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ADRENAL CRISIS DURING THE PERIOPERATIVE PERIOD

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FOREWORD / PREFACE

Adrenal crisis in the perioperative period is rare but clinically significant as it can rapidly develop from a hidden cortisol deficiency to refractory hypotension, shock, hypoglycaemia, electrolyte disturbance and death if not treated promptly. The peri-operative period is a time of heightened vulnerability for patients with known adrenal insufficiency, chronic glucocorticoid use, or unrecognised hypothalamic-pituitary-adrenal axis suppression, as cortisol requirements are increased by surgery, anaesthesia, fasting, infection, bleeding, and physiological stress after surgery [1-3]. The risk is that adrenal crisis can present as other more common peri-operative emergencies such as sepsis, anaphylaxis, haemorrhage or anaesthetic-induced cardiovascular instability. Therefore, prevention, early recognition and immediate administration of hydrocortisone are important safety measures [2,4]. This booklet offers a concise, evidence-based and practical resource for clinicians, trainees and perioperative teams. It is not intended to provide a general discussion of adrenal insufficiency, but rather to explain how adrenal crisis can be predicted, identified, and treated in practice during surgery and critical care.

KEY MESSAGES / LEARNING OBJECTIVES

By the end of this booklet, readers should be able to:

- Recognise perioperative adrenal crisis as a time-critical endocrine emergency, not merely an abnormal cortisol result.
- Identify high-risk patients, including those with primary adrenal insufficiency, pituitary or hypothalamic disease, recent adrenal surgery, and current or recent systemic glucocorticoid exposure.
- Explain why surgery, anaesthesia, fasting, infection and postoperative stress increase cortisol demand and may precipitate cardiovascular collapse when steroid cover is inadequate.
- Treat suspected adrenal crisis immediately; cortisol or ACTH sampling is useful when feasible, but must not delay hydrocortisone and fluid resuscitation.
- Differentiate adrenal crisis from common perioperative emergencies such as haemorrhage, sepsis, anaphylaxis, myocardial events and anaesthetic-related cardiovascular instability.
- Apply principles of perioperative steroid supplementation, postoperative monitoring, safe handover and tapering back to maintenance therapy.
- Use electronic records, digital alerts and emerging AI-supported tools as aids for risk identification, communication and surveillance, while maintaining clinical judgement and multidisciplinary escalation. These objectives emphasise prevention, early escalation and documentation across the preoperative clinic, operating theatre, recovery ward and ICU continuum, with clear pathways for communication between surgeons, anaesthetists, endocrinologists, intensivists and nursing teams.

INTRODUCTION AND SCOPE

Adrenal crisis is an acute, life-threatening endocrine emergency due to inadequate cortisol levels in response to physiological stress, which typically manifests as hypotension or shock, gastrointestinal symptoms, hypoglycaemia, hyponatraemia, and hyperkalaemia in primary adrenal insufficiency or altered consciousness [1,4]. This emergency is especially important in the perioperative period, as surgery, anaesthesia, fasting, infection, bleeding, and postoperative inflammatory stress all increase cortisol requirements, and oral steroid administration may be temporarily suspended, while the usual clinical features may be masked by anaesthesia or critical illness [2,3]. The perioperative period in this booklet is defined as the entire surgical care pathway, including preoperative assessment and medication planning, induction of anaesthesia, the intraoperative period, recovery, the early postoperative period, and escalation to the intensive care unit (ICU) if necessary [2].

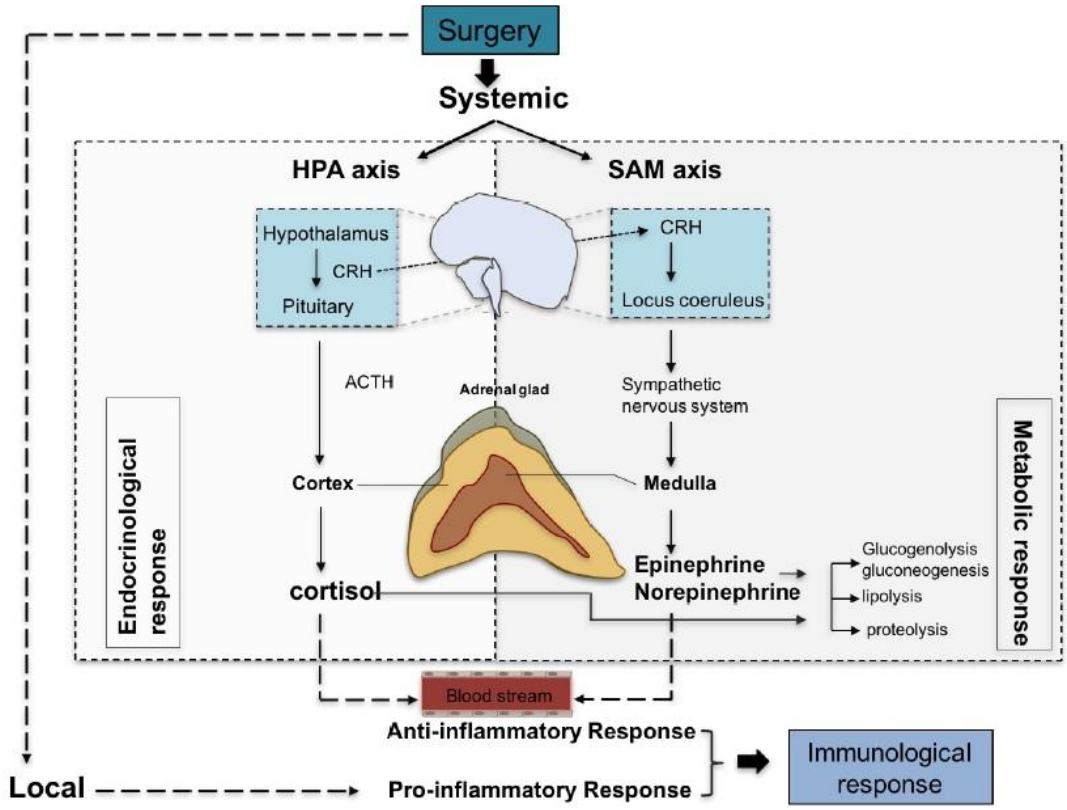
This booklet is for patients who have a known diagnosis of primary adrenal insufficiency, secondary or tertiary adrenal insufficiency, previous pituitary or adrenal disease, recent adrenal surgery, or current or recent systemic glucocorticoid use that may affect the hypothalamic-pituitary-adrenal axis [1-3]. This focus is relevant because adrenal insufficiency may continue after steroid reduction or discontinuation and recovery of adrenal function is highly variable from person to person [3]. Thus, perioperatively, risk assessment should not only be based on a formal diagnosis of Addison's disease, but also on the presence of diagnosed adrenal disease and/or HPA-axis suppression due to medication [1-3].

The scope is intentionally limited to peri-operative prevention, recognition, emergency treatment, and safe peri-operative escalation [2,4]. It is not intended to be a general textbook review of adrenal physiology, chronic adrenal insufficiency, Cushing's syndrome, endocrine testing or long-term outpatient follow-up [1,2]. Rather, it focuses on the anticipation, suspicion, and management of adrenal crisis in the surgical and anaesthetic setting, including handover, postoperative monitoring, and ICU overlap [2,4]. The ICU discussion is only included when it is directly relevant to the perioperative deterioration, refractory hypotension, requirement for vasopressors, and/or sepsis overlap and potential critical illness-related corticosteroid insufficiency [4]. Technology and AI are used to support risk identification, alerts, communication and monitoring, but not as a replacement for clinical judgement, emergency hydrocortisone administration or multidisciplinary escalation [5,6].

HPA AXIS PHYSIOLOGY AND SURGICAL STRESS

The hypothalamic-pituitary-adrenal axis is the main endocrine pathway through which the body maintains cortisol availability during basal conditions and acute physiological stress [7,8]. Under normal conditions, corticotrophin-releasing hormone from the hypothalamus stimulates pituitary adrenocorticotrophic hormone release, which then stimulates the adrenal cortex to produce cortisol [1,7]. Cortisol secretion follows a circadian rhythm, but this rhythm is modified during major stressors such as surgery, trauma, infection, blood loss, pain and critical illness [7,8].

Figure 1. HPA-axis response to surgical stress



Surgical stress activates the hypothalamus, pituitary gland and adrenal cortex, increasing cortisol availability during perioperative stress. Adapted from Yuki et al. [16].

Surgical Stress and Cortisol Demand

Surgery activates the HPA axis through tissue injury, nociceptive stimulation, inflammation, anxiety, fasting, blood loss and postoperative metabolic demand [7,8]. This response begins before or during induction, increases with intraoperative tissue trauma, and may persist after surgery, especially after major procedures or postoperative complications [7,8]. In major surgery, ACTH and cortisol secretion rise rapidly, although ACTH may return towards baseline earlier while cortisol remains elevated because of continuing inflammatory and metabolic signals [7].

Table 1. Perioperative Stressors Increasing Cortisol Demand

Perioperative stressor	Effect on cortisol demand	Clinical relevance
Tissue injury and inflammation	Increases stress signalling	Higher cortisol requirement
Fasting and interrupted oral intake	May interrupt usual steroid therapy	Risk of inadequate replacement
Anaesthesia and analgesia	May attenuate but not abolish stress response	At-risk patients still need steroid planning

Blood loss, infection or shock	Increases haemodynamic stress	May precipitate adrenal crisis
Postoperative complications	Prolongs stress response	Requires continued monitoring

Clinical Role of Cortisol During Surgery

The clinical purpose of the cortisol response is to support vascular tone, maintain responsiveness to catecholamines, promote gluconeogenesis, modulate inflammation and preserve cardiovascular stability during stress [1,7,8]. Anaesthesia can reduce some components of the surgical stress response, particularly nociceptive and sympathetic activation, but it does not remove the need for cortisol when physiological stress is significant [7,8]. The degree of cortisol requirement depends on the combined burden of surgical magnitude, anaesthetic technique, blood loss, inflammation, complications and the patient's adrenal reserve [2,7,8].

Adrenal Insufficiency and Failure of the Stress Response

In patients with intact adrenal function, the perioperative cortisol rise is usually adaptive [7]. In primary adrenal insufficiency, the adrenal cortex cannot produce adequate cortisol despite increased ACTH stimulation [1]. In secondary or tertiary adrenal insufficiency, pituitary or hypothalamic dysfunction limits ACTH drive and therefore reduces cortisol production during stress [1,3]. In patients exposed to systemic glucocorticoids, suppression of corticotrophin-releasing hormone and ACTH may reduce endogenous adrenal responsiveness, and recovery of HPA-axis function varies after dose reduction or discontinuation [3].

Link to Perioperative Adrenal Crisis

Perioperative adrenal crisis occurs when cortisol availability is insufficient for the degree of surgical, anaesthetic or postoperative stress [2,4]. The resulting pathophysiology may include impaired vascular responsiveness to catecholamines, hypotension, hypovolaemia, hypoglycaemia, altered consciousness and, in primary adrenal insufficiency, sodium and potassium disturbance [1,4]. Because these features overlap with haemorrhage, sepsis, anaphylaxis, myocardial events and anaesthetic complications, unexplained or refractory instability should always be interpreted in relation to steroid history and adrenal risk [2,4]. Perioperative steroid supplementation is therefore preventive: it replaces the cortisol surge that the patient cannot reliably generate during surgical stress [2,3].

PATIENTS AT RISK AND PERIOPERATIVE TRIGGERS

Patients at risk of perioperative adrenal crisis are those who cannot mount an adequate cortisol response to surgical, anaesthetic or postoperative stress [1-3]. Risk assessment should therefore not be limited to patients with a known diagnosis of Addison's disease, because clinically important adrenal insufficiency may also occur in patients with pituitary disease, hypothalamic disease, chronic glucocorticoid exposure, recent steroid withdrawal or previously unrecognised HPA-axis suppression [1-3,9]. The central perioperative question is whether the patient can produce enough cortisol when exposed to fasting, anaesthesia, tissue injury, inflammation, infection, blood loss or critical illness [2,9].

Primary adrenal insufficiency

Primary adrenal insufficiency is a high-risk condition because the adrenal cortex cannot produce sufficient cortisol, and mineralocorticoid deficiency may also impair sodium, potassium and volume regulation [1,4]. Common causes include:

- autoimmune adrenalitis,
- bilateral adrenalectomy,
- adrenal haemorrhage,
- infiltrative adrenal disease,
- infection and genetic or drug-related adrenal disorders [1].

In the perioperative setting, these patients are vulnerable because surgical stress increases cortisol demand while fasting, vomiting or nil-by-mouth status may interrupt routine oral steroid replacement [2,4]. Without adequate perioperative glucocorticoid cover, they may develop hypotension, hypovolaemia, hypoglycaemia, electrolyte disturbance and shock [1,4].

Secondary and tertiary adrenal insufficiency

Secondary and tertiary adrenal insufficiency occur when pituitary or hypothalamic dysfunction reduces ACTH drive and thereby limits cortisol production during stress [1,3]. These patients may have a history of pituitary tumours, pituitary surgery, cranial irradiation, traumatic brain injury, infiltrative disease or long-term suppression from exogenous glucocorticoids [1,3]. Unlike primary adrenal insufficiency, mineralocorticoid secretion is often relatively preserved because aldosterone is mainly regulated by the renin-angiotensin-aldosterone system [1]. However, perioperative risk remains clinically significant because cortisol deficiency alone can cause impaired vascular tone, reduced catecholamine responsiveness and refractory hypotension during acute stress [1,4].

Chronic Glucocorticoid Use and Recent Steroid Withdrawal

Patients taking chronic systemic glucocorticoids form a particularly important perioperative risk group [3,9]. The 2024 European Society of Endocrinology and Endocrine Society guideline identifies risk for glucocorticoid-induced adrenal insufficiency when exposure exceeds both a duration threshold of approximately three to four weeks and a dose greater than physiologic daily replacement, for example more than 15–25 mg hydrocortisone equivalent, 4–6 mg prednisone or prednisolone, 3–5 mg methylprednisolone, or 0.25–0.5 mg dexamethasone daily [3]. Suppression risk is influenced by dose, duration, potency, route, timing and individual susceptibility, and recovery after dose reduction or cessation varies substantially [3].

Therefore, patients who have recently reduced or stopped glucocorticoids should not automatically be considered safe unless adrenal recovery has been assessed or perioperative steroid cover is planned [3,9].

Table 2. Patient risk groups and perioperative concerns

Risk group	Why they are vulnerable	Perioperative concern
Primary adrenal insufficiency	Failure of adrenal cortisol production, often with mineralocorticoid deficiency	Shock, hypovolaemia and electrolyte disturbance
Secondary/tertiary adrenal insufficiency	Reduced ACTH drive from pituitary or hypothalamic dysfunction	Inadequate cortisol rise during surgical stress
Chronic systemic glucocorticoid users	Suppression of CRH and ACTH with reduced adrenal responsiveness	Crisis after missed doses, fasting or major surgery
Recent steroid withdrawal or taper	HPA-axis recovery may be incomplete	False reassurance if steroids were “stopped”
Undiagnosed adrenal insufficiency	No preoperative steroid plan or emergency documentation	First presentation may occur during or after surgery

Perioperative Triggers

Perioperative triggers are usually situations that increase cortisol demand, reduce steroid intake, or both [2,4,9]. Important triggers include major surgery, emergency surgery, trauma, infection, sepsis, haemorrhage, prolonged fasting, vomiting, bowel preparation, postoperative ileus, delayed resumption of oral medication and inadequate handover of steroid requirements [2,4,9]. Anaesthesia may also mask early warning symptoms such as weakness, nausea, abdominal pain, dizziness or confusion, meaning that the first recognised sign may be unexplained hypotension or poor response to fluids and vasopressors [2,4].

Undiagnosed Adrenal Insufficiency

Undiagnosed adrenal insufficiency deserves particular attention because surgical stress may reveal limited adrenal reserve for the first time [1,2]. Clues may include unexplained fatigue, weight loss, postural symptoms, recurrent hyponatraemia, hyperpigmentation in primary adrenal insufficiency, autoimmune disease, pituitary history, chronic opioid or glucocorticoid exposure, or previous unexplained perioperative collapse [1,3,4]. In practice, prevention depends on careful medication history, recognition of steroid exposure, preoperative communication, clear documentation and a low threshold for emergency hydrocortisone when adrenal crisis is suspected [2-4].

PREOPERATIVE IDENTIFICATION AND RISK ASSESSMENT

Purpose of Preoperative Risk Assessment

Preoperative identification is the most important opportunity to prevent perioperative adrenal crisis, because many crises occur when adrenal insufficiency or HPA-axis suppression is not recognised before surgical stress begins [2,4]. The assessment should determine whether the patient has diagnosed adrenal insufficiency, possible undiagnosed adrenal disease, pituitary or hypothalamic pathology, previous adrenal surgery, current glucocorticoid therapy or recent glucocorticoid withdrawal [1-3,9]. Risk assessment should be completed before elective surgery whenever possible, but it must also be performed rapidly in emergency surgery because lack of time does not remove the need for steroid cover in high-risk patients [2,4].

Focused Clinical History

A focused history should ask about primary adrenal insufficiency, Addison’s disease, adrenalectomy, congenital adrenal disorders, pituitary disease, pituitary surgery, cranial radiotherapy, traumatic brain injury and previous endocrine follow-up [1,3]. The clinician should also ask about previous adrenal crisis, unexplained perioperative collapse, severe hypotension during illness, recurrent vomiting with steroid omission, hospital admission for steroid replacement, or use of emergency hydrocortisone injection [1,4]. A previous adrenal crisis is particularly important because it indicates that the patient has already failed to meet cortisol demand during physiological stress [1,4].

Medication Review and Recent Steroid Exposure

Medication review is essential because glucocorticoid-induced adrenal insufficiency is commoner than many clinicians recognise and may persist after steroid reduction or cessation [3,9]. The review should include oral prednisolone, prednisone, hydrocortisone, dexamethasone and methylprednisolone, as well as repeated injectable steroids, high-dose inhaled steroids, potent topical steroids, intra-articular steroids and long-term nasal or rectal preparations where clinically relevant [3,9].

According to the 2024 European Society of Endocrinology and Endocrine Society guideline, risk of glucocorticoid-induced adrenal insufficiency should be considered when exposure exceeds approximately three to four weeks and the dose is greater than physiological replacement, for example above 15-25 mg hydrocortisone equivalent or 4-6 mg prednisone/prednisolone daily [3]. Recent steroid tapering or withdrawal should therefore be treated as a warning sign rather than reassurance, unless adrenal recovery has been demonstrated [3,9].

Table 3. Preoperative Risk-Assessment Questions for Perioperative Adrenal Crisis

Preoperative question	Why it matters	Action
Does the patient have known adrenal insufficiency?	Confirms inability to mount an adequate stress response [1,2]	Plan perioperative steroid cover
Has the patient used systemic steroids recently?	May indicate HPA-axis suppression [3,9]	Assess dose, duration, timing and route
Has there been a previous adrenal crisis?	Indicates proven vulnerability during stress [1,4]	Escalate early and document clearly
Does the patient carry a Steroid Emergency Card?	Alerts staff to adrenal-crisis risk and emergency treatment needs [10]	Record details and ensure team awareness
Is endocrine advice required?	Complex cases may need individualised planning [2,3]	Contact endocrinology/anaesthesia before surgery

Steroid Emergency Card and Patient-Held Alerts

The Steroid Emergency Card, medical alert bracelet, endocrine clinic letter and patient-held emergency plan should be checked and documented during preoperative assessment [4,10]. These tools are especially useful when patients present to unfamiliar hospitals, emergency departments or surgical teams, because they communicate the need for emergency hydrocortisone and steroid precautions [4,10]. However, absence of a card does not exclude risk, particularly in patients with recent glucocorticoid exposure, pituitary disease or undiagnosed adrenal insufficiency [1-3].

Communication with Anaesthesia, Endocrinology and the Perioperative Team

Communication is a core safety intervention [2,4]. The steroid plan should be visible in the anaesthetic assessment, surgical notes, drug chart, theatre checklist, recovery plan and postoperative handover [2]. Anaesthesia should be informed before induction, nursing staff should know when usual oral steroids are replaced by intravenous hydrocortisone, and pharmacy should help confirm steroid equivalents when the history is unclear [2,3,9].

Endocrinology input is particularly useful for uncertain HPA-axis suppression, complex pituitary disease, bilateral adrenal disease, adrenal surgery, pregnancy, paediatric transition cases or repeated perioperative instability [1-3]. In urgent cases, suspected adrenal crisis risk should be treated pragmatically: if the patient is high risk and cannot be assessed fully, perioperative hydrocortisone cover is safer than delaying surgery without steroid protection [2-4].

PREVENTION: PERIOPERATIVE STEROID SUPPLEMENTATION

Purpose of Perioperative Steroid Supplementation

Perioperative steroid supplementation aims to prevent adrenal crisis by replacing the cortisol surge that patients with adrenal insufficiency or HPA-axis suppression may be unable to generate during surgical stress [2,3,9]. The principle is preventive rather than diagnostic: *if the patient is known to have adrenal insufficiency, or is strongly suspected to be unable to mount an adequate stress response, steroid cover should be planned before anaesthesia, fasting and tissue injury occur [2-4].* In emergency surgery, uncertainty should not lead to omission of cover in a high-risk patient, because short-term hydrocortisone is safer than untreated adrenal crisis [2,4].

Continuation of Usual Glucocorticoid Therapy

The usual maintenance glucocorticoid should generally be continued until the time of surgery, unless the patient is specifically instructed otherwise by the perioperative or endocrine team [2,3,9]. Patients taking hydrocortisone, prednisolone or other systemic glucocorticoids should not have their treatment stopped abruptly before surgery, because withdrawal may precipitate adrenal insufficiency or glucocorticoid withdrawal symptoms [3,9]. Where oral intake is interrupted because of fasting, vomiting, bowel preparation, ileus or postoperative nil-by-mouth status, the key clinical task is to replace the missed oral glucocorticoid with an appropriate intravenous regimen [2,3,9].

Steroid Cover According to Surgical Stress

Steroid cover should reflect both patient risk and the expected degree of surgical stress [2,9,11]. Minor procedures under local anaesthesia may require continuation of usual steroid therapy with careful observation, whereas moderate or major operations usually require parenteral hydrocortisone at induction and continued postoperative coverage until the patient is clinically stable and able to resume oral medication [2,9,11]. The Association of Anaesthetists guideline recommends hydrocortisone 100 mg intravenously at induction for adult patients with adrenal insufficiency, followed by hydrocortisone 200 mg over 24 hours, usually by continuous infusion, until the patient can take double their usual oral glucocorticoid dose [2]. However, reviews of glucocorticoid-treated patients also emphasise that lower doses and shorter courses may be sufficient in some patients, particularly when surgical stress is limited and the patient is haemodynamically stable [9,11]. Therefore, local protocols, surgical magnitude, clinical status and specialist advice should guide final dosing [2,3,9].

Table 4. Perioperative Steroid-Cover Principles According to Surgical Context

Surgical context	Preventive principle	Practical implication
Minor procedure with reliable oral intake	Avoid interruption of usual glucocorticoid therapy [2,9]	Continue usual dose and monitor
Moderate surgery or uncertain oral absorption	Cover the stress response and missed oral therapy [2,9]	Use perioperative hydrocortisone according to protocol
Major surgery, emergency surgery or high-risk patient	Assume high cortisol demand [2,4]	Give IV hydrocortisone at induction and continue postoperative coverage
Postoperative fasting, vomiting or ileus	Oral steroids may not be absorbed [2,3]	Continue IV replacement until oral intake is reliable
Clinical deterioration or suspected crisis	Prevention has failed or demand has increased [4]	Treat immediately as adrenal crisis

Oral-to-Intravenous Transition and Postoperative Restart

The oral-to-intravenous transition is especially important in recovery and early ward care [2,4]. A patient may receive appropriate hydrocortisone in theatre but become vulnerable later if postoperative steroid orders are unclear, oral medication is withheld, or the handover fails to state when IV hydrocortisone should continue [2,4]. The postoperative plan should specify the route, dose, timing, review point and criteria for returning to oral therapy [2,3]. Once the patient is eating, drinking and haemodynamically stable, hydrocortisone is usually reduced back towards the patient's usual replacement regimen, often after a short period of increased oral dosing according to the local protocol and endocrine advice [2,3].

Communication and Documentation of the Steroid Plan

Prevention also requires clear communication. The steroid plan should appear in the anaesthetic chart, theatre checklist, medication prescription, recovery instructions and ward or ICU handover [2,4]. Nurses should know that delayed or omitted steroid doses in an adrenal-insufficient patient are safety-critical, not routine medication delays [4]. Surgeons and anaesthetists should recognise that postoperative infection, bleeding, hypotension or return to theatre may increase cortisol demand and require reassessment of steroid cover [2,4,9]. In this sense, supplementation is not a single dose given at induction; it is a perioperative safety pathway that continues until the patient is stable, absorbing oral medication and protected by a clear ongoing steroid plan [2-4].

INTRAOPERATIVE RECOGNITION

Intraoperative adrenal crisis is difficult to recognise because many classical symptoms of adrenal insufficiency are hidden by anaesthesia, surgical draping, analgesia, sedation and neuromuscular blockade [2,4]. Nausea, abdominal pain, weakness, dizziness, confusion and postural symptoms may be absent or impossible to assess during surgery [1,4]. For this reason, recognition in theatre usually depends on physiological deterioration, especially unexplained cardiovascular instability in a patient with known or suspected adrenal insufficiency, chronic glucocorticoid exposure or recent steroid withdrawal [2-4].

Refractory Hypotension and Poor Vasopressor Response

The most important intraoperative warning sign is hypotension that is disproportionate to the apparent surgical or anaesthetic context [2,4]. Adrenal crisis should be considered when hypotension persists despite usual corrective measures, including adjustment of anaesthetic depth, fluid administration, vasopressor support and correction of obvious reversible causes [2,4]. This is particularly important when there is no clear evidence of haemorrhage, myocardial event, anaphylaxis, sepsis, tension pneumothorax, embolic event or drug-related cardiovascular depression [2,4]. Poor response to catecholamines is clinically relevant because cortisol supports vascular tone and maintains vascular responsiveness to endogenous and exogenous catecholamines during stress [1,7].

Shock as the First Recognised Manifestation

Shock may be the first recognised manifestation, especially in emergency surgery, major abdominal surgery, trauma, sepsis, adrenal surgery or procedures complicated by bleeding or prolonged physiological stress [2,4]. In a patient with adrenal insufficiency, shock should not be attributed automatically to anaesthesia or blood loss until adrenal crisis has been considered [1,2,4]. The threshold for treatment should be low because emergency hydrocortisone is recommended when adrenal crisis is suspected, and treatment should not be delayed while waiting for biochemical confirmation [4].

Hypoglycaemia and Metabolic Clues

Hypoglycaemia is another important clue, particularly in children, frail patients, prolonged fasting, sepsis, liver disease or patients with limited glycogen reserve [1,4]. In adults, hypoglycaemia may be less prominent than hypotension, but it remains clinically relevant because cortisol contributes to gluconeogenesis and stress-related glucose maintenance [1,7]. Intraoperative or recovery-area glucose measurement should therefore be considered when an at-risk patient develops unexplained instability, delayed emergence, seizures, sweating, altered consciousness or unexpected deterioration [1,4].

Electrolyte Clues and Their Limitations

Electrolyte abnormalities may support the diagnosis but should not be required before treatment [1,4]. Hyponatraemia may occur in both primary and central adrenal insufficiency, while hyperkalaemia is more suggestive of primary adrenal insufficiency because mineralocorticoid deficiency impairs potassium and sodium regulation [1,4]. However, intraoperative electrolytes may be influenced by intravenous fluids, blood products, renal function, acid-base disturbance and timing of measurement [1,4]. A normal potassium level therefore does not exclude adrenal crisis, especially in secondary or tertiary adrenal insufficiency [1,3].

Intraoperative clue	Why it matters	Clinical response
Refractory hypotension	Commonest practical warning sign [2,4]	Consider adrenal crisis after immediate reversible causes are addressed
Poor vasopressor response	Cortisol supports catecholamine responsiveness [1,7]	Escalate and give emergency hydrocortisone if suspected
Shock without clear cause	May be the first visible sign under anaesthesia [2,4]	Treat urgently while continuing differential diagnosis
Hypoglycaemia	Reflects impaired stress glucose regulation [1,4]	Check glucose and correct promptly
Hyponatraemia or hyperkalaemia	Supports adrenal insufficiency, especially primary AI [1,4]	Do not wait for electrolytes before treatment

Intraoperative recognition is therefore a pattern-based judgement rather than a single diagnostic test [2,4]. The key question is whether the patient's instability is unexplained, refractory, and occurring in a person with adrenal risk [2-4]. If the answer is yes, emergency hydrocortisone should be administered while the team continues simultaneous assessment for haemorrhage, sepsis, anaphylaxis, myocardial events and anaesthetic complications [2,4].

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis of perioperative adrenal crisis is primarily clinical, because the patient may deteriorate before biochemical confirmation is available [1,4]. In theatre, recovery or ICU, adrenal crisis should be suspected when an at-risk patient develops unexplained hypotension, shock, hypoglycaemia, altered consciousness, hyponatraemia, hyperkalaemia or poor response to fluids and vasopressors [1,2,4]. Treatment must not be delayed while waiting for laboratory results, because suspected adrenal crisis is a time-critical emergency and hydrocortisone should be administered immediately when the clinical picture supports the diagnosis [4].

Cortisol, ACTH and Biochemical Assessment

Where feasible, blood should be drawn before hydrocortisone is given, but only if this can be done without delaying emergency treatment [1,4]. The most useful initial samples are serum cortisol and plasma ACTH, ideally collected before steroid administration, because they can later help distinguish primary adrenal insufficiency from central adrenal insufficiency [1].

- In primary adrenal insufficiency, cortisol is low or inappropriately low for the severity of illness, while ACTH is usually elevated [1].
- In secondary or tertiary adrenal insufficiency, ACTH may be low or inappropriately normal, reflecting impaired hypothalamic or pituitary drive [1,3].

However, perioperative interpretation of cortisol is complex because acute illness, assay variation, binding-protein changes, recent steroid administration and critical illness may affect measured values [1,3]. Therefore, laboratory testing supports but does not replace clinical judgement [1,4].

Dynamic Testing and Practical Diagnostic Approach

In a stable patient, dynamic testing such as the short Synacthen test may help confirm adrenal insufficiency, but this is usually not appropriate during immediate perioperative collapse [1,3]. Formal endocrine testing should be deferred until the patient is stabilised if emergency hydrocortisone is clinically required [1,4]. Similarly, normal electrolytes do not exclude adrenal crisis, particularly in secondary or tertiary adrenal insufficiency where aldosterone secretion may be preserved [1,3]. The absence of hyperkalaemia should therefore not falsely reassure clinicians when hypotension and adrenal risk are present [1,4].

A practical diagnostic approach should include:

- immediate assessment of airway, breathing, circulation and anaesthetic depth [2,4];
- confirmation of steroid history, adrenal disease, pituitary disease or recent glucocorticoid withdrawal [2,3];
- urgent blood glucose, electrolytes, renal function, lactate and arterial or venous blood gas where available [1,4];
- cortisol and ACTH sampling before hydrocortisone only if this causes no treatment delay [1,4];
- simultaneous search for common perioperative causes of shock [2,4].

Differential Diagnosis and Parallel Management

Differential diagnosis is essential because adrenal crisis often resembles other perioperative emergencies [2,4]. Haemorrhage should be considered when hypotension is associated with surgical blood loss, falling haemoglobin, tachycardia or poor perfusion [2]. Sepsis should be considered in emergency surgery, contaminated procedures, fever, raised lactate, vasopressor requirement or postoperative deterioration [4]. Anaphylaxis should be suspected when hypotension occurs suddenly after drug, latex, chlorhexidine, blood-product or antibiotic exposure, especially with bronchospasm, rash or airway oedema [2]. Myocardial ischaemia, arrhythmia, pulmonary embolism, tension pneumothorax, high neuraxial block, excessive anaesthetic depth and drug-related cardiovascular depression should also be actively assessed [2,4,9].

The key point is that differential diagnosis and adrenal-crisis treatment should occur in parallel [2,4]. Hydrocortisone administration does not prevent investigation of bleeding, sepsis, anaphylaxis or myocardial events, but delay in hydrocortisone may worsen shock in a cortisol-deficient patient [4]. Therefore, perioperative adrenal crisis should be treated as a clinical emergency when suspected, while the team continues a structured search for alternative or coexisting causes of deterioration [2,4].

EMERGENCY MANAGEMENT OF SUSPECTED ADRENAL CRISIS

Time-Critical Management and Initial Sampling

Suspected perioperative adrenal crisis should be managed as a time-critical emergency because cardiovascular collapse may progress rapidly if cortisol deficiency is not corrected [1,4]. Treatment should begin as soon as the diagnosis is suspected and must not wait for cortisol, ACTH or electrolyte results [1,4]. If blood can be drawn immediately, serum cortisol and plasma ACTH should be collected before steroid administration, but sampling must not delay hydrocortisone, fluid resuscitation or haemodynamic support [1,4].

Immediate Hydrocortisone Administration

The first specific treatment is immediate hydrocortisone. Adult guidance recommends hydrocortisone 100 mg by intravenous or intramuscular injection, followed by hydrocortisone 200 mg over 24 hours, preferably by continuous intravenous infusion, or alternatively 50 mg intravenously or intramuscularly every 6 hours where infusion is not practical [1,4].

In the perioperative setting, this emergency regimen may overlap with planned surgical steroid cover, but deterioration despite prophylaxis should still be treated as a possible adrenal crisis, and the adequacy of steroid delivery should be reviewed [2,4]. Hydrocortisone is preferred because it provides glucocorticoid activity and, at stress doses, also contributes to mineralocorticoid effects, which are especially relevant in primary adrenal insufficiency [1,4].

Fluid Resuscitation and Haemodynamic Support

Fluid resuscitation should occur in parallel with steroid administration. Adrenal crisis is commonly associated with hypovolaemia, vasodilation and impaired vascular responsiveness to catecholamines, so rapid intravenous isotonic saline is recommended unless there is a specific contraindication requiring a modified fluid strategy [1,4].

Intraoperative and ICU patients should have fluid therapy guided by haemodynamic status, blood loss, urine output, lactate, cardiac function and the wider differential diagnosis of shock [2,4]. If haemorrhage, sepsis, anaphylaxis, myocardial dysfunction, or pulmonary embolism is possible, those conditions should be investigated and treated simultaneously, rather than waiting to see whether hydrocortisone alone resolves the instability [2,4,9].

Glucose, Electrolyte and Acid-Base Correction

Glucose should be checked early because cortisol deficiency can impair gluconeogenesis and contribute to hypoglycaemia, particularly during fasting, sepsis, prolonged surgery, frailty or limited glycogen reserve [1,4]. Hypoglycaemia should be corrected promptly with intravenous glucose according to local emergency protocols, with repeated monitoring until the patient is stable [1,4].

Dextrose-containing fluids may be needed when hypoglycaemia persists or when the patient cannot resume oral intake, but this should not replace isotonic saline where hypovolaemia or shock is present [1,4]. Electrolyte and acid-base abnormalities should be assessed urgently but should not delay treatment [1,4]. Hyponatraemia may occur in primary, secondary or tertiary adrenal insufficiency, while hyperkalaemia is more suggestive of primary adrenal insufficiency because aldosterone deficiency affects renal sodium and potassium handling [1]. Potassium, sodium, renal function, glucose, lactate and blood gas results help assess severity, guide resuscitation and identify coexisting causes of deterioration [1,4]. Severe hyperkalaemia, acute kidney injury, acidosis or persistent hypoglycaemia should be managed according to institutional emergency protocols while hydrocortisone and volume replacement continue [1,4].

Practical Emergency Sequence

A practical emergency sequence is:

- call for senior anaesthetic, surgical and nursing help immediately [2,4];
- administer hydrocortisone 100 mg IV or IM without delay [1,4];
- draw cortisol and ACTH first only if this does not delay treatment [1,4];
- start rapid IV 0.9% saline or appropriate isotonic resuscitation [1,4];
- check and correct glucose, sodium, potassium, renal function, lactate and acid-base status [1,4];
- continue hydrocortisone 200 mg/24 hours or 50 mg every 6 hours [1,4];
- continue parallel assessment for bleeding, sepsis, anaphylaxis, myocardial events and anaesthetic complications [2,4,9];
- escalate to ICU if shock, vasopressor need, respiratory failure, severe electrolyte disturbance or diagnostic uncertainty persists [2,4].

Escalation, Ongoing Steroid Plan and Step-Down

Escalation is part of emergency management, not a sign of failure. Patients with persistent hypotension, vasopressor requirement, altered consciousness, severe metabolic disturbance, sepsis, major bleeding, poor urine output or repeated deterioration require senior multidisciplinary review and often ICU-level monitoring [2,4]. Endocrinology should be contacted once the patient is stabilised, but emergency hydrocortisone should not wait for endocrine review [1,4]. The postoperative plan should specify ongoing hydrocortisone, fluid strategy, glucose and electrolyte monitoring, timing of reassessment, criteria for transition back to oral therapy and documentation of the event as suspected adrenal crisis [2,4]. Once the patient is haemodynamically stable and oral intake is reliable, steroid dosing can be reduced gradually towards the usual replacement regimen, guided by clinical status, surgical stress, complications and specialist advice [2-4].

POSTOPERATIVE MONITORING AND HANDOVER

Postoperative monitoring is essential because adrenal crisis may occur after an apparently uneventful operation if steroid cover is stopped too early, oral intake is delayed, or complications increase cortisol demand [2,4]. Recovery-area and ward teams should therefore monitor haemodynamic stability, fluid balance, blood glucose, electrolytes, mental status, pain, nausea, vomiting and the patient’s ability to absorb oral medication [1,4]. Persistent hypotension, recurrent vomiting, hypoglycaemia, hyponatraemia, hyperkalaemia, poor urine output, fever, sepsis or unexpected clinical deterioration should prompt reassessment of steroid cover and consideration of adrenal crisis [1,2,4].

Steroid Continuation, Tapering and Oral Restart

Patients treated for suspected adrenal crisis should usually remain on hydrocortisone 200 mg over 24 hours, preferably by continuous intravenous infusion or 50 mg every 6 hours, until clinical recovery and specialist review [3,4]. In the postoperative setting, tapering should not be automatic; it should depend on haemodynamic stability, surgical stress, infection, bleeding, vasopressor requirement, oral intake and endocrine or senior clinical advice [2-4]. Once the patient is clinically stable and able to eat, drink and absorb medication, intravenous hydrocortisone can usually be stepped down to increased oral glucocorticoid replacement before returning gradually to the patient's maintenance regimen [2-4]. The exact taper should follow local protocol and specialist guidance, especially after major surgery, ICU admission or confirmed adrenal crisis [2-4].

Table 5. Postoperative Monitoring and Steroid-Restart Checklist

Postoperative issue	What to check	Why it matters
Recovery stability	Blood pressure, pulse, perfusion, urine output	Detects recurrent shock or under-replacement [2,4]
Oral restart	Eating, drinking, vomiting, ileus, absorption	Oral steroids are unsafe if not absorbed [2,4]
Metabolic monitoring	Glucose, sodium, potassium, renal function	Identifies hypoglycaemia and electrolyte clues [1,4]
Steroid prescription	Dose, route, timing, taper plan	Prevents omitted or premature stopped doses [2-4]
Safety-netting	Steroid card, emergency plan, discharge advice	Reduces future adrenal-crisis risk [4,10]

Handover and Documentation

Handover should clearly state the diagnosis or risk of adrenal insufficiency, the steroid regimen already given, the current hydrocortisone plan, when the next dose is due, criteria for oral restart, monitoring requirements and triggers for escalation [2,4]. This information should appear in the anaesthetic record, recovery notes, medication chart, ward handover and discharge summary [2,4]. Documentation should also record whether adrenal crisis was suspected, whether cortisol and ACTH were sampled, and whether endocrinology review is required [1,4].

Discharge Safety-Netting and Follow-Up

Discharge safety-netting is part of postoperative prevention. Patients should leave hospital with clear instructions on usual steroid dosing, temporary dose increase after illness or complications, when to seek urgent help, and the importance of carrying a Steroid Emergency Card or equivalent alert [4,10]. If a crisis occurred, follow-up with endocrinology should be arranged to review diagnosis, education, emergency hydrocortisone access and future perioperative planning [1,4].

ADRENAL CRISIS IN ICU

ICU admission may be required when suspected perioperative adrenal crisis presents as persistent postoperative shock, vasopressor requirement, altered consciousness, severe electrolyte disturbance, respiratory failure or diagnostic uncertainty [2,4]. In this setting, adrenal crisis is rarely obvious because it overlaps with common ICU problems such as sepsis, haemorrhage, myocardial dysfunction, drug effects and postoperative inflammatory response [2,4,12]. The ICU team should therefore treat adrenal crisis as a clinical possibility when a patient with known adrenal insufficiency, pituitary disease, adrenal disease, chronic glucocorticoid exposure or recent steroid withdrawal develops unexplained or refractory deterioration after surgery [1-4].

Postoperative Shock and Vasopressors

Postoperative adrenal crisis may appear as distributive or mixed shock with hypotension that responds poorly to fluids and vasopressors [1,4]. Cortisol supports vascular tone and catecholamine responsiveness; therefore, cortisol deficiency may contribute to persistent vasodilation and escalating vasopressor needs [1,7]. In practice, this means that a patient who remains hypotensive despite correction of anaesthetic depth, bleeding, fluid deficit, sepsis source control and myocardial causes should be reviewed for adrenal risk and missed steroid replacement [2,4]. If adrenal crisis is suspected, hydrocortisone should be administered immediately while shock management continues [4].

Sepsis Overlap

Sepsis is one of the most important differential diagnoses and may also be a trigger for adrenal crisis [4,12,13]. Fever, raised lactate, leucocytosis, vasopressor dependence, organ dysfunction and suspected infection should prompt sepsis management, including cultures, antimicrobial therapy, source control and haemodynamic resuscitation according to local protocols [12,13]. However, identifying sepsis does not exclude adrenal crisis, particularly in patients with established adrenal insufficiency or HPA-axis suppression [1-4]. In such patients, infection increases cortisol demand and may make usual replacement inadequate [1,4]. Therefore, ICU care should avoid a false either-or approach: the patient may require both sepsis treatment and emergency hydrocortisone for adrenal crisis [4,12,13].

Distinguishing Adrenal Crisis from CIRCI

Critical illness-related corticosteroid insufficiency is not identical to classic adrenal crisis [12,14]. Adrenal crisis usually refers to acute decompensation in a patient with known or unrecognised HPA-axis disease or glucocorticoid-induced suppression, where stress-dose hydrocortisone replaces a cortisol response that the patient cannot produce adequately [1-4]. CIRCI, by contrast, describes inadequate corticosteroid activity relative to the severity of critical illness, especially in prolonged or severe critical illness, and its diagnosis remains difficult [12,14]. The 2017 SCCM/ESICM guideline states that no single test reliably diagnoses CIRCI, although random cortisol and delta cortisol after cosyntropin may be used by clinicians [12]. Recent reviews further emphasise that acute critical illness often increases systemic cortisol availability through altered

binding proteins and metabolism, while prolonged ICU illness may lead to central suppression and acquired adrenal dysfunction [14].

This distinction matters because treatment decisions differ. In a patient with known adrenal insufficiency and perioperative collapse, treatment is emergency replacement for suspected adrenal crisis and should not wait for confirmatory testing [1,4]. In septic shock without known adrenal disease, corticosteroids are considered mainly to reduce vasopressor dependence and modulate shock physiology, not necessarily because the patient has classic adrenal failure [12,13]. ICU documentation should therefore specify whether hydrocortisone is being used for suspected adrenal crisis, perioperative steroid cover, vasopressor-dependent septic shock, or another ICU indication [2,4,12,13].

ICU Steroid Use and Monitoring

For suspected adrenal crisis, adult emergency guidance recommends hydrocortisone 100 mg IV or IM immediately, followed by 200 mg over 24 hours by infusion or 50 mg every 6 hours [1,4]. For adult septic shock, the 2024 SCCM focused update suggests corticosteroids and recommends against high-dose, short-duration regimens greater than 400 mg/day hydrocortisone equivalent for less than three days [13]. These ICU recommendations should not replace adrenal-crisis protocols in patients with established adrenal insufficiency; rather, they help guide management when sepsis and vasopressor-dependent shock coexist [4,12,13].

ICU monitoring should include blood pressure, vasopressor dose, lactate, urine output, mental status, temperature, glucose, sodium, potassium, renal function and fluid balance [1,4,12]. Hyperglycaemia, secondary infection, neuromuscular weakness, delirium and fluid or sodium disturbances should be considered during ongoing corticosteroid therapy, especially in prolonged ICU admission [13,14]. When the patient improves, steroid reduction should be planned deliberately. Transition from IV hydrocortisone to oral glucocorticoids requires haemodynamic stability, improving vasopressor requirement, reliable gastrointestinal absorption and a clear endocrine or senior ICU plan [2-4]. ICU discharge handover should document the indication for steroids, doses already given, current regimen, taper plan, oral restart criteria, adrenal-risk status and follow-up needs [2,4].

TECHNOLOGY SUPPORT IN PERIOPERATIVE ADRENAL-CRISIS PREVENTION

Technology has become an important support mechanism in perioperative safety because adrenal-crisis risk can easily be missed when patients move across multiple clinical areas. In the perioperative pathway, information passes through preoperative assessment, theatre, recovery, ward care and ICU, creating opportunities for steroid history, emergency-card status or hydrocortisone plans to be omitted. Technology cannot replace clinical judgement, but it can strengthen early recognition, prescribing accuracy, handover and postoperative surveillance when it is integrated into routine clinical workflows [2,4,10].

Electronic Health Records and Risk Identification

Electronic health records can be used to flag known adrenal insufficiency, pituitary disease, adrenalectomy, long-term glucocorticoid therapy, recent steroid withdrawal or previous adrenal crisis [3-5]. These alerts are particularly useful when patients move between preoperative clinics, emergency departments, theatres, recovery areas, wards and ICU, where steroid-risk information may otherwise be missed during handover [2,4].

Clinical Decision Support and Steroid Alerts

Steroid-risk flags should be designed to trigger practical action rather than simply add passive information to the record [5]. A useful alert should prompt clinicians to check the medication history, confirm whether the patient carries a Steroid Emergency Card, prescribe perioperative hydrocortisone where indicated, and document the steroid plan in the anaesthetic and postoperative handover [2,4,10]. Evidence from emergency care suggests that clinical decision support can shorten the time to hydrocortisone administration in patients with known adrenal insufficiency, indicating that electronic alerts may improve recognition and response in high-risk settings [5].

Digital Checklists and Postoperative Surveillance

Perioperative decision-support tools may also help standardise steroid supplementation according to patient risk, surgical stress and route of administration [2,3,9]. Digital checklists can remind teams to continue usual glucocorticoids, convert oral therapy to intravenous hydrocortisone when oral intake is unsafe, and specify criteria for restarting oral replacement after surgery [2-4]. In ICU and postoperative care, electronic dashboards can support monitoring of blood pressure, vasopressor dose, glucose, sodium, potassium, renal function, lactate and missed medication doses [1,4].

Artificial Intelligence: Potential and Limitations

Artificial intelligence may contribute to future perioperative safety by identifying patterns of deterioration, predicting postoperative complications, and supporting escalation decisions in recovery or ICU [6,15]. However, these tools should be viewed as adjuncts, not diagnostic authorities [6,15]. AI models may be affected by incomplete data, local population differences, workflow design, alert fatigue and poor external validation [6,15]. They cannot replace clinical suspicion, immediate hydrocortisone when adrenal crisis is suspected, or senior anaesthetic, endocrine and ICU review [2,4].

Therefore, the safest approach is to use technology to strengthen human decision-making: flag the risk early, communicate it clearly, prevent omitted steroid doses, and escalate deterioration rapidly [2,4,10].

PRACTICAL PROTOCOLS AND CHECKLISTS

Practical protocols reduce the risk of missed adrenal insufficiency, delayed hydrocortisone and poor postoperative communication [2,4]. These checklists should be adapted to local policy, but the core principle is that adrenal-crisis prevention must be visible before, during and after surgery [2,4,10].

Preoperative Checklist

Before surgery, the team should confirm:

- known primary, secondary or tertiary adrenal insufficiency [1-3];
- pituitary disease, adrenal disease, adrenalectomy or previous adrenal crisis [1,2,4];
- current or recent systemic glucocorticoid use, including recent tapering or withdrawal [3,9];
- whether the patient carries a Steroid Emergency Card, medical alert bracelet or endocrine letter [4,10];
- usual steroid dose, timing and route [2,3];
- whether fasting, vomiting, bowel preparation or ileus may interrupt oral steroid absorption [2,4];
- planned perioperative hydrocortisone regimen, including dose at induction and postoperative continuation [2,4];
- whether anaesthesia, surgery, recovery, ward and pharmacy teams are aware of the steroid plan [2,4].

Intraoperative Red Flags

During anaesthesia, adrenal crisis should be considered when an at-risk patient develops:

- hypotension disproportionate to surgical or anaesthetic findings [2,4];
- shock with poor response to fluids and vasopressors [1,4];
- unexplained hypoglycaemia, especially after fasting or prolonged surgery [1,4];
- hyponatraemia or hyperkalaemia, especially in primary adrenal insufficiency [1,4];
- deterioration without clear haemorrhage, anaphylaxis, myocardial event, sepsis or anaesthetic cause [2,4,9].

Emergency Algorithm

If adrenal crisis is suspected:

- Call for senior anaesthetic, surgical and nursing help immediately [2,4].
- Draw cortisol and ACTH only if this does not delay treatment [1,4].
- Give hydrocortisone 100 mg IV or IM immediately [1,4].
- Continue hydrocortisone 200 mg over 24 hours by infusion, or 50 mg IV/IM every 6 hours if infusion is unavailable [1,4].
- Start rapid isotonic fluid resuscitation, usually 0.9% saline, unless contraindicated [1,4].
- Check and correct glucose, sodium, potassium, renal function, lactate and acid-base disturbance [1,4].
- Continue simultaneous assessment for bleeding, sepsis, anaphylaxis, myocardial events and anaesthetic complications [2,4,9].
- Escalate to ICU if shock, vasopressor requirement, altered consciousness, severe metabolic disturbance or diagnostic uncertainty persists [2,4].

ICU and Postoperative Handover Checklist

Handover should state:

- why the patient is at adrenal-crisis risk [2,4];
- steroid doses already given and next dose due [2,4];
- current hydrocortisone route, dose and taper plan [2-4];
- glucose, electrolyte, fluid-balance and vasopressor monitoring needs [1,4,12];
- criteria for restarting oral steroid therapy [2-4];
- whether endocrinology review is required [1,4];
- discharge safety-netting, including Steroid Emergency Card, sick-day rules and future perioperative planning [4,10].

Clear documentation should appear in the anaesthetic record, medication chart, recovery notes, ICU or ward handover and discharge summary [2,4].

CONCLUSION

Adrenal crisis during the perioperative period is a preventable but potentially fatal emergency. Its danger lies in the fact that it may resemble common surgical and anaesthetic complications, including haemorrhage, sepsis, anaphylaxis, myocardial events and drug-related cardiovascular instability [2,4]. Safe care therefore depends on anticipation before surgery, clear steroid planning, early recognition of refractory hypotension or shock, and immediate hydrocortisone when adrenal crisis is suspected [1,2,4]. ICU involvement becomes essential when postoperative deterioration is complicated by vasopressor requirement, sepsis overlap, severe metabolic disturbance or diagnostic uncertainty [4,12,13]. Technology, steroid alerts and digital checklists may support safer systems, but they cannot replace clinical judgement or multidisciplinary escalation [5,6]. The central message is practical: identify risk early, maintain steroid continuity, treat suspected crisis without delay, document clearly, and protect the patient across the full perioperative pathway.

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