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Integrated Emergency, Nursing, and Family Medicine Approaches to the Recognition and Management of Adrenal Crisis

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Abstract

Background: Adrenal crisis is a life-threatening endocrine emergency caused by a severe deficiency of cortisol, often triggered by physiologic stress in individuals with underlying adrenal insufficiency. Despite being treatable, it carries a significant mortality rate, estimated at 0.5 deaths per 100 patient-years, primarily due to delays in recognition and intervention.

Aim: This article aims to outline the integrated, multidisciplinary approach required for the prompt recognition, emergency management, and long-term prevention of adrenal crisis, emphasizing roles across emergency medicine, nursing, and family medicine.

Methods: Management is centered on immediate parenteral glucocorticoid administration (100mg hydrocortisone IV/IM) and aggressive fluid resuscitation with isotonic saline. This is coupled with correction of hypoglycemia and electrolyte imbalances. Diagnosis relies on clinical suspicion based on a history of adrenal insufficiency, chronic steroid use, or presentation with refractory hypotension, and is supported by laboratory findings (e.g., hyponatremia, hyperkalemia, hypoglycemia).

Results: Prompt treatment leads to rapid clinical improvement, but delayed intervention results in high mortality and complications such as seizures, arrhythmias, and multi-organ failure. Patient education on "sick day rules" (stress-dose steroids) and access to emergency hydrocortisone injection kits are critical for preventing recurrent crises.

Conclusion: Adrenal crisis remains a preventable cause of death. Optimal outcomes depend on a high index of suspicion, immediate empiric therapy, and a coordinated interprofessional team strategy to ensure seamless care from emergency response to long-term community management.

Keywords: Adrenal crisis, Adrenal insufficiency, Hydrocortisone, Glucocorticoid, Emergency management, Sick day rules, Interprofessional care.

1. Introduction

Adrenal crisis, often termed Addisonian crisis, constitutes an acute and potentially fatal manifestation of adrenal insufficiency that demands immediate recognition and intervention. Epidemiological data indicate a substantial mortality burden among affected patients, with reported rates approximating 0.5 deaths per 100 patient years, underscoring the persistent lethality of this endocrine emergency despite advances in care [1]. The clinical course can be abrupt, with patients deteriorating rapidly in community settings or shortly after hospital presentation when diagnosis or treatment is delayed. The condition arises from inadequate endogenous cortisol availability, the primary glucocorticoid responsible for maintaining hemodynamic stability, metabolic homeostasis, and the adaptive response to physiologic stress. Insufficient cortisol may result from intrinsic adrenal failure or from disrupted hypothalamic-pituitary-adrenal axis signaling due to secondary or tertiary etiologies; irrespective of cause, the result is an inability to meet increased cortisol

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demands during stressors, which precipitates the crisis state [2].

Distinguishing chronic, compensated primary adrenal insufficiency, commonly known as Addison disease and managed with stable long-term glucocorticoid replacement, from acute adrenal crisis is essential because the latter represents a time-sensitive deterioration in physiologic status requiring parenteral glucocorticoid administration and supportive care. The clinical presentation of adrenal crisis is protean and initially nonspecific. Early symptoms commonly include profound fatigue, generalized weakness, anorexia, nausea, vomiting, abdominal pain, back pain, diarrhea, lightheadedness, hypotension, and syncope; these manifestations may rapidly progress to obtundation, metabolic encephalopathy, refractory hypotension, and distributive or mixed shock if not treated expeditiously [3][4]. Such symptom overlap with other acute medical and surgical conditions complicates early detection and contributes to diagnostic delay. Laboratory features may show electrolyte disturbances, including hyponatremia and hyperkalemia in primary adrenal failure, hypoglycemia in severe cases, and nonspecific markers of acute illness; however, definitive diagnosis during the emergency may not be practical and should not delay empiric therapy when clinical suspicion is high.

The standard of care for a suspected adrenal crisis includes immediate administration of parenteral glucocorticoids, intravenous fluid resuscitation, correction of electrolyte and glucose derangements, and identification and treatment of precipitating causes such as infection, volume loss, trauma, or abrupt withdrawal of chronic glucocorticoid therapy [2]. Preventive strategies focus on patient education and system-level readiness. Instruction on so-called sick day rules, whereby patients increase their oral glucocorticoid dosage two to threefold during minor intercurrent illnesses and to higher increments for major stressors, reduces the risk of progression to crisis. Ensuring patient access to injectable hydrocortisone and training patients or caregivers in intramuscular administration for situations of vomiting or inability to tolerate oral medication form critical components of prevention [5][6]. Despite these established measures, a lack of uniformity in the operational definition of adrenal crisis has fostered inconsistency in clinical recognition, reporting, and research. Expert panels and reviews have proposed varying criteria, reflecting the heterogeneous clinical picture and the interplay of absolute and relative hemodynamic compromise in different patients. A pragmatic and recent operational definition advanced by Rushworth and colleagues in 2019 conceptualizes adrenal crisis as an acute decline in health status accompanied by either absolute hypotension, defined as systolic blood pressure below 100 mm Hg, or relative hypotension, defined as a systolic pressure at least 20 mm Hg lower than the patient's typical baseline [3].

This approach highlights the importance of individualized hemodynamic thresholds and recognizes that some patients present with a marked deviation from their norm despite not meeting conventional absolute hypotension cutoffs. A critical clinical expectation embedded in this definition is the rapid responsiveness to parenteral glucocorticoids; typically, clinicians should observe a marked reduction in hypotension within the first hour following steroid administration and progressive symptomatic and physiologic improvement over the subsequent hours if the episode represents true adrenal crisis [3]. This temporal criterion serves both as a diagnostic aid and as a marker of therapeutic adequacy. The need for immediate empiric treatment based on clinical grounds rather than awaiting confirmatory laboratory assays remains a central tenet of practice because delays in glucocorticoid replacement correlate with worse outcomes. Concurrently, the heterogeneity of existing definitions complicates epidemiologic surveillance and interventional research, and it underscores the need for broader consensus that integrates objective hemodynamic parameters, biochemical markers where available, and early treatment response. Clinicians across emergency medicine, nursing, and family medicine must therefore maintain a high index of suspicion for adrenal crisis in patients with known adrenal insufficiency, in those exposed to potential precipitants, and in undifferentiated shock states where cortisol deficiency may be contributory. Emphasis on patient education, availability of parenteral hydrocortisone, and system-level protocols for rapid steroid administration constitutes the practical framework for reducing morbidity and preventing avoidable mortality attributable to this treatable endocrine catastrophe [1][2][3][4][5][6].

Etiology

Thomas Addison first described adrenal insufficiency in 1855 [7]. His report established the clinical entity now known as primary adrenal failure. The therapeutic landscape changed after the discovery of cortisone by Hench, Kendall, and Reichstein in the late 1940s [8][9]. That discovery transformed patient outcomes and lifespans. Historical shifts in causation followed advances in treatment and public health. In the 1930s tuberculosis accounted for the majority of cases. Estimates from that era place tuberculous adrenalitis at roughly 70 percent of primary adrenal failure. Modern patterns differ by region. In high income settings autoimmune adrenalitis, referred to as Addison disease, now dominates as the leading cause of primary adrenal insufficiency. In lower income settings tuberculosis remains the principal etiology [10]. Primary adrenal insufficiency results from loss of adrenal cortical function. The defining biochemical profile includes diminished cortisol and elevated adrenocorticotropic hormone. Autoimmune

destruction of the adrenal cortex constitutes the commonest mechanism in many settings. Other causes include surgical removal of both glands and congenital defects in cortisol biosynthesis such as congenital adrenal hyperplasia. Infectious destruction of the glands remains relevant. Mycobacterium tuberculosis can produce chronic infectious adrenalitis and progressive fibrosis of the adrenal cortex. Acute bilateral adrenal hemorrhage following fulminant meningococcal sepsis produces Waterhouse Friderichsen syndrome and rapid loss of adrenal function. Less common infectious agents and infiltrative processes may also cause primary failure [11][12][13][14].

Secondary adrenal insufficiency arises from inadequate pituitary ACTH secretion or from prolonged suppression of the hypothalamic pituitary adrenal axis by exogenous glucocorticoids. Chronic exposure to systemic glucocorticoids downregulates ACTH output and provokes adrenal atrophy. Clinically important suppression may occur after surprisingly low doses administered for prolonged intervals. Evidence indicates that prednisone at doses as low as 5 mg daily for four weeks can impair axis function. Routes of administration other than oral systemic therapy can contribute. Intra articular steroid injections topical steroid preparations and inhaled steroid formulations have all been implicated in causing central suppression. Structural lesions of the pituitary or hypothalamus such as tumors or infiltrative disease may also produce secondary adrenal failure by disrupting ACTH production. The biochemical pattern of secondary insufficiency differs from primary disease by the absence of mineralocorticoid deficiency in most cases because aldosterone synthesis remains under renin angiotensin control [15]. Adrenal crisis most frequently occurs in individuals with a known diagnosis of primary or secondary adrenal insufficiency. However, an acute crisis may represent the initial clinical presentation. Roughly half of patients ultimately diagnosed with Addison disease present first with an acute crisis. Case series report that a substantial minority of adrenal crises lack an identifiable antecedent cause in routine evaluation. One study documented unexplained crises in approximately ten percent of patients [16][17][18][19].

Precipitating events for adrenal crisis span infectious insults to physiologic stressors and medication changes. Gastrointestinal and influenza like illnesses remain the most common precipitants in contemporary case series [3][6][20]. Infectious triggers include bacterial mycobacterial fungal parasitic and viral pathogens. Severe viral infections such as COVID 19 have been observed as precipitating factors in recent reports [19][21]. Surgical procedures trauma childbirth and pregnancy may overwhelm adrenal reserve and trigger crisis. Exposure to extreme heat or cold and intense physical exertion can function as stressors in vulnerable patients. Emotional distress has been associated with crisis onset in some reports [19][22]. Medication related causes require particular attention. Nonadherence to maintenance glucocorticoid replacement represents a preventable mechanism of crisis. Abrupt cessation of long term glucocorticoid therapy provokes central adrenal insufficiency and may precipitate life threatening cortisol deficiency [23]. Certain drugs accelerate cortisol clearance or inhibit steroid synthesis and therefore increase risk. Thyrotoxicosis accelerates cortisol metabolism and can unmask unsuspected adrenal insufficiency. Initiation of levothyroxine in an untreated patient may precipitate crisis by increasing metabolic demands on an inadequate adrenal system [24]. Antiadrenal agents such as mitotane metyrapone and ketoconazole impair steroidogenesis and have been reported as precipitants. Modern oncologic therapies have added new iatrogenic causes. Immune checkpoint inhibitors and selected tyrosine kinase inhibitors can cause immune mediated or direct endocrine toxicity that culminates in adrenal insufficiency and crisis [25][26][27].

Patients with polyglandular autoimmune syndromes have heightened vulnerability to adrenal crisis because multiple endocrine axes may be compromised concurrently. Concomitant thyroid disease can obscure adrenal insufficiency. Hypothyroid patients exist in a low metabolic state that may mask signs of cortisol deficiency. Beginning thyroid hormone replacement in such patients increases metabolic rate and reveals latent adrenal insufficiency through hypotension or hypoglycemia. Autoimmune polyglandular syndromes may include combined involvement of thyroid parathyroid adrenal and pancreatic islets and therefore require vigilance for evolving adrenal failure [24][28]. Epidemiologic patterns of precipitating events underscore the interaction between a fixed deficit in cortisol reserve and variable external stresses. Minor intercurrent illness may require only oral dose escalation in compliant patients. Major physiologic stressors demand prompt parenteral replacement and supportive measures. The heterogeneity of triggers complicates both clinical recognition and prevention strategies. Infections and surgical stress present diagnostic challenges because their manifestations may overlap with features of cortisol deficiency. Moreover, medication interactions and diagnostic overshadowing by other acute pathologies contribute to delayed diagnosis. Recognition of etiologic categories informs prevention. In primary disease patient education on stress dose management and provision of emergency injectable hydrocortisone reduce risk. In secondary disease clinicians must account for iatrogenic suppression when planning glucocorticoid tapering and when prescribing drugs known to alter glucocorticoid bioavailability. In patients receiving immune checkpoint inhibitors oncology teams must

monitor endocrine function and coordinate early endocrine consultation when symptoms suggest insufficiency. In settings with endemic tuberculosis public health measures and timely treatment of active infection remain central to reducing tuberculous adrenalitis.

Pathophysiology connects etiology to clinical course. Loss of cortisol impairs vascular responsiveness to catecholamines and blunts gluconeogenesis. Aldosterone deficiency present produces salt loss hyperkalemia and volume depletion. The combined hemodynamic metabolic and electrolyte derangements drive the acute presentation. Rapid reversal of these abnormalities with parenteral glucocorticoid administration underlies the therapeutic rationale for immediate empiric treatment in suspected cases. Despite improved understanding and better treatments adrenal crisis persists as a cause of morbidity and mortality. Regional differences in etiologic frequency persist across eras and health systems. Autoimmune mechanisms dominate in developed settings. Infectious causes such as tuberculosis remain important in lower resource settings. Iatrogenic factors linked to expanding pharmacologic and oncologic therapies have created new pathways to adrenal failure. Recognition of this evolving etiologic landscape should guide surveillance of clinical protocols and patient education. Clinicians across primary secondary and acute care must maintain vigilance for adrenal insufficiency in patients with compatible histories in order to prevent progression to crisis and to provide timely lifesaving therapy [11][12][13].

Adrenal Crisis Risk Factors

Patients with a documented history of adrenal insufficiency or a prior adrenal crisis face the highest risk of recurrent acute decompensation. Prior episodes indicate limited cortisol reserve or failures in stress-dose management. Individuals with primary adrenal insufficiency carry greater intrinsic risk than those with secondary adrenal insufficiency because primary disease often involves impairment of both glucocorticoid and mineralocorticoid synthesis, which amplifies the likelihood of hypotension, electrolyte disturbance, and volume depletion during intercurrent stressors [16][29]. Chronic glucocorticoid therapy constitutes a major risk axis. Long-term systemic steroids suppress the hypothalamic-pituitary-adrenal axis and produce adrenal atrophy. Abrupt reduction or discontinuation of any glucocorticoid preparation may precipitate acute cortisol deficiency. Clinically relevant suppression may follow not only oral systemic therapy but also corticosteroid administered by topical, inhaled, or intra-articular routes. Failure to recognize the systemic effects of nonoral formulations increases the risk of adrenal crisis when therapy is stopped, interrupted, or when additional physiologic stress occurs. Drug interactions and medications that alter cortisol synthesis or clearance represent an important and preventable group of risk factors. Enzyme inducers such as rifampin, phenytoin, phenobarbital, and carbamazepine accelerate glucocorticoid metabolism and can lower effective cortisol levels in vulnerable patients [30][31][32]. Herbal remedies that induce cytochrome P450 enzymes, such as St John's wort, produce a similar effect. Antifungal agents such as ketoconazole and fluconazole inhibit steroidogenesis or alter steroid metabolism and can precipitate insufficiency when used alone or in combination with other suppressive factors. Etomidate suppresses 11β-hydroxylase and can induce acute adrenal insufficiency in critically ill patients. Recognition of these pharmacologic risks is essential when initiating, discontinuing, or combining therapies that affect adrenal function.

Anticoagulant therapy increases the risk of adrenal hemorrhage, an uncommon but catastrophic cause of acute adrenal failure. Hemorrhagic destruction of one or both adrenal glands produces rapid loss of steroid output and can present with shock. Additional medications with hormonal activity such as megestrol acetate and medroxyprogesterone have been associated with HPA axis perturbation and may alter cortisol dynamics, thereby increasing vulnerability to crisis in susceptible patients [33][34][35]. Pregnancy confers heightened risk, particularly in the third trimester. Physiologic increases in cortisol binding and changes in steroid metabolism may reduce free cortisol availability during periods of stress. Labor and the peripartum period impose substantial physiologic demands that can unmask inadequate adrenal reserve, so pregnant patients with known or suspected insufficiency require anticipatory dose adjustments and close monitoring [36]. Advanced age emerges as another risk factor. Older adults may harbor multiple comorbidities, polypharmacy, and diminished physiological reserve, all of which magnify the impact of relative cortisol deficiency and increase the probability of clinical decompensation [3].

Comorbidity burden independently raises risk. Cardiovascular disease, chronic kidney disease, chronic lung disease, and active infection compound the hemodynamic and metabolic stresses that reveal or worsen adrenal insufficiency [16][29]. Autoimmune type 1 diabetes commonly coexists with adrenal autoimmunity. Patients with type 1 diabetes have higher rates of adrenal insufficiency and face specific hazards because glycemic instability and hypoglycemia may coexist with cortisol deficiency, complicating diagnosis and increasing morbidity [3]. Structural adrenal pathology, including metastatic disease to the adrenals and adrenal hemorrhage from any cause, represents a direct anatomic route to cortisol failure and rapid clinical collapse [37][38].

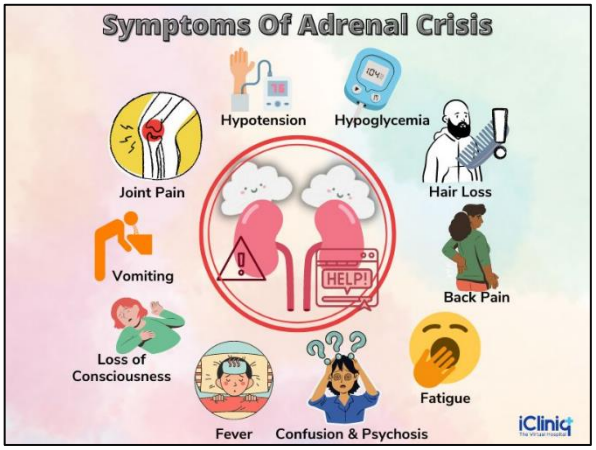

Figure-1: Symptoms of adrenal crisis.

Patients with autoimmune polyglandular syndromes type 1 and type 2 require special consideration. Multiple endocrine axes can be affected concurrently or sequentially in these syndromes, creating unpredictable interactions among thyroidal adrenal and pancreatic function. Thyroid hormone replacement in an undiagnosed or untreated patient can increase metabolic demand and precipitate adrenal crisis. The coexistence of multiple glandular autoimmune processes increases the probability that adrenal insufficiency will go unrecognized until stress unmasks a deficit [39][40]. Risk stratification must incorporate the interplay of baseline adrenal reserve, precipitating exposures, comorbid conditions, and pharmacologic influences. Identification of patients at risk allows preemptive measures: structured education on stress dosing, provision of emergency injectable glucocorticoid, careful medication review to avoid interactions that reduce cortisol availability, and coordinated management during pregnancy, surgery, or acute illness. These steps reduce the incidence of preventable crisis and improve outcomes in patients who remain vulnerable because of underlying disease or therapy.

Epidemiology

The true prevalence of adrenal crisis within the general population is difficult to establish because of diagnostic variability, underreporting, and differences in healthcare access. The condition primarily affects individuals with adrenal insufficiency, and data from cohort studies suggest that between 6% and 8% of these patients experience an adrenal crisis each year. This translates to approximately 4 to 6 adrenal crises per 100 patient years among those diagnosed with adrenal insufficiency [20]. Despite progress in diagnosis, hormone replacement, and patient education, the overall incidence remains consistently high. Studies demonstrate that even well-educated patients who receive comprehensive training on sick day management and emergency hydrocortisone use continue to experience crises, highlighting the unpredictable and multifactorial nature of this condition [19]. Mortality associated with adrenal crisis persists as a major concern. In a well-informed patient cohort, the mortality rate reached 6%, indicating that education alone cannot completely mitigate the risk of fatal outcomes [19]. This persistent mortality reflects the acute and rapidly progressive nature of adrenal crisis, in which even brief treatment delays can lead to circulatory collapse, electrolyte imbalance, and multi-organ failure. The data emphasize the need for early recognition, access to emergency steroids, and system-wide readiness to treat suspected cases. Among individuals with Addison disease, the annual frequency of adrenal crisis remains near 8%, showing little decline over decades despite medical advances [41]. These figures underscore that adrenal crisis continues to represent a critical, recurrent, and preventable cause of morbidity and mortality in patients with adrenal insufficiency.

Pathophysiology

The pathophysiology of adrenal crisis remains incompletely defined. Examining normal glucocorticoid function clarifies how hormone loss produces the clinical syndrome. Glucocorticoids act across multiple systems with permissive suppressive stimulatory and preparative roles in the stress response [42]. Loss of these functions removes several layers of physiologic reserve and produces rapid systemic decompensation when an acute stressor occurs. Adrenal crisis denotes acute, severe deficiency of cortisol and in many cases aldosterone. The hypothalamic release of corticotropin releasing hormone in response to stress drives anterior pituitary secretion of adrenocorticotropic hormone. ACTH stimulates the adrenal zona fasciculata to synthesize cortisol from cholesterol via cytochrome P450 enzymes [43]. Interruption at any level of this axis or destruction of adrenal cortical tissue leads to inadequate cortisol availability relative to physiologic demand. Cortisol serves as the primary mediator of the human stress response. It supports vascular tone by permitting catecholamine action at adrenergic receptors and by modulating vascular smooth muscle responsiveness. Cortisol restrains systemic inflammation by inhibiting proinflammatory cytokine production and by impairing T cell proliferation and signaling, thereby limiting uncontrolled immune activation [44]. Cortisol promotes glucose availability through hepatic gluconeogenesis and by supporting glycogen synthesis. It facilitates mobilization of amino acids and free fatty acids to supply substrates for gluconeogenesis and tissue metabolism. Loss of cortisol therefore produces a combined hemodynamic metabolic and immunologic failure that manifests clinically as hypotension hypoglycemia and an inappropriate inflammatory response.

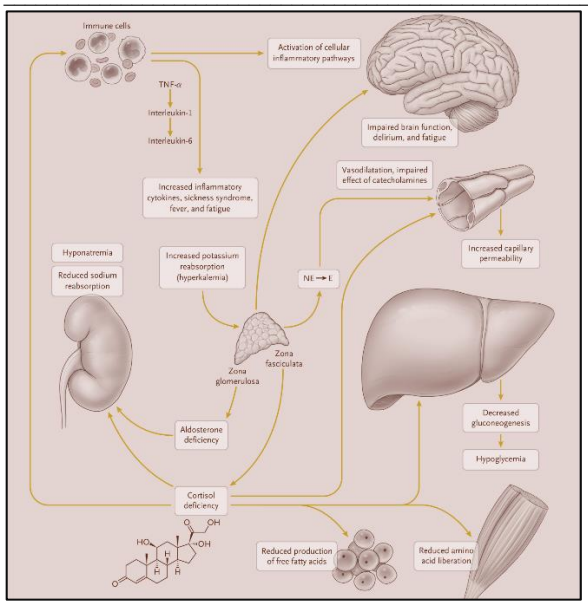

Figure-2: Adrenal Crisis pathophysiology.

Aldosterone deficiency accompanies adrenal cortical failure in primary disease and magnifies circulatory instability. Aldosterone maintains sodium retention and potassium excretion at the renal collecting duct. When aldosterone is absent renal sodium loss and potassium retention cause extracellular volume contraction hyperkalemia and metabolic acidosis. Volume depletion reduces venous return cardiac output and renal perfusion. The resulting fall in arterial pressure produces postural hypotension reflex tachycardia and, if uncorrected, circulatory collapse. Impaired renal perfusion further concentrates nitrogenous waste and elevates blood urea nitrogen and creatinine, signaling end organ hypoperfusion [43]. Metabolic sequelae of cortisol and aldosterone loss converge. Hypoglycemia emerges from failed hepatic glucose production and impaired counter regulatory responses. Hyperkalemia and acidosis result from aldosterone deficiency and from cell membrane shifts during volume loss. These derangements impair cellular function and potentiate cardiovascular instability. The combined electrolyte and metabolic disturbances accelerate progression to multisystem organ dysfunction if not reversed. Glucocorticoid support for adrenergic responsiveness underlies the characteristic refractory hypotension of adrenal crisis. Cortisol upregulates adrenergic receptor expression and downstream signaling pathways. In cortisol deficient states catecholamines fail to sustain vascular tone despite intravenous fluids and vasopressors. Clinically this presents as hypotension that does not correct with volume resuscitation alone and that responds only after parenteral glucocorticoid replacement [45]. The hemodynamic failure often displays a rapid time course and can progress to distributive or mixed shock.

Immune and inflammatory pathways modify the clinical picture. Loss of cortisol mediated restraint permits exaggerated cytokine release during infection or tissue injury. That dysregulated immune response may worsen capillary leak and vasodilation and may increase metabolic demand. Concurrent infection can both precipitate crisis and amplify its severity. Tissue level effects further explain organ dysfunction. Cortisol affects myocardial contractility vascular resistance and renal autoregulation. Its absence reduces myocardial sensitivity to catecholamines and impairs cardiac output. The kidney suffers from decreased perfusion and from direct effects on tubular sodium handling. Hepatic gluconeogenic failure limits energy substrate supply to brain and other vital organs. In summary adrenal crisis reflects failure of core endocrine mechanisms that preserve hemodynamic stability metabolic balance and immune control during stress. The loss of cortisol removes permissive support for catecholamines and for gluconeogenesis. If aldosterone is also deficient sodium loss potassium retention volume depletion and acidosis accelerate shock. The interplay of hormonal deficits with infection medication effects and physiologic stressors produces a rapidly progressive syndrome. Rapid recognition and prompt parenteral glucocorticoid administration restore the permissive functions of cortisol and reverse the pathophysiologic cascade [42][43][44][45].

Effects of Glucocorticoids on the Immune System

Glucocorticoids function as central modulators of the immune response through multiple convergent mechanisms that restrain cytokine production alter leukocyte trafficking and suppress antigen driven lymphocyte activation. Immune activation triggered by infectious or noninfectious stressors elevates cytokines such as interleukin 1 interleukin 2 interleukin 6 tumor necrosis factor alpha and tumor necrosis factor gamma and thereby stimulates the hypothalamic pituitary adrenal axis with consequent rise in circulating glucocorticoids [46][47]. Elevated glucocorticoid concentrations feedback on innate and adaptive immune compartments to inhibit transcription of proinflammatory cytokines reduce expression of adhesion molecules that mediate leukocyte extravasation and impair dendritic cell maturation and function [48][49]. At the cellular level glucocorticoids interfere with nuclear factor kappa B signaling and other transcriptional pathways that sustain cytokine cascades. They also induce lymphocyte redistribution out of the peripheral circulation and promote apoptosis of selected T lymphocyte subsets thereby limiting clonal expansion and effector function. These effects jointly reduce febrile responses attenuate capillary leak and preserve vascular integrity during stress. When glucocorticoid availability is absent or inadequate under conditions of severe stress the regulatory brake on cytokine networks fails and an uncontrolled inflammatory response may ensue. Exuberant cytokine release produces systemic vasodilation increased capillary permeability and profound interstitial fluid shifts. The ensuing

hypovolemia reduces effective circulating volume and can precipitate distributive or hypovolemic shock. Fever and tissue edema further compromise microvascular perfusion and oxygen delivery which amplifies organ dysfunction. Thus, the immune dysregulation that characterizes adrenal crisis links inflammatory overactivity to hemodynamic collapse.

Glucocorticoid deficiency also perturbs musculoskeletal and mineral metabolism in ways that may influence clinical course. Cortisol modulates thyroid axis output and bone cell biology. In the absence of normal glucocorticoid signaling there may be relative increases in pituitary thyroid stimulating hormone with downstream elevations of thyroid hormone that accelerate bone resorption and mobilize calcium [28][50][51]. Proposed mechanisms for hypercalcemia in adrenal insufficiency include disinhibition of renal 1 alpha hydroxylation of vitamin D increased intestinal calcium absorption preservation of osteoblast survival and enhanced proximal tubular calcium reabsorption associated with intravascular volume contraction. The precise relative contributions of these pathways remain incompletely defined and warrant further investigation [28][50][51]. Fluid homeostasis is sensitive to glucocorticoid status because cortisol exerts tonic suppression on hypothalamic antidiuretic hormone secretion [52][53]. Glucocorticoid deficiency permits inappropriate or excessive ADH release with resultant water retention and hyponatremia in many patients. Paradoxically adrenal crisis may also present effective hypovolemia because impaired vascular tone and aldosterone deficiency drive sodium wasting and reduced intravascular volume. The combined effects on ADH and mineralocorticoid function produce complex derangements in intravascular volume and serum osmolality that complicate resuscitation. Cortisol is essential for metabolic adaptation to stress and for maintenance of glucose homeostasis [54]. It promotes hepatic gluconeogenesis supports glycogen synthesis and induces relative insulin resistance to preserve circulating glucose for vital organs. In cortisol deficient states gluconeogenesis is impaired peripheral glucose utilization is increased, and counter regulatory responses are blunted. These alterations predispose symptomatic and severe hypoglycemia particularly during intercurrent illness or fasting states.

Central appetite regulation is also altered by changes in CRH and glucocorticoid feedback [55][52]. Corticotropin releasing hormone exerts an anorexigenic effect during stress. Exogenous or endogenous glucocorticoids suppress CRH release and thereby tend to increase appetite. Conversely, inadequate glucocorticoid tone during adrenal insufficiency leaves CRH unchecked and contributes to anorexia and poor oral intake, which further exacerbates metabolic instability. Electrolyte disturbances reflect the distinction between primary and central adrenal failure. Primary adrenal cortical destruction produces loss of aldosterone with consequent renal sodium loss hyponatremia hyperkalemia volume depletion and metabolic acidosis [18][56]. In secondary or tertiary adrenal insufficiency aldosterone secretion is usually preserved because it remains under renin angiotensin control and therefore mineralocorticoid related electrolyte abnormalities are less prominent [57][56]. The combination of glucocorticoid and mineralocorticoid deficits in primary disease magnifies hemodynamic compromise and the risk of rapid deterioration. Collectively the effects of glucocorticoids on immune modulation fluid balance glucose metabolism appetite and electrolyte handling explain the multisystem manifestations of adrenal crisis and the rapid clinical response that follows prompt parenteral glucocorticoid replacement [46][47][48].

History and Physical

A meticulous history is the cornerstone of evaluating a patient with suspected adrenal crisis. Eliciting prior diagnoses of adrenal insufficiency or previous episodes of adrenal crisis immediately elevates clinical suspicion. Documentation of chronic glucocorticoid therapy is essential because abrupt cessation or failure to implement stress dose escalation during intercurrent illness commonly precipitates life threatening cortisol deficiency [58][59]. Inquiry must therefore address adherence to prescribed regimens, recent changes in dosing, and events that might have interfered with oral intake, such as vomiting or severe gastrointestinal illness. Recent infections, particularly gastroenteritis and respiratory tract infections, recent surgical procedures, major trauma, heat or cold exposure, and any substantial physiologic or emotional stress should be recorded, since such events frequently unmask inadequate adrenal reserve and precipitate acute decompensation. A careful medication review is indispensable. Systemic oral steroids require focused assessment, but the clinician must also identify alternative steroid exposures that can suppress the hypothalamic pituitary adrenal axis, including inhaled corticosteroids, topical steroid preparations, intra articular steroid injections, and less obvious systemic exposures such as depot steroid formulations. Documentation of over the counter agents and herbal supplements is necessary, given that enzyme inducing products such as St John’s wort and prescribed enzyme inducers can alter steroid metabolism and thereby influence adrenal function [58][59]. The history must also probe for recent initiation of medications that alter cortisol metabolism or biosynthesis, including antifungal agents, anticonvulsants, and certain anticancer therapies, because these agents can either precipitate insufficiency or unmask previously compensated disease.

Personal and family histories of autoimmune disease are highly relevant. The presence of

autoimmune thyroid disease type 1 diabetes or other autoimmune endocrinopathies raises the likelihood of polyglandular autoimmune syndromes and therefore increases the pretest probability of concurrent adrenal insufficiency. Recurrent unexplained hypoglycemia in individuals with type 1 diabetes, particularly when resistant to standard corrective measures, should prompt urgent consideration of adrenal insufficiency as a contributing factor [60]. Likewise, a history of chronic fatigue, unexplained weight loss, salt craving, amenorrhea, or progressive hyperpigmentation may indicate longstanding adrenal cortical failure that has not previously been recognized. Identifying precipitating factors during the history provides both diagnostic clues and immediate management priorities. Nonadherence to maintenance replacement therapy and abrupt glucocorticoid withdrawal remain preventable but common causes of crisis. Intercurrent infection is the most frequent proximate trigger and may co present with signs that obscure the endocrine origin of the presentation. Surgical stress, labor and delivery, severe gastroenteritis with volume loss, and major trauma all produce physiologic demands that exceed the reduced cortisol reserve seen in adrenal insufficiency. Recognition of these antecedent events should lower the threshold for empiric parenteral glucocorticoid therapy given the high risk of rapid deterioration.

The initial clinical picture is frequently nonspecific and may include weakness, profound fatigue, anorexia, nausea, vomiting, fever, lower chest or abdominal pain, back pain, dizziness, somnolence, and cognitive impairment. These symptoms may progress rapidly to hypotension, altered mental status, obtundation, and circulatory collapse if not treated [3][61]. Children may present differently, with failure to thrive, marked weight loss, and severe hypoglycemia that can lead to seizures. Less common manifestations include an acute abdomen like presentation that can mimic surgical emergencies, psychiatric symptoms such as depression, decreased libido, and menstrual irregularities. Because the spectrum of presentation spans multiple organ systems, clinicians must maintain a high index of suspicion in any patient with unexplained hemodynamic instability or with symptoms disproportionate to commonly diagnosed conditions. Physical examination complements the history and frequently yields important diagnostic information. Vital sign assessment often reveals fever, tachycardia, and orthostatic hypotension. Measurement of orthostatic changes in blood pressure and heart rate can expose inadequate intravascular volume or impaired vascular responsiveness. Patients with primary adrenal insufficiency may show hyperpigmentation of the skin and buccal mucosa due to chronic elevation of proopiomelanocortin derived peptides; identifying such stigmata supports the diagnosis of primary cortical failure [62]. Conversely evidence of chronic exogenous steroid exposure such as facial rounding, dorsocervical fat pad, truncal adiposity, striae, and cutaneous thinning indicates long term glucocorticoid use and suggests potential central suppression of the HPA axis.

Abdominal and chest examination may reveal tenderness that can be mistaken for intra-abdominal pathology. Marked hyperpyrexia is occasionally observed, with temperatures exceeding 40.5 degrees Celsius in severe inflammatory or infectious precipitants [5][20][41]. As cortisol stores become exhausted, patients may progress to frank circulatory collapse with cyanosis, profound hypotension, and reduced consciousness. In the absence of prompt glucocorticoid replacement, the trajectory is toward coma and death. The history and physical examination together should prioritize identification of treatable precipitants, assessment of the degree of hemodynamic compromise, and recognition of features that distinguish primary from central adrenal failure, because mineralocorticoid deficiency in primary disease influences fluid and electrolyte management. Given the rapid progression and high mortality risk associated with adrenal crisis clinicians must act on the history and examination findings without delay, initiating empirical parenteral glucocorticoids and supportive measures when clinical suspicion is high, while concurrently obtaining targeted laboratory and imaging studies to refine diagnosis and guide ongoing therapy [58][59][60][3][61][62][63].

Evaluation

Initial assessment of a patient with suspected adrenal crisis must prioritize rapid acquisition of targeted laboratory data while recognizing that definitive management should not be delayed for test completion [63]. Baseline serum chemistry panels, a complete blood count with differential, measurements of plasma cortisol and adrenocorticotropic hormone, and assays of aldosterone and renin provide the biochemical foundation for differentiating primary from secondary or tertiary causes and for documenting the metabolic derangements that underlie clinical instability. Thyroid function tests should form part of the initial evaluation because coexisting thyroid disease commonly coexists with autoimmune adrenal disorders and because thyroid hormone replacement may alter cortisol requirements [63]. The classic laboratory constellation observed in adrenal crisis reflects the combined loss of glucocorticoid and, in primary disease, mineralocorticoid activity. Hyponatremia frequently occurs due to renal sodium wasting and inappropriate antidiuretic hormone activity. Hyperkalemia reflects aldosterone deficiency and predicts primary adrenal cortical failure. Hypoglycemia arises from impaired hepatic gluconeogenesis and diminished counterregulatory responses and is particularly prevalent and clinically consequential in pediatric populations. Elevated serum creatinine and blood urea nitrogen commonly identify prerenal azotemia produced by volume depletion and

reduced renal perfusion. Hypercalcemia may be present and can be multifactorial in origin, stemming from volume contraction, increases in biologically active vitamin D, or alterations in bone turnover described elsewhere in the pathophysiology literature [28][50][51]. Normocytic normochromic anemia with relative lymphocytosis and eosinophilia often accompanies glucocorticoid deficiency because cortisol normally suppresses eosinophil counts. An unanticipated preservation or elevation of eosinophil levels in a hemodynamically unstable patient should raise suspicion for adrenal insufficiency, since an intact stress response would typically produce eosinopenia. Renin activity is commonly elevated in primary adrenal failure owing to renal sodium loss and reduced effective arterial volume, whereas aldosterone is inappropriately low for the degree of hypotension and hypovolemia in such cases. ACTH concentrations provide critical discriminative value: elevated or high normal ACTH favors primary adrenal failure while low or low normal ACTH suggests central causes [15].

Clinical practice mandates that laboratory assessment serve diagnostic and management functions without imposing treatment delay. If logistical constraints permit, blood for cortisol and ACTH should be drawn immediately prior to steroid administration, but empirical parenteral hydrocortisone should be given when clinical suspicion is high because prompt replacement materially alters survival [64]. Performing dynamic testing such as the ACTH stimulation test in the acute unstable patient is not recommended until the patient is hemodynamically stabilized and the clinical picture has clarified. Once stabilization is achieved, stimulation testing and further endocrine evaluation can refine the diagnosis and guide long term replacement strategies [64]. Adjunctive diagnostic studies complement biochemical testing and aid in identifying precipitating causes or anatomic pathology. An electrocardiogram frequently provides rapid, actionable information; hyperkalemia may manifest as peaked T waves and widened QRS complexes, whereas marked hypercalcemia occasionally shortens the QT interval. Surveillance for occult infection as a common precipitant of crisis requires blood cultures, urinalysis with culture, and chest radiography. Cross sectional abdominal imaging, preferably computed tomography, is indicated when adrenal hemorrhage is suspected because it may reveal hemorrhagic enlargement, adrenal calcification consistent with prior tuberculosis, or focal masses suggestive of metastatic disease. In the context of secondary adrenal insufficiency, neuroimaging of the sella turcica using computed tomography or magnetic resonance imaging may disclose pituitary macroadenomas, infiltrative disease, or features of empty sella that explain central ACTH deficiency [65].

Interpretation of laboratory abnormalities must be integrated with the clinical context because single values often carry limited specificity. For example, hyponatremia in adrenal crisis may reflect a mixture of salt loss from mineralocorticoid deficiency and water retention due to inappropriate ADH. Hyperkalemia becomes most diagnostic when present in conjunction with hypotension, hyperreninemia, and low aldosterone levels. Hypoglycemia should trigger immediate correction because it compounds neurologic risk and may be the dominant presenting abnormality in infants and children. The presence of thyroid axis abnormalities should prompt careful deliberation before replacement therapy; the Society for Endocrine Emergency Guidelines advises against initiating thyroid hormone unless the TSH exceeds 10 mU/L because exogenous thyroxine can increase cortisol clearance and precipitate deterioration in untreated adrenal insufficiency [15]. Laboratory monitoring extends beyond the initial diagnostic phase and informs ongoing resuscitation and replacement. Serial measurements of serum electrolytes, creatinine, glucose, and acid base status guide fluid and electrolyte management. Trends in inflammatory markers and microbiologic results guide the search for infectious precipitants and the need for antimicrobial therapy. Repeat endocrine testing after stabilization, including formal ACTH stimulation testing, allows definitive classification of the adrenal disorder and supports tailored long term endocrine follow up [64]. In summary, evaluation of suspected adrenal crisis combines an urgent, focused laboratory strategy with targeted imaging and bedside studies. Clinicians must obtain essential hormonal and metabolic data expeditiously while initiating empiric parenteral glucocorticoid therapy when indicated. Additional investigations to identify precipitating causes and to differentiate primary from central adrenal failure should proceed in parallel, with dynamic endocrine testing deferred until after clinical stabilization [63][15][64][65].

Treatment / Management

An adrenal crisis constitutes a life threatening endocrine emergency that requires immediate recognition, aggressive supportive care, and prompt hormone replacement, ideally within an intensive care environment given the potential for rapid hemodynamic deterioration and multiorgan dysfunction [66]. The cornerstone of therapy is prompt parenteral glucocorticoid administration, with hydrocortisone recognized as the agent of choice because it combines potent glucocorticoid activity with mineralocorticoid effect at physiologic and stress doses; when clinical suspicion is high in a patient with known adrenal insufficiency or in any unstable patient in whom adrenal failure is plausible, empiric administration of stress dose steroids should not be delayed for confirmatory testing [66]. For adults the widely accepted regimen begins with an immediate

100 mg bolus of hydrocortisone given intravenously or intramuscularly, followed by either repeated doses totaling 200 mg over the subsequent 24 hours, commonly administered as 50 mg every six hours, or as a continuous intravenous infusion delivering an equivalent total daily dose; isotonic crystalloid resuscitation should accompany steroid replacement, with an initial bolus of 1 liter of normal saline or of 5 percent dextrose in 1 liter of normal saline followed by guided maintenance fluids according to hemodynamic response and laboratory indices [3].

	Acute management	Discharge planning
Adrenal crisis	• IV crystalloids • 100 mg IV hydrocortisone followed by 50-100 mg of IV hydrocortisone every 6 hours[11]	• Education on the signs and symptoms of adrenal insufficiency and adrenal crisis • Consider prescription of rescue steroids • Medic-Alert bracelet to inform possibility of adrenal insufficiency • Endocrinology referral • Determine feasibility of opioid taper
Chronic OIAI	• Hydrocortisone 15-20mg per 24 hours in 2-3 divided doses. • If borderline abnormal CST, consider 10mg daily or stress doses only with close monitoring[11] • Stress dosing for severe illness, surgery, or trauma • Endocrinology consult	

Figure-3: Adrenal Crisis Management.

Pediatric management adapts dosing to body surface area and physiologic requirements, with an initial hydrocortisone dose of 50 to 100 mg per square meter administered intravenously or intramuscularly, followed by an additional 50 to 100 mg per square meter distributed over the next 24 hours either in divided boluses every six hours or via continuous infusion, and with fluid resuscitation commencing with 20 milliliters per kilogram of isotonic saline and repeated as necessary to a cumulative 60 milliliters per kilogram within the first hour while addressing hypoglycemia with dextrose at 0.5 to 1 gram per kilogram when indicated [31][67]. Parallel to hormone and volume replacement, management requires frequent assessment of electrolyte status, glucose, acid base balance, and renal perfusion, with correction of hyperkalemia, hyponatremia, and hypoglycemia guided by standard critical care protocols. Early involvement of endocrinology optimizes diagnostic evaluation, guidance on the need for mineralocorticoid replacement, and the transition from acute parenteral therapy to an appropriate maintenance regimen. Mineralocorticoid replacement with fludrocortisone is not routinely required during the acute phase when hydrocortisone is provided at stress doses that exceed 50 mg daily, because hydrocortisone exerts sufficient mineralocorticoid activity at those doses; the need for fludrocortisone should be reassessed once the glucocorticoid dose is tapered to maintenance levels and in consultation with endocrine specialists [70]. Contemporary evidence favors continuous intravenous hydrocortisone infusion over intermittent bolus dosing for achieving stable plasma cortisol profiles and for reducing temporal fluctuations in hemodynamic and metabolic parameters [68]; continuous infusion facilitates titration to physiologic targets and may simplify the transition to oral replacement as clinical improvement ensues. Once the patient demonstrates sustained hemodynamic stability and metabolic recovery, a planned, gradual taper of glucocorticoid dosing should commence to avoid recurrent insufficiency and to permit endocrine reassessment [69].

When hydrocortisone is unavailable or contraindicated, alternative parenteral glucocorticoids may be employed with attention to relative glucocorticoid potency and lack of mineralocorticoid activity; prednisolone may be given as an initial bolus of 25 mg followed by two additional 25 mg doses within the first 24 hours and an ongoing equivalent daily prednisone regimen approximating 50 mg total, methylprednisolone may be administered at approximately 40 mg every 24 hours, and dexamethasone may be used at 4 mg every 24 hours though it is the least preferred option because it lacks mineralocorticoid effect and complicates subsequent biochemical testing for cortisol and ACTH [3][31]. Concomitant management must address and treat identifiable precipitants; when infection precipitates adrenal crisis, timely empiric antimicrobial therapy matched to the suspected source and local resistance patterns is essential while cultures and other diagnostic studies are obtained. Supportive measures include vasopressor therapy for refractory hypotension after volume optimization, ventilatory support when respiratory failure occurs, renal support for severe azotemia, and close monitoring for complications such as adrenal hemorrhage or coagulopathy. Finally, discharge planning should include education on stress dosing, provision of emergency injectable hydrocortisone for home use when appropriate, written action plans, and coordination for endocrinology follow up to define long term replacement needs and to mitigate the risk of recurrent crisis.

Differential Diagnosis

An adrenal crisis presents with a constellation of nonspecific systemic signs that overlap with many acute medical conditions; clinicians must therefore maintain a broad differential while prioritizing rapid identification of life threatening causes. Hypotension that is refractory to conventional fluid resuscitation and vasopressor therapy constitutes a cardinal clinical clue that should prompt immediate consideration of adrenal crisis, particularly in patients with a known history of adrenal insufficiency or recent glucocorticoid exposure [71]. The presenting symptom complex often includes altered mental status, gastrointestinal symptoms such as nausea vomiting and abdominal pain, fever, and generalized weakness. These features are shared by multiple syndromes that cause circulatory collapse metabolic derangement or acute inflammatory responses and discriminating adrenal crisis from these

alternatives rests on integrating historical signals medication exposures biochemical abnormalities and the pattern of hemodynamic response to standard therapies [5].

Shock of any etiology occupies the initial tier of the differential diagnosis because the hemodynamic profile may be indistinguishable at first evaluation. Hypovolemic shock due to hemorrhage severe dehydration or massive fluid losses from gastrointestinal or renal sources must be excluded by focused history physical examination and point of care assessments including bedside ultrasonography and measurement of hemoglobin and lactate. Cardiogenic shock resulting from acute myocardial dysfunction or mechanical cardiac complications produces hypotension often accompanied by pulmonary edema and elevated cardiac biomarkers and should be investigated through electrocardiography cardiac enzymes and transthoracic echocardiography. Obstructive shock due to pulmonary embolism tension pneumothorax or cardiac tamponade demands urgent imaging and invasive assessment because these conditions require specific mechanical interventions. Distributive shock including septic shock and anaphylaxis may mimic adrenal insufficiency with vasodilation and capillary leak; the presence of a clear infectious source severe leukocytosis or positive cultures supports sepsis while allergic stigmata or rapid bronchospasm localize anaphylaxis [5].

Endocrine emergencies enter the differential when metabolic perturbations predominate. Thyrotoxicosis can precipitate circulatory collapse with fever and agitation and is accompanied by suppressed TSH and elevated free thyroid hormones. Diabetic emergencies such as diabetic ketoacidosis or the hyperosmolar hyperglycemic state present with profound dehydration acid base disturbance or severe hyperglycemia and are distinguished by characteristic laboratory profiles and ketone bodies. Myxedema coma, the extreme manifestation of hypothyroidism, may simulate adrenal crisis through altered mental status hypothermia and hyponatremia but typically evolves more indolently and features markedly low thyroid hormone levels. Pituitary apoplexy or expanding sellar masses may present acutely with headache visual disturbance and central adrenal insufficiency; neuroimaging and assessment of other pituitary axes help differentiate central causes from primary adrenal failure [71]. Gastrointestinal disorders frequently mimic adrenal crisis because abdominal pain vomiting and fever are common to both. An acute surgical abdomen such as appendicitis diverticulitis or intestinal obstruction may dominate the clinical picture and necessitate rapid surgical evaluation. Severe gastroenteritis and prolonged poor oral intake provoke hypovolemia and electrolyte imbalance that can unmask adrenal insufficiency or independently cause hypotension. Careful abdominal examination laboratory assessment and appropriate imaging are essential to avoid missing a surgical cause.

Hematological, oncologic and metastatic processes must be considered. Adrenal metastases from melanoma breast lung or other cancers can produce progressive adrenal destruction and eventual insufficiency; imaging may reveal bilateral adrenal masses or hemorrhagic transformation. The history of immune checkpoint inhibitor therapy heightens suspicion for autoimmune, or treatment induced hypophysitis or primary adrenalitis and obliges prompt endocrine evaluation. Coagulopathy or anticoagulant therapy raises the risk of bilateral adrenal hemorrhage, a catastrophic cause of sudden adrenal failure that may present abdominal or flank pain and rapid hemodynamic decline [71]. Obstetric considerations include hyperemesis gravidarum and pregnancy associated physiologic changes that alter cortisol binding and demand. Pregnant patients may require adjusted diagnostic thresholds and prompt endocrinology involvement because third trimester stressors and labor can precipitate decompensation. Infectious precipitants ranging from localized bacterial infections to systemic sepsis and emerging viral pathogens must be assessed and treated concurrently if present. Finally psychological stress severe trauma and recent major surgery are common precipitants that may reveal previously compensated adrenal insufficiency. The clinician must synthesize medication history including chronic glucocorticoid use topical or inhaled steroids enzyme inducing drugs and agents that alter cortisol metabolism because iatrogenic suppression or drug interactions can mimic or precipitate adrenal crisis. Laboratory patterns such as hyponatremia hyperkalemia hypoglycemia elevated renin and discrepant ACTH values provide discriminating data that reorient the differential away from alternative diagnoses and toward adrenal insufficiency. Given the high mortality associated with missed or delayed treatment clinicians should adopt a low threshold for empiric glucocorticoid administration while concurrently pursuing the above differential considerations and targeted diagnostic studies [5][71].

Prognosis

The prognosis of adrenal crisis depends largely on the speed of diagnosis and the immediacy of treatment initiation. Although timely administration of intravenous glucocorticoids and aggressive fluid resuscitation can lead to full recovery, mortality remains high, primarily due to delays in recognition and intervention. The condition's rarity contributes to this persistent challenge, as many healthcare professionals lack routine exposure to adrenal crisis cases and may not promptly identify its presentation or appreciate its life-threatening potential. A retrospective analysis conducted in the United Kingdom reported that adrenal crisis accounted for approximately 10% of all deaths among individuals

diagnosed with primary or secondary adrenal insufficiency, underscoring the ongoing need for clinical vigilance and system-level preparedness [72]. Patients whose adrenal crisis is promptly recognized and treated with intravenous fluids and parenteral hydrocortisone typically demonstrate rapid clinical improvement and favorable recovery outcomes. Restoration of hemodynamic stability, correction of electrolyte disturbances, and reversal of metabolic abnormalities can occur within hours after proper therapy is initiated. However, the prognosis worsens substantially in cases where diagnosis is delayed, treatment is inadequate, or the patient presents in a state of advanced circulatory collapse or coma.

Mortality risk is significantly higher in patients with severe comorbidities or coexisting endocrine dysfunctions such as uncontrolled diabetes mellitus or thyroid disease, as these conditions compound metabolic instability. Individuals with recurrent adrenal crises, chronic infections, or poor adherence to maintenance steroid therapy also exhibit poorer outcomes. Cognitive impairment and functional decline may persist in survivors who experienced prolonged hypotension or hypoglycemia during the acute event, and these patients often require structured rehabilitation, including physical or occupational therapy, to restore baseline functional capacity. Preventive strategies have a direct impact on long-term prognosis. Patient education regarding the need for stress-dose steroid adjustments during illness or surgery, the availability of emergency hydrocortisone injections, and adherence to maintenance therapy significantly reduce recurrence and mortality. Regular endocrinology follow-up and the use of medical alert identification facilitate early intervention during emergencies. Despite therapeutic advances, adrenal crisis continues to represent a preventable cause of death among individuals with adrenal insufficiency, highlighting the critical importance of rapid recognition, appropriate emergency management, and lifelong preventive care [72].

Complications:

An adrenal crisis represents one of the most severe medical emergencies in endocrinology, capable of producing fatal outcomes even when recognized and treated promptly [2]. The range of complications associated with adrenal crisis extends far beyond immediate hemodynamic instability. The profound hormonal imbalance precipitates a cascade of metabolic and systemic effects that can culminate in multi-organ dysfunction. Electrolyte abnormalities, particularly hyponatremia, hyperkalemia, and hypoglycemia, are among the most prominent and clinically dangerous consequences. Severe hyponatremia may lead to cerebral edema and seizures, while hyperkalemia poses a substantial risk of cardiac arrhythmias and sudden cardiac arrest. Persistent or profound hypoglycemia can result in confusion, convulsions, and coma, further complicating resuscitative efforts and increasing the likelihood of neurological sequelae [71]. When hypotension remains untreated, prolonged tissue hypoperfusion can induce ischemic injury in vital organs. This can lead to acute kidney injury, hepatic dysfunction, myocardial ischemia, and ultimately multiple organ failure. In addition, the underlying precipitating cause—such as infection, trauma, or surgical stress—may independently contribute to systemic inflammatory responses, compounding the overall physiological insult [62]. Secondary complications, including disseminated intravascular coagulation, acute respiratory distress syndrome, or metabolic acidosis, may also develop in patients with protracted shock.

Beyond the acute episode, patients recovering from an adrenal crisis often face long-term complications that affect functional capacity and quality of life. Despite adherence to steroid replacement therapy, many individuals continue to experience residual fatigue, cognitive dysfunction, and emotional disturbances. Depression, chronic exhaustion, and reduced stress tolerance are frequently reported, limiting work capacity and social functioning. These issues significantly diminish overall life satisfaction and increase the risk of recurrent crises, especially in patients lacking consistent endocrinological follow-up or adequate education regarding stress-dose adjustments [73]. The mortality rate associated with adrenal crises remains unacceptably high despite advances in medical knowledge and treatment availability. Deaths are often linked to respiratory infections, cardiovascular events, and cerebrovascular accidents [1]. The underlying mechanism is thought to involve the additive effects of severe hypotension, metabolic derangements, and immune suppression caused by inadequate or delayed corticosteroid administration. Retrospective data have indicated a mortality rate of up to 6% among individuals who experienced an adrenal crisis, underscoring the persistent clinical challenge posed by delayed recognition and insufficient emergency intervention [19].

Patient dissatisfaction with emergency management of adrenal crisis remains considerable, reflecting ongoing deficiencies in healthcare system preparedness and professional awareness. A reported satisfaction rate of only 66% in patients treated for adrenal crisis in emergency departments highlights the need for improved clinical protocols and healthcare worker education [74]. This gap reinforces the importance of systematic patient training, provision of emergency steroid identification cards, and widespread access to injectable hydrocortisone kits. In summary, adrenal crisis carries the dual burden of immediate life-threatening complications and lasting impairment of health and quality of life. Effective prevention through early diagnosis, rapid initiation of glucocorticoid therapy, and structured patient education programs remains the cornerstone for

reducing both morbidity and mortality associated with this condition.

Patient Education

Patient education constitutes a principal strategy for reducing morbidity and mortality from adrenal crisis because many affected individuals lack a prior diagnosis and because timely self-management or early presentation to care alters outcomes [71]. Clinicians must provide clear, practical instruction that enables patients and caregivers to recognize early signs of adrenal insufficiency and to implement stress dosing without delay. Education should emphasize the sick day protocol whereby patients increase their baseline oral glucocorticoid during intercurrent illness or physiologic stress to approximate the normal cortisol surge that accompanies stress. Specific instructions should be given for febrile illnesses: patients should double their usual oral glucocorticoid dose for fevers above 100.4 °F (38 °C) and should triple the dose for fevers exceeding 102.2 °F (39 °C). Guidance must also cover noninfectious stressors that require dose escalation, including trauma, surgery, and other major procedures, and clinicians should provide explicit dose targets and routes for oral and parenteral administration when oral intake is compromised [23].

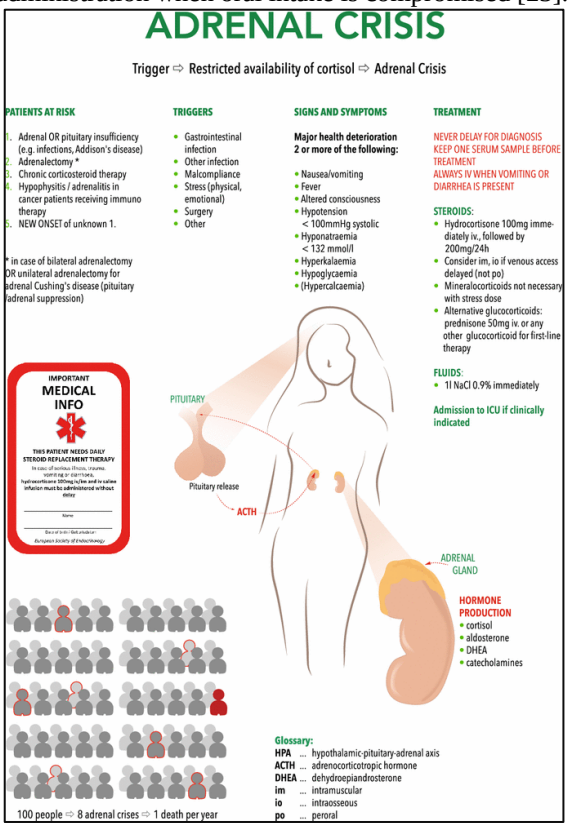

Figure-4: Understanding Adrenal Crisis.

Education should extend beyond numeric dose changes to practical skills; patients and caregivers must learn intramuscular injection technique for hydrocortisone or dexamethasone, how to prepare and use emergency saline for intravenous access when appropriate, and when to seek emergency care rather than attempt home management. Patients should be advised about transient increases in glucocorticoid requirements for intense emotional stressors and given a simple rule, such as a single additional 10 mg hydrocortisone dose in selected severe psychosocial events, while stressing that such measures do not replace medical evaluation when physiological symptoms develop [23]. Clinicians should review the spectrum of prodromal and acute symptoms to improve early recognition, including nausea, vomiting, abdominal pain, unexplained weight loss, dizziness or syncope, confusion, hypoglycemia, fever, and subjective deterioration in wellbeing, and they should instruct patients to act promptly when these symptoms occur. Identification tools must be provided; every patient with adrenal insufficiency should carry a steroid emergency card that documents the diagnosis, current replacement regimen, sick day rules, and precise parenteral dosing instructions—100 mg hydrocortisone IV or IM as an initial bolus followed by 200 mg over 24 hours given as 50 mg IV or IM every six hours—so that unfamiliar healthcare personnel can deliver appropriate, time sensitive therapy [15][69].

In addition to a written card, patients should wear medical alert identification that communicates adrenal insufficiency to first responders and emergency clinicians, because this simple identifier expedites empiric steroid administration during acute presentations when history taking is limited [31][69]. An emergency kit should be assembled and maintained in an accessible location at home and during travel; the kit should contain injectable hydrocortisone sodium succinate 100 mg vials or, when hydrocortisone is unavailable, parenteral dexamethasone 4 mg vials, sterile normal saline for reconstitution, appropriate syringes and needles, and clear stepwise instructions for reconstitution and intramuscular administration so that trained caregivers can act decisively in the event of vomiting or inability to tolerate oral therapy [15]. Education must address medication interactions and potential iatrogenic precipitants; patients should be counseled to inform all prescribers about their adrenal insufficiency, to avoid abrupt cessation of chronic glucocorticoids, and to alert clinicians when new drugs known to alter cortisol metabolism or synthesis are prescribed. Clinicians should provide tailored counseling for special circumstances such as pregnancy, major surgery, and intercurrent severe illness, and they should coordinate perioperative plans with surgical and anesthesia teams to ensure appropriate stress dosing and postoperative monitoring.

Regular reinforcement of education is essential; follow up with an endocrinologist should be scheduled at least annually for adults and every three to six months for children to reassess replacement regimens, to review sick day rules, and to update emergency plans as clinical circumstances change. Structured education programs that include written

materials, demonstration of injection technique, and opportunities for patients to rehearse emergency scenarios improve retention and self-efficacy and reduce preventable crises. Finally, system level measures complement individual education: clinicians should provide clear documentation in electronic health records, issue emergency letters for travel, and liaise with primary care and emergency services so that emergency steroid protocols are known and can be enacted rapidly. Patient education therefore must be comprehensive, practical, and repetitive, combining symptom awareness, concrete sick day rules, competency in parenteral administration, provision of emergency supplies and identification, and scheduled specialist follow up to reduce the incidence and severity of adrenal crises and to improve long term outcomes [71][23][15][69].

Other Issues

Clinicians must maintain a high index of suspicion for adrenal crisis in any patient who presents with circulatory collapse that remains refractory to adequate fluid resuscitation and vasopressor therapy. Refractory hypotension despite appropriate initial resuscitative measures is a cardinal clinical clue that should prompt immediate consideration of cortisol deficiency, particularly in older patients and in those with multiple comorbid conditions or coexisting endocrine disorders. Altered mental status in the context of endocrine disease portends a higher risk of adverse outcome and should lower the threshold for empiric glucocorticoid administration. Prompt recognition is essential because the clinical trajectory of untreated adrenal insufficiency may be rapid and progressive. Biochemical abnormalities provide additional diagnostic guidance but should not delay therapy. The concurrence of hyponatremia, hyperkalemia, and hypoglycemia with hypotension raises strong suspicion for primary adrenal cortical failure, whereas isolated hypotension with low to normal potassium may indicate central causes. The presence of electrolyte derangements consistent with mineralocorticoid deficiency should immediately orient management toward parenteral hydrocortisone while concurrent diagnostic evaluation proceeds. Clinicians should draw appropriate blood samples for cortisol, ACTH, electrolytes, glucose, and renal indices at the earliest opportunity, but obtaining these investigations must not postpone the administration of 100 mg hydrocortisone IV or IM when the clinical probability of crisis is high [76].

Understanding etiologic categories refines both diagnostic reasoning and therapeutic priorities. Primary adrenal insufficiency results from direct adrenal destruction with biochemical features of low cortisol and elevated ACTH and, commonly, aldosterone deficiency manifested by sodium loss and potassium retention. Secondary adrenal insufficiency results from deficient pituitary ACTH output and presents with low cortisol and low to normal ACTH, while mineralocorticoid function is typically preserved. Structural, infectious, hemorrhagic, infiltrative, and autoimmune processes can produce primary failure. Central etiologies include pituitary adenomas, hypophysitis, and other lesions that disrupt ACTH secretion. Recognition of the underlying category informs decisions about mineralocorticoid replacement, the need for neuroimaging, and the anticipated course of recovery [76].

An ACTH stimulation test may be useful for diagnostic clarification once the patient is clinically stable, but dynamic testing in the acute unstable patient is not appropriate because it may delay lifesaving therapy. Similarly, thyroid hormone replacement should be avoided in patients with suspected untreated adrenal insufficiency until appropriate glucocorticoid coverage has been established. The clinician must therefore sequence interventions to prioritize hemodynamic stabilization and replacement of deficient corticosteroids before pursuing corrective endocrine therapies that might increase metabolic demand. Awareness of precipitating factors is critical for prevention and for targeted management. Gastrointestinal infections are among the most common proximate triggers, but any physiologic stressor—from trauma and surgery to severe emotional distress—can exceed a reduced cortisol reserve and precipitate crisis. Adrenal crisis may present in patients with a prior diagnosis of adrenal insufficiency who fail to implement stress dosing, in patients who abruptly stop exogenous glucocorticoids, and in individuals who carry no prior diagnosis and whose first manifestation is acute decompensation. Medication interactions that alter cortisol synthesis or metabolism and anticoagulant related adrenal hemorrhage represent iatrogenic pathways to abrupt adrenal failure and must be actively considered during evaluation [76].

Patient and caregiver education forms a central pillar of long term management and prevention. Instruction on stress dose rules, recognition of early symptomatic changes, carriage of medical alert identification and an emergency steroid card, and competency intramuscular injection for emergency hydrocortisone are practical measures that reduce the incidence of preventable crises. Regular endocrinology follow up, and multidisciplinary coordination ensure that perioperative and intercurrent illness plans are in place and that medication changes that affect the hypothalamic pituitary adrenal axis are managed proactively. Finally, optimal care depends on a team approach. Emergency clinicians, intensivists, endocrinologists, pharmacists, nurses, and primary care providers must coordinate assessment, stabilization, diagnostic evaluation, and discharge planning. Pathways that facilitate rapid empiric steroid administration, parallel diagnostic testing, and clear communication about stress dosing during transitions of care improve outcomes. Institutional readiness, clinician education, and patient empowerment together reduce diagnostic delay and mitigate the

substantial morbidity and mortality associated with adrenal crisis [76].

Enhancing Healthcare Team Outcomes

The management of adrenal crisis requires the combined expertise of family medicine physicians, emergency medicine specialists, and nursing professionals, supported by pharmacists and endocrinologists. The complexity and rapid progression of this condition demand precise coordination and shared clinical responsibility among all team members. Each discipline contributes specific functions that collectively determine the quality and outcome of care. In the emergency setting, early recognition and rapid intervention form the cornerstone of management. Emergency physicians are often the first to evaluate patients presenting with unexplained hypotension, hypoglycemia, or altered consciousness. Their primary role involves immediate clinical stabilization through intravenous fluids, administration of parenteral hydrocortisone, correction of electrolyte imbalances, and management of potential precipitating factors. They must maintain a high degree of suspicion for adrenal crisis in patients with refractory shock unresponsive to standard resuscitative measures. Timely diagnosis prevents irreversible organ failure and death. Emergency physicians also ensure effective communication with endocrinology and critical care services for ongoing management. Their vigilance and rapid clinical judgment are decisive in improving survival and reducing complications associated with adrenal crisis [76].

Nursing professionals represent the foundation of continuous monitoring and patient support during all phases of care. In the acute phase, nurses maintain close observation of vital signs, mental status, urine output, and hemodynamic parameters. They play a direct role in fluid management, drug administration, and immediate response to changes in patient condition. Critical care and emergency nurses are instrumental in recognizing early deterioration, preventing complications such as hypoglycemia and severe hypotension. Their clinical vigilance facilitates early intervention before irreversible shock develops. In addition to technical roles, nurses provide education to patients and families about long-term management. They teach the importance of adherence to steroid replacement therapy, the necessity of stress dosing during illness, and the recognition of early warning symptoms. By ensuring comprehension of these preventive strategies, nurses reduce the recurrence of adrenal crises and hospital readmissions. Family medicine physicians provide continuity and preventive care after the acute crisis is resolved. Their role extends beyond treatment to long-term management, monitoring, and education. They oversee follow-up visits to evaluate recovery, optimize glucocorticoid and mineralocorticoid dosing, and manage comorbid conditions such as diabetes or thyroid disorders that may exacerbate adrenal instability. They identify psychosocial barriers that affect adherence and coordinate with endocrinologists for medication adjustments. Family physicians also ensure that patients and their families understand the importance of medical alert identification, emergency hydrocortisone injection kits, and preventive measures during intercurrent illnesses. Their involvement bridges the gap between hospital care and community management, ensuring continuity and reducing the likelihood of recurrent crises [76].

Pharmacists play an essential supportive role by ensuring appropriate medication selection, dosing, and patient counseling. They educate patients on avoiding abrupt cessation of corticosteroids, potential side effects, and interactions with other drugs that may impair cortisol metabolism. Their collaboration with physicians enhances medication safety and prevents avoidable adverse events. Effective interprofessional collaboration strengthens all these efforts. Clear communication between emergency physicians, nurses, family physicians, and endocrinologists ensures a unified approach that minimizes delays in diagnosis and treatment. Shared documentation systems and structured communication protocols improve accuracy and efficiency, preventing duplication or omission of care. Ethical practice underpins this teamwork. Each professional upholds informed consent, patient autonomy, and confidentiality. The integration of these principles into clinical decisions supports trust and compliance, which are critical in managing a chronic, life-threatening condition like adrenal insufficiency. When executed effectively, this team-based model yields measurable benefits. Mortality rates decline due to faster recognition and intervention. Readmission rates drop as patients become more informed and self-sufficient. Medication adherence improves through coordinated counseling. Quality of life increases as patients regain stability and confidence in managing their condition. Thus, the collaboration between emergency medicine, nursing, and family medicine forms the structural core of adrenal crisis management. Their shared commitment to vigilance, communication, and patient education transforms a potentially fatal endocrine emergency into a manageable and preventable condition, advancing both patient outcomes and the overall quality of healthcare delivery [76].

Conclusion:

In conclusion, adrenal crisis is a time-sensitive, fatal endocrine emergency whose successful management hinges on a seamless, integrated approach across healthcare disciplines. The cornerstone of treatment is the immediate administration of parenteral hydrocortisone and vigorous fluid resuscitation, which can rapidly reverse the life-threatening hemodynamic and metabolic collapse. However, the persistent

mortality associated with this condition underscores critical gaps in recognition and system-level preparedness. To mitigate this, a high clinical index of suspicion is essential, particularly for patients with known adrenal insufficiency, those on chronic glucocorticoids, or any individual presenting with unexplained, refractory shock. Beyond acute intervention, long-term prevention is paramount. This relies on comprehensive patient education delivered by an interprofessional team, ensuring patients and caregivers understand "sick day rules," can administer emergency injections, and consistently use medical alert identifiers. The collaborative efforts of emergency physicians, nurses, family doctors, and endocrinologists are vital to bridge the gap between acute emergency care and sustained community management. Ultimately, enhancing outcomes requires a unified strategy that combines rapid clinical response with robust preventive education and follow-up, transforming a potentially catastrophic event into a manageable condition.

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