

Monitoring and Management of Endocrine-Related Side Effects Associated with Immune Checkpoint Inhibitor Therapy

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Principles of endocrine immune-related adverse events (irAEs) caused by immune checkpoint inhibitors (ICIs)

- **Most common:** thyroiditis, hypophysitis, adrenalitis, and endocrine pancreatitis
- **Symptoms are nonspecific:** fatigue, nausea, weight change, dizziness, hypotension, polyuria/polydipsia, general “unwellness”
- **Laboratory screening is essential** rather than waiting for a classic presentation
- **Plan for lifelong follow-up** of ICI-induced hypothyroidism, insulin-dependent diabetes, and adrenal insufficiency

Best practices checklist

- **Embed TSH, free T4 (FT4), AM cortisol (off steroids), and random blood glucose** into baseline and periodic ICI lab panels
- **Act promptly** on abnormal endocrine results (don’t “file and forget”)
- **Involve endocrinology early** for suspected pituitary disease, adrenal insufficiency, insulin-dependent diabetes, or complex thyroid presentations
- **Reassure patients** that most endocrine irAEs are manageable with hormone replacement **and** do not necessarily require stopping ICIs

When to consult endocrinology

- **Urgent** (same-day phone call; consider ER)
 - Morning cortisol <80 nmol/L (and not on exogenous steroids)
 - Any suspicion of adrenal crisis (hypotension, syncope, severe vomiting, confusion)
 - Pattern of central hypothyroidism (hypophysitis; low FT4 with low/normal TSH ± low cortisol)
 - Suspected diabetic ketoacidosis or very high glucose (>16 mmol/L), especially if symptomatic
 - Prolonged hyperthyroidism suggesting Graves disease
- **Semi-urgent** (routine referral)
 - Persistent hypothyroidism difficult to titrate, or possible pituitary involvement
 - New insulin-dependent diabetes once stabilized, for long-term management
 - Any endocrine irAE you are not comfortable managing yourself

Quick reference chart for abnormal laboratory findings

Laboratory findings	Likely issue	Next steps
Thyroid		
High TSH, low FT4	Primary hypothyroidism (thyroiditis)	Start levothyroxine; continue IO; use TSH to titrate.
Low TSH, high/normal FT4, prolonged thyrotoxicosis	Graves hyperthyroidism	Beta-blocker; call endocrinology ; consider TRAb/scan.
Pituitary		
Low FT4 with low/normal TSH	Central hypothyroidism (hypophysitis)	Check cortisol; treat adrenal axis first; call endocrinology .
Adrenal (patient not on systemic steroids)		
AM cortisol <100 nmol/L (and >80 nmol/L)	Suspicious for adrenal insufficiency	Assess ACTH and basic electrolytes; call endocrinology
AM cortisol <80 nmol/L	Adrenal insufficiency (primary or central)	Treat as urgent; call endocrinology ; consider ER if unwell
Pancreas		
Random glucose 11–15 mmol/L	Evolving type 1-like diabetes vs. steroid/type 2	Glucometer; consider oral ± basal insulin; close follow-up within days; call endocrinology
Random glucose >16 mmol/L or symptomatic	High-risk pre-DKA/DKA	Full labs; urgent assessment ; send to ER ; likely insulin-dependent diabetes.

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