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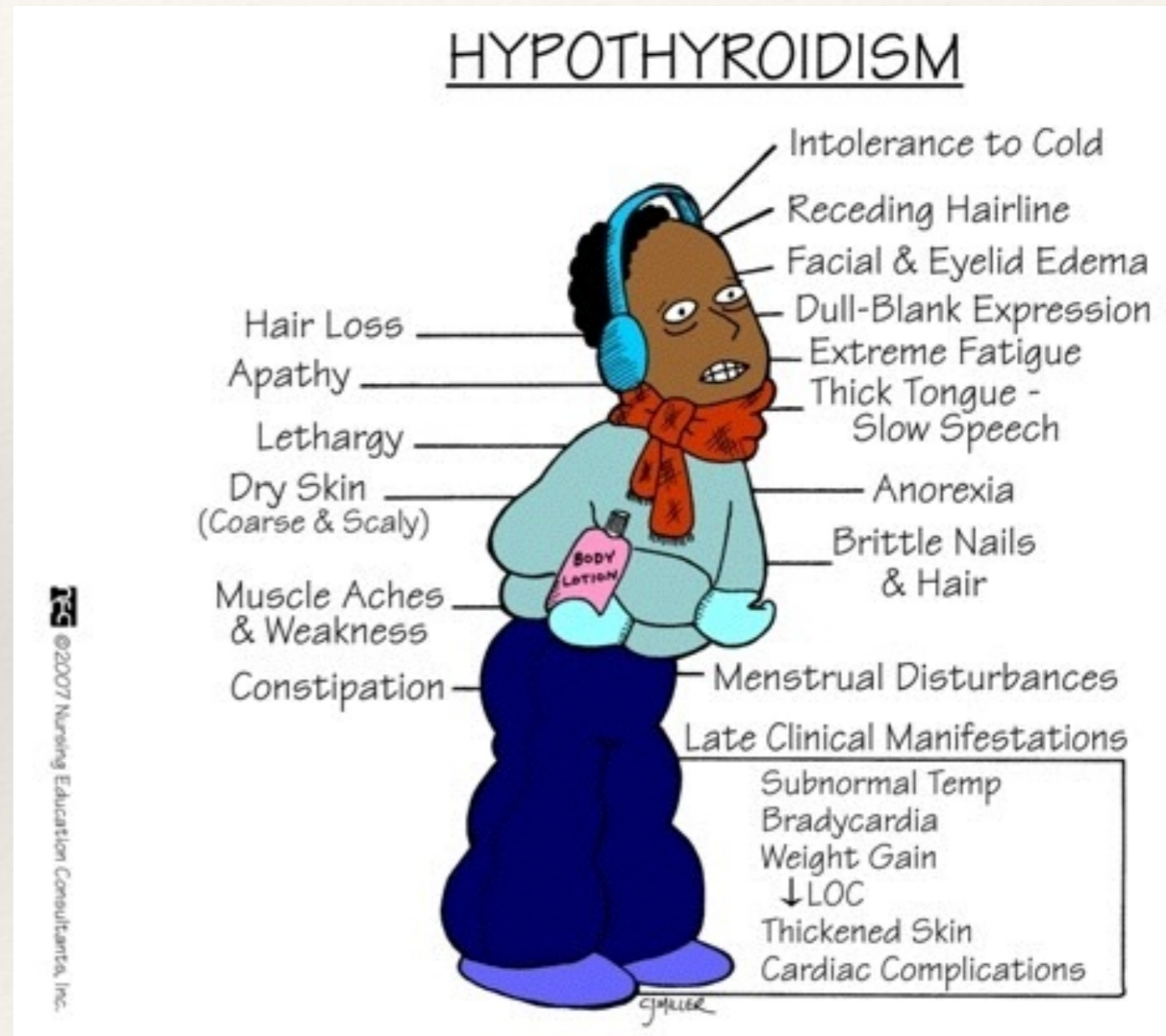
# Hypothyroidism and Depression: Use of TSH as a Diagnostic Tool and the Role of Thyroid Supplement Therapy in Psychiatric Practice

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# Hypothyroidism

- ❖ General medicine texts always include the list to the right, but they often miss DEPRESSION as a symptom of hypothyroidism- found in 38% of hypothyroid patients<sup>1</sup>
- ❖ hypothyroidism has been associated and studied with unipolar, non-psychotic depression
- ❖ hypothyroidism and depression- in hypothyroidism the serotonin synthesis is decreased and administration of T3 increases the brain levels of serotonin and its 5-HIAA catabolite





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# The Psychiatric Hypothyroid Patient

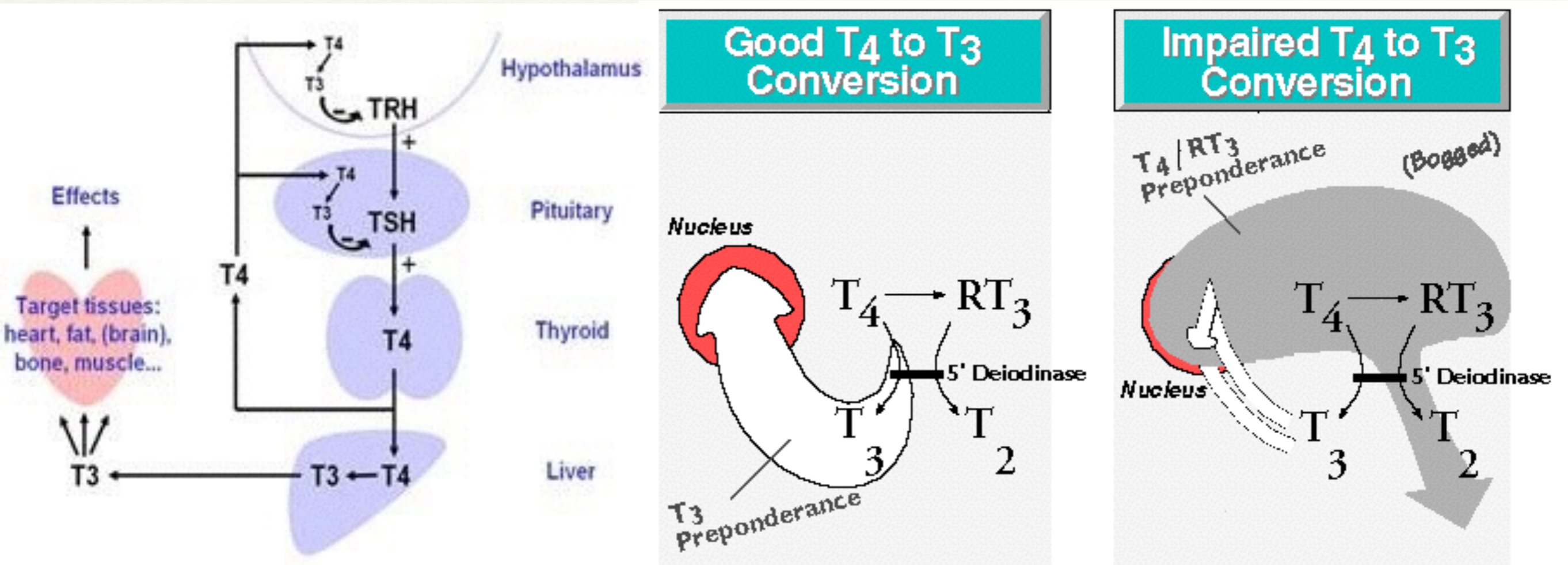
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Cognitive changes: decreased memory retention, psychomotor slowing, reduced attention span

Vegetative symptoms : hypersomnia, fatigue, lethargy, apathy, anergia, low libido

Mood changes : depression, mood instability, mania, anxiety

# Before Diagnosis... We Need to Know the Mechanism





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# Diagnostic Testing

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1. If thyroid dysfunction is suspected clinically, the preferred initial test is serum TSH.
2. If the serum TSH level is abnormal, the TSH should be rechecked along with a free T4 level.

The results of these laboratory tests diagnose the patient's thyroid condition.

**-Primary hypothyroidism-** TSH level is increased ( $>3.5 - 4.0$  mIU/l) and the free T4 is low ( $<.8$  ng/l) —> treat hypothyroidism (Hashimoto's thyroiditis, Iodine Deficiency, Iatrogenic-radioiodine therapy, thyroidectomy, medication ex: Lithium)

**-Subclinical hypothyroidism-** TSH level is increased and the free T4 level is normal (.8-1.8) —> repeat testing of TSH and free T4 levels in 4-6 months because TSH levels may spontaneously normalize or progress to clinical hypothyroidism; antithyroid peroxidase antibodies testing for Hashimoto's

**-Secondary hypothyroidism-** TSH is low or normal and free T4 is low —> measure additional pituitary hormones and MRI of the sella turcica region in the head testing for pituitary tumor

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# Treating

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Options for treating depression with triiodothyronine (T3):

1. Augmenting response – T3 is added to ongoing antidepressant monotherapy because the patient has not responded adequately, MC indication.
2. Accelerating response – T3 plus a tricyclic antidepressant are started simultaneously at the beginning of treatment to provide a more rapid response compared with tricyclic monotherapy. **However, a faster response to treatment does not increase the number of patients who respond by the end of treatment.**

Treatment Consideration:

-remission after antidepressant monotherapy occurs in 28 to 47 % of patients<sup>1</sup>



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# Treating: Augmenting the Response

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Antidepressant monotherapy vs. thyroid hormone plus an antidepressant at the beginning of treatment does not increase the probability of response or remission.

## 1. University of Toronto meta-analysis in 1996

Four randomized trials (444 patients with unipolar major depression) compared T3 plus SSRI with placebo plus an SSRI and found no evidence that T3 enhanced the effect of an SSRI.

## 2. University of Amsterdam study in 2004

Eight-week trial compared triiodothyronine (T3; 50 mcg per day) plus sertraline (50 to 200 mg per day) vs. placebo plus sertraline in 153 patients with major depression - response and remission were comparable for the two groups

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# triiodothyronine=T3

## liothyronine (Cytomel)= tablet or injectable solution

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- ❖ Take one-half hour to one hour before breakfast. Take on an empty stomach.
- ❖ Absorption in the GI tract ranges from 40% to 80%. The majority of the T3 is absorbed from the jejunum and upper ileum.
- ❖ foods that decrease absorption- infant soy formula, cotton seed meal, walnuts, and high-fiber foods
- ❖ drugs that decrease absorption
  - psych and neuro drugs- Carbamazepine, Phenytoin, SSRI, TCA
  - weight loss drugs- Orlistat and bile acid sequestrants (Cholestyramine, Colestipol, Colesevelam)
  - vitamins/supplements- Fe<sup>+</sup>, Ca<sup>+</sup>, NaI
  - others- Warfarin, Ciprofloxacin, Theophylline
- ❖ Side effects- opposite of hypothyroidism symptoms (i.e. heart palpitations, sweating, weight loss, etc.)
- ❖ Side effects of long term use- osteoporosis and heart arrhythmia



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# T4 vs T3

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Why T3 and not the more commonly used T4, levothyroxine (Synthroid)?

- ❖ many psychiatric studies performed with T3 —> many psychiatrists are more comfortable using T3 with depression

The cons to using T3?

- ❖ T3 is absorbed from the intestine very rapidly —> mild thyroid hormone toxicity (hyperthyroidism) possible
- ❖ Even though TSH is most commonly and the best marker to monitor treatment, some physicians use TSH, T4, and T3 to monitor treatment. Measuring T4 level is not accurate when T3 is administered. If T4 is used to monitor the adequacy of treatment when T3 is administered, it shows a low level of T4 which can lead to the erroneous decision to administer more T3.

Armour thyroid- contains both T4 and T3 derived from a pig

- ❖ No known benefits to taking natural version
- ❖ More expensive and not always carried in pharmacies
- ❖ Not used in studies

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# Problematic Groups to Treat

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- ❖ Treatment is Ineffective

1. Malabsorption Diseases (Inflammatory Bowel Diseases, Celiac Disease, etc)

- ❖ Cautious Use:

1. elderly patients
2. diabetes mellitus

- ❖ T3 contraindications:

1. adrenal insufficiency
2. unstable angina
3. recent myocardial infarction or compromised cardiovascular function



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# T3 compared to other adjunct treatments

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- Lithium

- effective, but side effect profile is severe- requires close follow-ups

- Lithium levels, renal function tests, TSH tests

- Lithium has a SE profile that includes hypothyroidism<sup>1</sup>

- The noncompliant patient- withdrawal symptoms from abrupt stopping of medication are much greater in Lithium than T3

- 2nd Generation Antipsychotic

- meta-analysis of 16 randomized trials lasting 4 to 12 weeks, compared adjunctive 2nd Generation with placebo in 3480 patients with non-psychotic, unipolar major depression who failed at least one course of antidepressant monotherapy.

- Remission occurred in more patients who received an adjunctive antipsychotic compared with placebo (31% versus 17%).

- However, discontinuation because of adverse effects was greater in patients who received an antipsychotic (9 versus 2 percent).

- Movement disorders and antihistamine effects associated with weight gain

- Adding a second antidepressant/ Combination therapy

- Common approach, but is the logic sound? Inconsistent evidence from randomized trials to support this practice. Trials that included a placebo have yielded inconsistent results, and other studies did not include a placebo control.

- serotonin syndrome or a hypertensive crisis- can occur with an MAOI plus an SSRI, a SNRI, or a tricyclic

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# Sources

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- ❖ Uptodate
- ❖ PsychCentral, Is Thyroid Dysfunction Driving Your Depression, Margarita Tartakovsky, M.S.
- ❖ slide 2: 1 <http://www.ncbi.nlm.nih.gov/pubmed/15388067>
- ❖ slide 5:1 <http://www.uptodate.com/contents/unipolar-depression-in-adults-augmentation-of-antidepressants-with-thyroid-hormone/abstract/12-14?utdPopup=true>
- ❖ slide 6:1 <http://www.currentpsychiatry.com/home/article/identifying-hypothyroidisms-psychiatric-presentations/190d5808f9bdd646cf3a8560587e35cc.html#bib7>