

The effect of non-thyroidal illness on thyroid hormone levels.

Thyroid function tests in non-thyroidal illness (non-drug causes):

In acute and severe non-thyroidal illnesses, there may be fluctuations in thyroid function tests which do not reflect thyroid dysfunction. An understanding of the effects of non-thyroidal illness in euthyroid individuals can be extrapolated to individuals with previously controlled hypothyroidism. This may avoid inappropriate changes to thyroid medications while in hospital.

In acute illness, a decrease in thyroid stimulating hormone (TSH), free thyroxine (FT4) and free 3,5,3-triiodo-L-thyronine (FT3) are most often reported in previously euthyroid individuals although TSH and FT4 may be elevated.^{1, 2} Decreases in these values often mirror the clinical status of the patient and TSH levels decrease proportionally to illness severity.¹ This change may occur within hours of illness onset. Normalization can occur in a little as 24h or much longer in extended illness.¹ FT4 levels are normal or low in very ill patients and the half-life decreases from 7 days to between 1 and 5 days.¹ FT3 levels may be normal or low. Inhibition of peripheral 5-monodeiodination by cytokines, elevated cortisol levels (endogenous or exogenous) and starvation inhibits the conversion of T4 to T3 in tissues.^{1,3} Alterations in the hypothalamic-pituitary set point may prevent the expected increase in TSH in response to low thyroid hormone levels.¹ A euthyroid clinical presentation is often observed even in the presence of low free T3 levels which may be compensated, in part, by an up-regulation of tissue T3 receptors. In the majority of patients, these levels will normalize following the resolution of illness. To further complicate this, a transient increase in TSH up to 20mU/mL may be measured during recovery from illness while FT4 and FT3 return to physiological levels.^{1,3} Despite low TSH levels, the benefit of LT4 supplementation in previously euthyroid individuals has not been demonstrated in clinical studies and a no consistent reduction in mortality in critically ill patients has been found.¹ The current recommendation is to not treat based on abnormal thyroid function tests in acute illness in a previously euthyroid patient unless there are clinical signs of a thyroid disorder.⁵

Thyroid function tests in previously controlled hypothyroidism in illness:

Many studies evaluating the results of thyroid function tests in acute illness exclude patients with thyroid dysfunction. Clinical hypothyroid and hyperthyroid states may worsen or complicate illness and thus an approach to interpreting thyroid function tests in acute illness was needed. The presentation of clinical hypothyroidism includes fatigue, lethargy, deafness, bradycardia, atrial fibrillation, hypotension, constipation, muscle cramping and reduced motor activity.^{1, 6} If left unrecognized, it may prolong treatment and worsen cardiac outcomes.¹ These signs and symptoms may also result in misdiagnosis in the elderly if attributed incorrectly to diseases of aging such as Alzheimer's or to depression.¹ In a study of patients with hypothyroidism in the ICU, required levothyroxine doses increased however this may have been attributed medications increasing stomach pH and high calorie density enteral solutions rather than acute changes in thyroid function.⁷

Only clinical hyperthyroidism secondary to over supplementation will be addressed here. Signs and symptoms of clinical hyperthyroidism from over supplementation include agitation, insomnia, palpitations, diarrhea, proximal myopathy and weight loss.^{1, 6} Untreated hyperthyroidism is associated with new and worsening atrial fibrillation and death.¹

Gina's approach to assessment of thyroid function tests in acute illness

Thyroid Function Prior to Illness	TSH	FT4 (if available)	Physical Assessment	Thought Process	Plan
Euthyroid	--/↓/↑	--/↓	No S/Sx clinical hypothyroidism	<ul style="list-style-type: none"> --/↓ in TSH and/or --/↓ FT4 common in non-thyroidal illness ↑ TSH is less common in non-thyroidal illness but has been reported 	<ul style="list-style-type: none"> No clinical S/Sx of thyroid dysfunction Do not supplement with LT4 No benefit and may cause harm
	↑	--/↓	S/Sx clinical hypothyroidism	<ul style="list-style-type: none"> ↑ TSH and --/↓ T4 with S/Sx clinical hypothyroidism may indicate thyroid dysfunction NYD Assess risk vs. benefit of LT4 	<ul style="list-style-type: none"> Consider supplementing as appropriate for hypothyroidism if TSH > 20mU/L Start at lower dose if possible Monitor clinical response and side effects closely
Hypothyroidism (current Tx LT4)	--/↓/↑	--/↓	No S/Sx clinical hypothyroidism	<ul style="list-style-type: none"> --/↓ in TSH and/or --/↓ FT4 common in non-thyroidal illness 	<ul style="list-style-type: none"> Reassess post-recovery phase of illness to ensure LT4 dose not too high (2-4 weeks) Note: TSH may be transiently elevated following acute illness
	--/↓	--/↓	S/Sx clinical hypothyroidism	<ul style="list-style-type: none"> Concurrent severe non-thyroidal illness responsible for S/Sx? E.g. CHF and fatigue Rule out factors contributing to clinical S/Sx Thyroid function tests results not reliable indicator of thyroid function in acute illness 	<ul style="list-style-type: none"> If strong suspicion of clinical hypothyroidism reassess post-recovery phase of illness (excluding myxedema)
	↓	↑/↓	S/Sx clinical hyperthyroidism	<ul style="list-style-type: none"> Medications or disease states contributing to S/Sx? Dose increase on hospital admission? Assess risk vs. benefit of ↓ LT4 	<ul style="list-style-type: none"> Consider ↓ LT4 dose as indicated Monitor clinical response and side effects closely
	↑	--/↓	S/Sx clinical hypothyroidism	<ul style="list-style-type: none"> Concurrent severe non-thyroidal illness responsible for S/Sx? Possible undertreated hypothyroidism 	<ul style="list-style-type: none"> Consider ↑ LT4 dose as indicated Monitor clinical response and side effects closely

S/Sx: signs and symptoms

The Bottom Line:

Thyroid tests alone are not sufficient for assessing thyroid function in an acutely ill patient. In previously euthyroid patients, non-thyroidal illness may cause fluctuations in thyroid function tests and are often normal or low but may be elevated as well. Treatment is not recommended in the absence of clinical signs and symptoms supporting the laboratory measurement. In patients with previous thyroid dysfunction, a thorough history and assessment of the current clinical state is necessary. Thyroid function tests may be misleading as these are known to be altered in acute illness. Assessment of both TSH and FT4 may be valuable (a low TSH and an elevated FT4 would be more consistent with over supplementation than a low TSH and FT4). The relationship between TSH and FT4 should be considered when assessing thyroid function rather than absolute values. Conversely, uncontrolled thyroid dysfunction can prolong hospital admission and worsen patient outcomes both directly through adverse cardiac outcomes and indirectly through misdiagnosis. Monitor for new medications in hospital which may alter the pharmacokinetics or pharmacodynamics of thyroid medications.

References

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