

### Understanding Endocrinopathies in Your Patients

Some oncology medications may cause endocrine disorders, also known as endocrinopathies, such as hypothyroidism, hyperthyroidism, adrenal insufficiency, and hypophysitis.<sup>1</sup>

The following guide covers signs, symptoms, and evaluation of endocrinopathies.

### Hypothyroidism

#### Signs and symptoms of hypothyroidism<sup>2</sup>:

Common signs and symptoms of hypothyroidism may include:

Bradycardia	Hair loss/diffuse alopecia	Weight gain
Tiredness/weakness	Difficulty concentrating and poor memory	Dyspnea
Cold intolerance	Constipation	Hoarse voice

#### Guidelines recommend consultation with a specialist for<sup>3,4</sup>:

- An atypical pattern of thyroid function test results (TSH and free  $T_4$ )
- Symptoms that have become severe
- Patients who have multiple chronic conditions

#### Serum TSH is recommended to screen for thyroid dysfunction<sup>3</sup>:

- $\bullet$  For improved diagnostic accuracy, assess both serum TSH and free  $T_4$ 
  - -Overt hypothyroidism: TSH above the upper limit of the reference range with a subnormal free  $T_4$
  - -Subclinical hypothyroidism: Serum TSH above the upper reference limit in combination with normal free  $\mathrm{T}_{\!_4}$
- Diurnal variation in serum TSH values is common
  - -TSH tends to be lowest in the late afternoon and highest at bedtime
- Not all patients who have mild TSH elevations have hypothyroidism
- $T_4$  = thyroxine; TSH = thyroid-stimulating hormone.

If hypothyroidism or hyperthyroidism is determined, consult the prescribing information for any oncology products prescribed as part of your patient workup.

# Hyperthyroidism

### Signs and symptoms of hyperthyroidism<sup>5</sup>:

Common signs and symptoms of hyperthyroidism may include:

Tachycardia	Goiter	Weight loss
Hyperactivity/irritability/ dysphoria	Fatigue and weakness	Polyuria
Heat intolerance	Diarrhea	Oligomenorrhea

*IFRCK* 

#### Guideline recommendations for suspected hyperthyroidism<sup>6</sup>:

- Perform a comprehensive health history and physical examination, including heart rate, blood pressure, respiratory rate, and body weight
- Evaluate thyroid size
- Check for thyroid tenderness, symmetry, and nodularity
- Evaluate pulmonary, cardiac, and neuromuscular function
- ·Assess for peripheral edema, eye signs, or pretibial myxedema

#### Serum TSH is recommended to screen for hyperthyroidism<sup>6</sup>:

- $\cdot$  For improved diagnostic accuracy, assess serum TSH, free T<sub>4</sub>, and total T<sub>3</sub>
  - -Overt hyperthyroidism: Typically serum TSH is subnormal (<0.01 mU/L), while serum free  $T_4$ ,  $T_3$ , or both are elevated
  - -Subclinical hyperthyroidism: Typically serum TSH concentration is subnormal, while serum free  $T_4$  and total  $T_3$  or free  $T_3$  levels are normal

#### Consultation with a specialist is recommended when<sup>6</sup>:

- Patients require a level of care typically provided in centers with specific expertise
- Cardiac evaluation may be needed (eg, for older patients)
- Assessment and development of a treatment plan for thyrotoxic manifestations, including potential cardiovascular and neuromuscular complications, is needed

 $T_3$  = triiodothyronine;  $T_4$  = thyroxine; TSH = thyroid-stimulating hormone.

### Adrenal Insufficiency

#### Signs and symptoms of adrenal insufficiency<sup>7</sup>:

Adrenal insufficiency affects all systems in the human body, leading to a wide range of symptoms, which may include:

Orthostatic hypotension	Weight loss	Nausea or vomiting
Fatigue	Light headedness with standing	Diarrhea
Anorexia	Hyperpigmentation of skin and gums	Dehydration and hypotension
Weakness		

If adrenal insufficiency is left untreated, it may eventually lead to an adrenal crisis. This is where symptoms appear quickly and severely, and without medical attention, it can be fatal.<sup>8</sup>

Serum cortisol is recommended to screen for adrenal insufficiency<sup>8,9</sup>:

- Evaluate morning fasting cortisol and adrenocorticotropic hormone (ACTH) levels
  - -Follow up with an ACTH stimulation test if results are inadequate
  - -A morning serum cortisol of <140 nmol/L (5 μg/dL) in combination with increased ACTH levels (twice the upper normal limit) is confirmative of primary adrenal insufficiency<sup>8</sup>

If adrenal insufficiency or hypophysitis is determined, consult the prescribing information for any oncology products prescribed as part of your patient workup.



# Hypophysitis

#### Signs and symptoms of hypophysitis<sup>10</sup>:

Because symptoms may vary patient to patient, diagnosis can be extremely difficult.

Common signs and symptoms of hypophysitis may include:

Adrenal insufficiency	Hypothyroidism	Visual disturbance
Headache	Hypogonadism	Polydipsia/polyuria

#### Guideline recommendations for suspected hypophysitis<sup>9</sup>:

- Evaluate morning fasting cortisol and ACTH levels in addition to the following:
  - -TSH and free  $T_4$
  - -For premenopausal women: Evaluate FSH, LH, and estradiol
  - -For men: Evaluate FSH, LH, and testosterone
  - -Glucose and basic electrolytes panel (Na, K)
- Perform a brain MRI
- In patients with cardiovascular instability, adrenal crisis should be ruled out, as well as sepsis (cultures, imaging as indicated)

FSH = follicle-stimulating hormone; LH = luteinizing hormone; MRI = magnetic resonance imaging; T<sub>4</sub> = thyroxine; TSH = thyroid-stimulating hormone.

#### **References:**

 Nogueira E, Newsom-Davis T, Morganstein DL. Immunotherapy-induced endocrinopathies: assessment, management and monitoring. *Ther Adv Endocrinol Metab.* 2019. doi:10.1177/2042018819896182
Jameson J, Mandel SJ, Weetman AP. Hypothyroidism. In: Loscalzo J, Fauci A, Kasper D, Hauser S, Longo D, Jameson J, eds. *Harrison's Principles of Internal Medicine*, 21st ed. McGraw Hill; 2022. 3. Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Hypothyroidism. *Nat Rev Dis Primers*. 2022;8(1):30. doi:10.1038/ s41572-022-00357-7
Garber JR, Cobin RH, Gharib H et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Endocr Pract*. 2012;18(6):988-1028. doi:10.4158/EP12280.GL
Jameson JL, Mandel SJ, Weetman AP. Hyperthyroidism and other causes of thyrotoxicosis. In: Loscalzo J, Fauci A, Kasper D, Hauser S, Longo D, Jameson J, eds. *Harrison's Principles of Internal Medicine*, 21st ed. McGraw Hill; 2022. 6. Ross DS, Burch HB, Cooper DS et al. 2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid*. 2016;26(10):1343-1421. 7. Fitzgerald PA. Primary adrenal insufficiency (Addison Disease). In: Papadakis MA, McPhee SJ, Rabow MW, McQuaid KR, eds. *Current Medical Diagnosis & Treatment 2023*. McGraw Hill; 2023. 8. Hahner S, Ross RJ, Arlt W et al. Adrenal insufficiency. *Nat Rev Dis Primers*. 2021;7(1):19. 9. Barroso-Sousa R, Ott PA, Hodi FS, Kaiser UB, Tolaney SM, Min L. Endocrine dysfunction induced by immune checkpoint inhibitors: practical recommendations for diagnosis and clinical management. *Cancer*. 2018;124(6):1111-1121. doi:10.1002/cncr.31200 10. Prete A, Salvatori R. Hypophysitis. In: Feingold KR, Anawalt B, Boyce A et al, eds. Endotext. MDText.com, Inc.; 2021.



Copyright © 2022 Merck & Co., Inc., Rahway, NJ, USA and its affiliates. All rights reserved. US-NON-11458  $\,12/22$