



Adrenal Crisis in Internal Medicine: A Preventable Emergency Still Missed at the Bedside

Mohammed Alkhanafsa ¹

Dear Editor,

Adrenal crisis remains one of the most preventable yet potentially fatal endocrine emergencies encountered in internal medicine. It is estimated to occur in approximately 6-8 adrenal crises per 100 patient-years among patients with adrenal insufficiency, and crisis-related mortality has been reported up to 6% [3, 4]. Recognition is often delayed because the presentation overlaps with sepsis, hypovolemia, gastroenteritis, hypoglycemia, and undifferentiated shock. This diagnostic ambiguity is clinically important: adrenal crisis is a time-sensitive clinical diagnosis that should not wait for laboratory confirmation.

Adrenal insufficiency may be primary, secondary, or glucocorticoid-induced. Although primary and secondary adrenal insufficiency are uncommon, glucocorticoid-induced adrenal insufficiency is increasingly relevant to internists because glucocorticoids are prescribed across inflammatory, respiratory, rheumatologic, neurologic, and oncologic conditions [1, 2]. Risk is not limited to long-term oral therapy; inhaled, topical, intranasal, intra-articular, and repeated short courses may suppress the hypothalamic-pituitary-adrenal axis. However, the level of risk depends on dose, duration, potency, route and frequency of exposure, cumulative courses, recent tapering, and interacting medications, particularly potent CYP3A4 inhibitors [2]. Current or recent glucocorticoid exposure should therefore be actively sought.

Other causes are also important in general medicine. Chronic opioid therapy may cause secondary adrenal insufficiency and should be considered early in the medication history. Immune checkpoint inhibitors have added a modern risk category through hypophysitis, isolated adrenocorticotrophic hormone deficiency, and, less commonly, primary adrenalitis [5]. These risks are especially relevant on oncology wards, emergency units, and medical admission units.

The most important avoidable error is therapeutic hesitation. Current guidance emphasizes that emergency treatment should not be delayed while awaiting cortisol or adrenocorticotrophic hormone results [3, 4]. If blood can be drawn immediately, cortisol and adrenocorticotrophic hormone samples are useful, but treatment must proceed without delay. In adults with suspected adrenal crisis or strong risk factors, hydrocortisone 100 mg should be given intravenously or intramuscularly, followed by hydrocortisone 200 mg over 24 hours by continuous

CORRESPONDING AUTHOR

Mohammed Alkhanafsa

(Department of Internal Medicine, Hamad Medical Corporation, Doha, Qatar)

malkhanafsa@hamad.qa

A COMPLETE LIST OF THE AUTHORS' AFFILIATIONS
IS AVAILABLE AT THE END OF THE ARTICLE.

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intravenous infusion or 50 mg every 6 hours, together with rapid isotonic saline and correction of hypoglycemia or electrolyte disturbance when present [3, 4]. Hydrocortisone remains first-line because it provides both glucocorticoid and mineralocorticoid activity. If adrenal insufficiency is suspected but confirmation is still required and immediate cortisol measurement is important, dexamethasone may be used as an alternative because it does not interfere with serum cortisol measurement; this should not delay definitive stress-dose glucocorticoid therapy.

In routine practice, adrenal crisis is missed because symptoms are nonspecific: profound fatigue, abdominal pain, vomiting, dizziness, fever, hypotension, and altered mental status may be attributed to infection or dehydration [1, 4]. Laboratory clues include hyponatremia, hyperkalemia in primary adrenal insufficiency, hypoglycemia, eosinophilia, and unexplained renal impairment, but normal electrolytes or glucose do not exclude adrenal crisis [1, 4].

A practical response is to embed adrenal crisis recognition into acute-care workflows. In the emergency department and medical admission unit, adrenal crisis should be considered in patients with unexplained hypotension, shock, hypoglycemia, hyponatremia, hyperkalemia, or acute gastrointestinal illness, especially when there is known adrenal disease, pituitary disease, autoimmune endocrinopathy, chronic opioid therapy, immune checkpoint inhibitor exposure, bilateral adrenal disease, or current or recent glucocorticoid exposure [1-5]. Medication reconciliation should specifically ask about oral, inhaled, injected, topical, and intranasal glucocorticoids and recent tapering.

Prevention should be treated as a core safety intervention. Patients with known adrenal insufficiency, and those at substantial risk during glucocorticoid tapering, should receive written sick-day rules, clear stress-dose glucocorticoid instructions, advice for vomiting or inability to tolerate oral medication, and access to emergency injectable hydrocortisone when available [2, 3]. When speaking with patients, the term "steroids" may be clearer, but clinical documentation should specify glucocorticoids. Steroid emergency cards or medical alert identification should be regarded as practical harm-reduction tools. The safety gap is system-level and requires multidisciplinary collaboration among prescribers, pharmacists, nurses, and discharge staff, not only individual clinician vigilance.

The message for internists is simple: in suspected adrenal crisis, treat first and confirm later. Empiric hydrocortisone should be used when adrenal crisis is suspected or relevant risk factors are present, alongside fluids, antibiotics, and vasopressors when clinically indicated. Improving awareness, medication reconciliation, discharge education, and emergency planning could reduce preventable adrenal-crisis morbidity and death.

AUTHORS' DETAILS

1. Department of Internal Medicine, Hamad Medical Corporation, Doha, Qatar

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