2 mg) under supervised conditions, measuring T₄ concentrations at 4-24 hours thereafter. An increment of at least of 2.5 times the baseline FT₄ suggest pseudomalabsorption.
- In conclusion, if efforts to encourage regular daily consumption of L-T₄ are unsuccessful, options include observed therapy, or reduction of the frequency of L-T₄ ingestion to twice weekly, or weekly with a starting dose equal to the weight-adjusted dose one would prescribe in a daily administration regimen (i.e. 7 times the daily dose)



secondary hypothyroidism

- In patients with secondary hypothyroidism, the primary biochemical treatment goal should be to maintain the serum **freeT₄** values in the **upper half of the reference range**.
- However, the serum free T₄ target level may be reduced in older patients or patients with comorbidities, who may be at higher risk of complications of thyroid hormone excess



- **levothyroxine**

levothyroxine

- Prescription of brand name levothyroxine, or alternatively maintenance of the same generic preparation is advised.
- **Switches** between levothyroxine products could potentially result in variations in the administered dose and should generally be avoided for that reason(particular concern in frail patients, those with thyroid cancer, and the pediatric age group).
- It seems **reasonable** for a patient to **remain on a given L-T4 product** as long as possible, and if a change in product is made then thyroid function tests should be rechecked.
- **In patients with thyroid cancer**, especially when a desired goal TSH is relevant for curtailing possible disease recurrence or progression, it is **important to maintain L-T4 product stability**.

levothyroxine

- An **acidic pH** in the **stomach**(during fasting conditions) appears to be important for subsequent intestinal absorption
- With L-T₄ therapy, there will be a transient peak in serum **T₄** and **FT₄** levels of about **15% magnitude** about **4 hours after L-T₄ administration**
- Steady state levels of T₄ and TSH are generally achieved in 6 weeks (approximately 5-6 half-lives) after initiation of therapy
- The **absorption** of an orally administered dose of L-T₄ is about **70-80%** under optimum, fasting, conditions.
- Because co-administration of food and levothyroxine is likely to impair levothyroxine absorption, we recommend that, if possible, levothyroxine be consistently taken either **60 minutes before breakfast** or **at bedtime** (**3 or more hours after the evening meal**), for optimal, consistent absorption.
- if consumption of L-T₄ one hour before breakfast is not feasible, a **bedtime** regimen may be the **next best choice** (**Another regimen 30 minutes before breakfast**)

levothyroxine

- Thyroid hormone therapy should be initiated as an initial full replacement or as partial replacement.
- When deciding on a starting dose of levothyroxine, the patient's weight, lean body mass, pregnancy status, etiology of hypothyroidism, degree of TSH elevation, age, and general clinical context, including the presence of cardiac disease, should all be considered
- Dose adjustments should be made when there are large **changes in body weight**, with **aging**, and with **pregnancy**, with TSH assessment 4-6 weeks after any dosage change
- Other factors to consider when initiating L-T4 therapy include patient age and underlying comorbidities, both of which tend to decrease the daily hormonal requirement
- The daily **L-T4 dose** is more dependent on **lean body mass** than total body weight, which explains why the elderly often require lower doses of L-T4

levothyroxine

- One approach is to base the **starting dose** on the serum TSH level, with full replacement doses (**1.6-1.8 mcg/kg** body weight) being required when the serum **TSH is markedly elevated**, and **lower doses** (e.g., **25-50 mcg**) being required in **milder** degrees of hypothyroidism, e.g., where the serum **TSH is ≤ 10 mIU/L** or the patient has **SCH**.
- L-T4 doses in **thyroid cancer** patients requiring TSH suppression are generally higher and on the order of **2.1-2.7 mcg/kg**.
- Patients who are athyreotic(thyroidectomy) generally require a higher L-T4 dose than patients with Hashimoto's thyroiditis.
- all the studies found a lower dose requirement in post-menopausal women.
- L-T4 replacement doses tend to decrease with age.

levothyroxine

- the **target** of **TSH** typically being **0.5 to 3.5 or 4** mIU/L.
- **Dose adjustments** are usually made **4-6 weeks** after thyroid hormone is initiated.
- In general, L-T₄ dose adjustments of **12.5 to 25 mcg/day** are made(up or down); the serum **TSH** is then **repeated in 4-6 weeks, until** the TSH **target** has been reached. **Thereafter**, serum TSH should be measured in **4-6 months** and **then yearly** to assure stability.
- Changes in L-T₄ requirements occur with progression of thyroid failure (higher), aging (lower), weight loss (lower), and pregnancy (higher), and many other factors, such as concomitant medications, altered intestinal absorption, and medication adherence, to name a few.
- levothyroxine should be separated from other potentially interfering medications and supplements. **4-hour separation** is traditional.

the potential deleterious effects of excessive L-T₄

- deleterious effects of iatrogenic thyrotoxicosis include atrial fibrillation and osteoporosis particularly TSH values below **0.1** mIU/L, especially in older persons and postmenopausal women

THANKS FOR YOUR ATTENTION

