How to Cite:
Alfawaz, F. S., Alsaadi, M. M., Alotaibi, S. S., Al Anazi, N. A., Alotaibi, A. B., Al-Arej, I. M., Alsayegh, A. S., Alduaybi, M. A., Al Owias, M. I. Z., Alnughaymishi, A. A. S., Aldawsari, H. F. H., Alqahtani, A. S., Alanezi, B. S., & Al-Shuwayman, A. A. (2021). Cushing's syndrome: An in-depth review of pathophysiology, diagnosis, and manifestations. *International Journal of Health Sciences*, *5*(S1), 1388–1402.
https://doi.org/10.53730/ijhs.v5nS1.15303

Cushing's syndrome: An in-depth review of pathophysiology, diagnosis, and manifestations

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International Journal of Health Sciences E-ISSN 2550-696X © 2021.
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Manuscript submitted: 01 Jan 2021, Manuscript revised: 09 Jan 2021, Accepted for publication: 15 Jan 2021

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***Abstract*---Background:** Cushing's syndrome results from prolonged exposure to elevated glucocorticoids, leading to significant morbidity and mortality. Despite its historical identification over a century ago, challenges remain in diagnosing and treating this condition due to its non-specific symptoms and complex underlying mechanisms. **Aim:** This review aims to elucidate the pathophysiology, diagnostic approaches, and treatment options for Cushing's syndrome to enhance clinician understanding and improve patient outcomes. **Methods:** A comprehensive literature review was conducted, synthesizing data on the etiology, classification, and epidemiology of Cushing's syndrome. The review categorized Cushing's syndrome into ACTH-dependent and ACTH-independent forms, highlighting diagnostic challenges and therapeutic strategies, including surgical, medical, and radiation options. **Results:** The findings reveal that Cushing's syndrome predominantly arises from either endogenous factors (e.g., pituitary adenomas, ectopic ACTH production) or exogenous glucocorticoid use. ACTH-dependent Cushing's disease accounts for the majority of cases, particularly in women aged 25-40. The review also identifies key diagnostic tools, including biochemical tests and imaging studies, and discusses the importance of recognizing both overt and subtle clinical presentations. **Conclusion:** Cushing's syndrome remains a complex endocrine disorder requiring a multifaceted approach for accurate diagnosis and effective management. Continued research is necessary to better understand its pathophysiological mechanisms and to develop improved treatment strategies tailored to individual patient needs.

***Keywords*---**Cushing's syndrome, glucocorticoids, ACTH-dependent, ACTH-independent, diagnosis, treatment options.

Introduction

Extended exposure to increased blood levels of glucocorticoids causes Cushing's syndrome. The classical clinical condition that bears Harvey Cushing's name was first described more than a century ago. Even the most experienced endocrinologists still face difficulties in diagnosing and treating this illness. Even though the diagnosis is frequently obvious in its most severe form, clinicians must take the diagnosis into consideration in its early stages due to the prevalence of numerous non-specific symptoms, such as depression, muscle weakness, and obesity. Over the past century, the wide range of tests needed for diagnosis and differential diagnosis has increased, necessitating careful

interpretation. The metabolic disturbance linked to Cushing's syndrome is associated with a markedly elevated risk of death when it is severe and left untreated. However, subtler increases in cortisol can also have a significant effect on blood pressure and glycemic control, which may result in significant morbidity. The treatment of Cushing's syndrome is often complex and may involve a number of strategies, such as medication, surgery, and radiation therapy.

Pathophysiology, etiology, and epidemiology:

In normal physiological functioning, the ultimate product of the hypothalamo-pituitary-adrenal (HPA) axis is the glucocorticoid cortisol, which is secreted from the zona fasciculata of the adrenal gland in response to adrenocorticotrophin (ACTH) released from the pituitary gland. The secretion of ACTH is stimulated by corticotrophin-releasing hormone (CRH) and vasopressin from the hypothalamus. Cortisol exerts negative feedback on both CRH and vasopressin in the hypothalamus, as well as on ACTH in the pituitary gland. In healthy individuals, cortisol levels exhibit a circadian rhythm, peaking between 07:00 and 08:00, decreasing throughout the day, reaching their lowest point around midnight, and beginning to rise again at 02:00. The disruption of this circadian rhythm, along with the loss of the normal feedback mechanisms of the HPA axis, leads to chronic exposure to elevated circulating cortisol levels, resulting in the clinical manifestation of endogenous Cushing's syndrome (1, 2). Additionally, the administration of various synthetic steroids with glucocorticoid activity in excessive amounts can result in exogenous Cushing's syndrome. This form is the most prevalent cause of Cushing's syndrome encountered in clinical practice, often resulting from treatment for chronic conditions such as asthma or rheumatological diseases. Clinicians must diligently investigate for exogenous sources of corticosteroids, which may be delivered through topical, inhaled, or injected routes. The etiology of Cushing's syndrome can be broadly categorized into two groups: ACTH-dependent and ACTH-independent.

ACTH-dependent forms are characterized by excessive production of ACTH, stimulating all three layers of the adrenal cortex, which leads to bilateral adrenal hyperplasia and hypertrophy. This results in an increased adrenal weight, often displaying micronodular or, at times, macronodular changes. As a consequence, there is an elevation in circulating glucocorticoids, typically accompanied by a lesser increase in serum androgens.

ACTH-independent forms represent a heterogeneous collection of conditions characterized by low plasma ACTH levels, either due to adrenal glucocorticoid hypersecretion or as a result of the exogenous administration of glucocorticoids. Apart from adrenal adenomas—which primarily secrete glucocorticoids—other endogenous adrenal conditions typically show elevated levels of androgens and sometimes steroid precursors. The microscopic and macroscopic characteristics of unaffected adrenal tissue largely depend on the underlying etiology of the disorder. Cushing's syndrome can be classified based on its underlying causes into ACTH-dependent and ACTH-independent categories. The **ACTH-dependent** forms include pituitary-dependent Cushing's syndrome, also known as Cushing's disease, which arises from excessive ACTH production by the pituitary gland. Other ACTH-dependent causes involve ectopic ACTH syndrome, where ACTH is

produced by non-pituitary tumors, and ectopic CRH syndrome, which is extremely rare. Additionally, there may be cases of exogenous ACTH administration contributing to this syndrome. In contrast, the **ACTH-independent** forms are characterized by conditions that do not involve elevated ACTH levels. These include adrenocortical adenoma and adrenocortical carcinoma, which are tumors of the adrenal cortex. Another condition, known as ACTH-independent bilateral macronodular adrenal hyperplasia (AIMAH), is now referred to as bilateral macronodular adrenocortical disease (BMAD) (3). Other examples include idiopathic micronodular adrenocortical disease (i-MAD) and primary pigmented (micro)nodular adrenocortical disease (PPNAD), which can be associated with the Carney complex (c-PPNAD) or occur idiopathically (i-PPNAD). McCune-Albright syndrome and the administration of exogenous glucocorticoids also contribute to the development of Cushing's syndrome.

ACTH-Dependent Cushing's Syndrome
Cushing's Disease:

Pituitary-dependent Cushing's syndrome, commonly referred to as Cushing's disease, is the predominant cause of endogenous Cushing's syndrome, representing 60-80% of all cases. Epidemiological studies conducted in Europe indicate an incidence ranging from 0.7 to 2.4 cases per million annually (4, 5). This condition is notably more prevalent in women, typically occurring in individuals aged 25 to 40. Cushing's disease is almost exclusively attributed to a corticotroph adenoma (6, 7). While instances of apparent nodular corticotroph hyperplasia (in the absence of a CRH-producing tumor) have been reported, these are rare in extensive surgical series (8, 9), and the existence of such cases remains contentious. Most tumors identified are intrasellar microadenomas, measuring less than 1 cm in diameter, although macroadenomas comprise approximately 5-10% of cases, with potential for extrasellar extension or invasion. Cases of genuine pituitary corticotroph carcinomas, which present with extra-pituitary metastases leading to Cushing's syndrome, have also been infrequently documented (10, 11).

Despite extensive investigation, the molecular pathogenesis underlying corticotroph adenomas is still not fully understood, although current evidence leans toward a primary pituitary disorder rather than a hypothalamic one (12). Recent findings suggest that about one-third of these adenomas are attributed to a somatic mutation that causes the constitutive activation of USP8, a deubiquitinase that enhances the expression of the EGF receptor on corticotroph cells (13). Additionally, corticotroph adenomas can occasionally be linked to familial syndromes, including MEN1, MEN2, Carney Complex, or familial isolated pituitary adenoma syndrome, associated with mutations in the menin gene (MEN1), the RET oncogene, PRKR1A, and the AIP gene, which codes for aryl hydrocarbon receptor-interacting protein (14). Very rarely, Cushing’s disease has been observed in patients with McCune-Albright and Beckwith-Wiedemann syndromes, where ACTH-independent Cushing’s syndrome is more prevalent. Up to 40% of older individuals with long-standing Cushing’s disease may develop ACTH-dependent macronodular adrenocortical hyperplasia. In these cases, the adrenal glands often appear enlarged, occasionally exhibiting prominent nodules, but invariably show signs of internodular hyperplasia (15, 16). ACTH levels in

these patients may be lower than expected, and the resolution of hypercortisolemia can be delayed following the apparent removal of the pituitary tumor.

Ectopic ACTH Syndrome and Ectopic CRH Tumors

The majority of remaining cases of endogenous ACTH-dependent Cushing's syndrome, aside from Cushing's disease, are linked to non-pituitary tumors that secrete ACTH, collectively known as ectopic ACTH syndrome. Ectopic ACTH production arises from a variety of tumor types, which can be categorized into two broad groups: highly malignant carcinomas and less aggressive neuroendocrine tumors. However, it is important to recognize that this classification represents a spectrum rather than a strict dichotomy. In endocrine center investigations, where more subtle tumors are often examined, the predominance of bronchial neuroendocrine tumors becomes apparent, accounting for up to 25% of ectopic ACTH-dependent Cushing's syndrome cases. Following these, small-cell lung carcinoma ranks second, responsible for approximately 19% of ectopic Cushing's syndrome occurrences (17-19). Additionally, around 16% of patients with ectopic ACTH sources remain unidentified and necessitate repeated imaging for diagnosis. The ectopic ACTH syndrome is observed more frequently in men and typically manifests after the age of 40, although it should always be considered as a potential diagnosis, even in pediatric patients.

Etiology of Ectopic ACTH Syndrome in Patients (17-19)
Tumor Type and Associated Percentages in Ectopic Cushing's Syndrome Cases

In a review of selected literature involving 398 cases, the following tumor types and their corresponding percentages of total reported cases of ectopic Cushing's syndrome are noted: lung carcinoma at 18.8%, bronchial neuroendocrine tumors at 25.4%, thymic neuroendocrine tumors at 7.3%, medullary cell carcinoma at 4.5%, pancreatic or gastrointestinal neuroendocrine tumors at 11.8%, pheochromocytoma/paraganglioma at 3.8%, neuroendocrine tumors of unknown primary origin at 6.0%, occult tumors at 16.1%, and miscellaneous malignant tumors at 6.3%. The precursor molecule for ACTH, pro-opiomelanocortin (POMC), is expressed not only in the normal pituitary gland but also in various normal extra-pituitary tissues, as well as in certain tumors, such as those found in the lung and testis (20). The precise mechanism through which these non-corticotroph tumors express the POMC gene remains incompletely elucidated, although it may be associated with hypomethylation of the POMC promoter (21, 22). Generally, these tumors produce greater amounts of POMC compared to ACTH, which differs from the production profile observed in Cushing's disease. In addition to synthesizing ACTH and POMC, these tumors may also generate other pre-ACTH precursor peptides, commonly referred to as "big" ACTH (23, 24). The presence of these peptides may aid in the differential diagnosis of these tumors (25); however, clinical assays for their detection are not routinely available. Isolated ectopic production of corticotropin-releasing hormone (CRH) is challenging to diagnose and is exceedingly rare, with only a limited number of confirmed cases documented in the literature (26). Typically, patients exhibiting

ectopic CRH secretion also produce ACTH, making the distinction between the two of minimal practical significance.

ACTH-Independent Cushing's Syndrome:

ACTH-independent causes of Cushing's syndrome, excluding exogenous glucocorticoids, encompass a diverse range of diseases. The predominant pathology associated with this condition is adrenal adenoma or carcinoma. Although adrenal carcinoma may exhibit atypical histological features that do not conform to classic malignancy criteria, it can generally be distinguished based on several factors, including weight (exceeding 100g), nuclear pleomorphism, necrosis, mitotic activity, and vascular or lymphatic invasion. These characteristics are included in the Weiss scoring system, which is utilized to differentiate between adenomas and carcinomas. Adrenal adenomas most frequently present around the age of 35 and are notably more prevalent in women, with an incidence rate of approximately 0.6 per million per year (5). In contrast, adrenal cancer has an incidence of roughly 0.2 per million per year (5) and is one and a half times more common in women. The age distribution for adrenal cancer is bimodal, peaking during childhood and adolescence as well as between 40 and 50 years (1, 27). Approximately 50-60% of adrenocortical carcinomas secrete adrenal hormones, with glucocorticoids and adrenal androgens being the most frequently produced (28).

Bilateral macronodular adrenocortical disease (BMAD), formerly referred to as ACTH-independent bilateral macronodular adrenal hyperplasia (AIMAH), represents a rare variant of Cushing's syndrome characterized by notably enlarged nodular adrenal glands (greater than 5 cm) with nodules exceeding 1 cm observable on imaging. Most cases of BMAD are sporadic, though a limited number of familial instances have been documented (29). The etiology remains largely unknown, but in some cases, the nodules have been shown to express elevated levels of receptors typically present on the adrenal gland or ectopic receptors that can stimulate cortisol production. Most patients present with subclinical Cushing's syndrome. A well-documented instance of this is food-dependent Cushing's syndrome, wherein ectopic glucose-dependent insulinotropic polypeptide (GIP) receptors on the adrenal glands respond to GIP released postprandially, leading to hypercortisolemia (30). Treatment with octreotide may alleviate the syndrome (31); however, its efficacy diminishes after a few months due to the down-regulation of somatostatin receptors in the intestine (32). Additionally, abnormal expression of various receptors, including vasopressin, β-adrenergic, luteinizing hormone/human chorionic gonadotropin, serotonin, angiotensin, leptin, glucagon, interleukin-1, and thyroid-stimulating hormone, has been described and linked functionally to cortisol production (32). BMAD tissue may express multiple aberrant receptors (33). Approximately one-third of patients with BMAD exhibit inactivating germline mutations in the tumor suppressor gene ARMC5 (armadillo repeat containing protein 5), with each nodule demonstrating additional independent hits in the same gene; familial forms of BMAD have also been identified (34). Heterozygous germline pathogenic variants in the KDM1A gene, which encodes lysine-specific demethylase 1, have been reported in GIP-dependent Cushing's syndrome associated with BMAD (35). Furthermore, germline mutations in MEN1, FH (fumarate hydratase gene), and

ACP (familial polyposis coli gene) have been discovered in some individuals with BMAD (36, 37).

Cushing's syndrome resulting from bilateral nodular adrenal disease can also be observed in McCune-Albright syndrome (38). This syndrome is characterized by fibrous dysplasia of bone, café-au-lait pigmentation of the skin, and endocrine dysfunction, which may involve hyperfunction of the pituitary, thyroid, adrenal glands, or, most commonly, the gonads, leading to precocious puberty. This condition arises from an activating mutation in the GNAS gene, which encodes the α-subunit of the G protein responsible for stimulating cyclic adenosine monophosphate (cAMP) formation. Such mutations occur in a mosaic pattern during early embryogenesis (39). When this mutation affects certain adrenal cells, it results in the constitutive activation of adenylate cyclase, leading to nodule formation and glucocorticoid excess, while the unaffected normal adrenal cortex undergoes atrophy (40, 41). Primary pigmented nodular adrenal disease (PPNAD), also known as micronodular adrenal disease, constitutes another uncommon form of Cushing's syndrome. This condition is characterized by small or normal-sized adrenal glands containing cortical micronodules (averaging 2–3 mm) that may appear dark or black in color. The internodular cortex is typically atrophic, which is in contrast to the condition observed in ACTH-dependent macronodular hyperplasia (42). Cases of PPNAD have been reported without accompanying Cushing's syndrome. A bilateral adrenalectomy is considered curative for this condition. Approximately 70% of PPNAD cases occur as part of the Carney complex, which is associated with various other abnormalities, including cardiac myxomas, skin or breast myxomas, hyperpigmentation, and a range of endocrine disorders (such as sexual precocity, Sertoli cell, Leydig cell, or adrenal rest tumors, as well as acromegaly). Cushing's syndrome manifests in approximately 30% of cases within the Carney complex. The tumor suppressor gene PRKAR1A (type 1A regulatory subunit of protein kinase A) has been found to be mutated in over 70% of patients with this complex. A few instances of pituitary corticotrophinoma have been documented in patients with Carney complex, including one individual who exhibited both adrenal and pituitary Cushing's syndrome (43, 44). In isolated cases of PPNAD, mutations in both PRKAR1A and the phosphodiesterase 11A (PDE11A) gene have been demonstrated (45, 46). A missense mutation of the ACTH receptor resulting in its constitutive activation has also been linked to ACTH-independent Cushing's syndrome (47). Additionally, other exceedingly rare causes of Cushing's syndrome have been identified, including adrenal rest tissue found in the liver, adrenal beds, or associated with the gonads, which may produce hypercortisolemia, typically following adrenalectomy in the context of ACTH-dependent disease (48, 49). Ectopic cortisol production has also been noted in ovarian carcinoma cases (50).

Clinical Manifestations of Cushing's Syndrome

Cushing's syndrome presents a range of clinical manifestations due to chronic exposure to excess glucocorticoids, varying from mild, subclinical symptoms to more severe manifestations. The classic depiction of the syndrome involves significant truncal obesity paired with limb wasting, facial rounding, and other symptoms such as hirsutism, muscle weakness, spontaneous bruising, vertebral fractures, hypertension, and diabetes mellitus. However, such pronounced cases

are less frequently encountered today (52-54). Diagnosing Cushing's syndrome can be challenging, as many symptoms—like lethargy, depression, obesity, and menstrual irregularities—are common in the general population. Thus, a targeted investigative approach focusing on more specific features indicative of glucocorticoid excess is crucial. Noticing the development of multiple signs and symptoms over time can assist in making a diagnosis; long-term sequential photographs can be beneficial in documenting the progression toward a Cushingoid state.

The manifestations depend on the duration and severity of glucocorticoid exposure. In severe cases, particularly with ectopic ACTH secretion (e.g., from small cell carcinoma), symptoms of hypercortisolism may be overshadowed by malignancy-related symptoms, such as weight loss and anorexia. Reports indicate a mean time to diagnosis for Cushing's syndrome of approximately 34 months, varying by the underlying cause; the shortest time is observed in ectopic Cushing's syndrome (14 months), followed by ACTH-independent cases (30 months), and the longest in Cushing's disease (38 months) (55). The nature of steroid excess is dictated by the underlying condition. For instance, adrenal adenomas typically secrete glucocorticoids, while ACTH-dependent diseases or carcinomas often result in hyperandrogenism. The following data illustrates the presenting features of Cushing's syndrome and their prevalence among patients (43-45):

- Weight gain/obesity: 81-97%
- Muscle weakness/tiredness: 46-67%
- Round face: 88-92%
- Skin thinning: 84%
- Easy bruising: 21-62%
- Edema: 48-50%
- Purple wide striae: 35-84%
- Hirsutism: 56-81%
- Acne: 19-64%
- Female balding: 13-51%
- Dysmenorrhea: 35-84%
- Reduced libido: 33-100% (higher in men)
- Hypertension: 68-90%
- Mental health disorders: 26-62%
- Recurrent infections: 14-25%
- Diabetes/impaired glucose tolerance: 43-50%
- Fractures: 21-56%

The combination of Cushingoid features varies based on the underlying cause's natural progression. Patients with ectopic ACTH syndrome may exhibit severe metabolic symptoms, including anorexia and myopathy, alongside glucose intolerance. This may lead to hypokalemic alkalosis and peripheral edema, suggesting potential malignancies like small cell lung carcinoma or high-grade neuroendocrine tumors. Conversely, those with low-grade ACTH-producing bronchial carcinoids often develop classic Cushingoid features due to prolonged hypercortisolemia prior to diagnosis. Patients with adrenal carcinomas experience rapid symptom onset, which may include abdominal pain and palpable tumors.

These tumors can secrete both mineralocorticoids and androgens, differentiating them from benign adenomas that typically only secrete cortisol (56). In women, symptoms of androgen excess, such as acne and hirsutism, are often evident. Moreover, approximately 10% of patients with adrenal incidentalomas may present with "subclinical" Cushing's syndrome, now referred to as mild autonomous cortisol secretion (MACS), characterized by mild hypercortisolism without prominent Cushing's symptoms (57). In women, a significant proportion of circulating androgens is of adrenal origin, leading to symptoms of adrenal hyperandrogenism. Common signs of Cushing's syndrome include obesity and truncal fat distribution, often resulting in abdominal obesity and characteristic fat deposition in the face ("moon face") and upper back ("buffalo hump") (52, 58). Rarely, fat accumulation in the epidural space can cause neurological deficits (59), and retroorbital fat deposition may result in exophthalmos (60). In children, generalized weight gain combined with growth retardation can raise suspicion for the syndrome (2). Other distinctive signs include proximal myopathy, wide purple striae, osteoporosis, thin skin, and easy bruising. Screening studies indicate that no cases of Cushing's syndrome were reported among individuals with obesity lacking specific Cushingoid features, hence routine screening in such cases is generally not advised (61).

Proximal muscle myopathy affects 40-70% of individuals with active Cushing's syndrome due to glucocorticoid catabolism. Assessing muscle function, such as climbing stairs or rising from a seated position, can help evaluate myopathy. Symptoms may worsen due to hypokalemia resulting from concurrent mineralocorticoid activity, but this weakness is typically absent in pseudo-Cushing's states (1). Myopathy may not fully resolve post-treatment of hypercortisolism (62). Osteoporosis affects about 50% of adults with Cushing's syndrome (63) and can be assessed through bone densitometry or fracture history, particularly vertebral fractures linked to trabecular bone loss from glucocorticoids, which inhibit osteoblast function (64). These fractures can lead to height loss, while rib fractures may be painless and exhibit excessive callus formation. Additionally, osteonecrosis, especially of the femoral head, can occur, particularly after prolonged high-dose glucocorticoid therapy (65). Post-treatment and bone density often significantly improves (66-68). Skin and subcutaneous tissue changes are also indicative of Cushing's syndrome. Hypercortisolism leads to skin thinning, detectable via "cigarette paper" texture on the dorsum of the hand (Liddle's sign). Consideration of the patient's age and gender is essential, as natural atrophy can complicate diagnosis. Classic facial plethora results from both skin thinning and loss of subcutaneous fat, leading to easy bruising that may be mistaken for senile purpura or coagulation issues. "Violaceous" striae greater than 1 cm in diameter, often found on the abdomen but also in other areas, are nearly pathognomonic for Cushing's syndrome. Narrower, colored striae can be present but should be differentiated from typical healed striae commonly observed postpartum.

Conclusion

Cushing's syndrome, characterized by chronic glucocorticoid excess, poses significant clinical challenges due to its diverse presentations and underlying mechanisms. This review has explored the intricate pathophysiology, emphasizing

the hypothalamo-pituitary-adrenal (HPA) axis's disruption as central to the disorder's development. The two primary classifications of Cushing's syndrome—ACTH-dependent and ACTH-independent—highlight the importance of distinguishing between endogenous causes, such as pituitary adenomas or ectopic ACTH secretion, and exogenous factors like glucocorticoid medications. The complexities in diagnosing Cushing's syndrome stem from its array of non-specific symptoms, often leading to delayed recognition and treatment. The necessity of a thorough evaluation involving biochemical assays and advanced imaging techniques cannot be overstated, as they are crucial in confirming diagnoses and ruling out other conditions. Additionally, a better understanding of the molecular underpinnings, particularly in cases like Cushing's disease, can pave the way for targeted therapies that address the specific etiology of the syndrome. Treatment options for Cushing's syndrome are multifaceted, encompassing surgical interventions, pharmacotherapy, and radiation therapy. The choice of treatment is often dictated by the underlying cause, the patient's overall health, and the disease's severity. While surgical resection of tumors, particularly pituitary adenomas, remains a cornerstone of treatment, medical management has evolved with the advent of novel pharmacological agents aimed at controlling cortisol production. In conclusion, Cushing's syndrome requires a coordinated approach involving endocrinologists, surgeons, and primary care providers to optimize patient outcomes. Continuous research into its pathophysiology and treatment strategies will further enhance understanding and management of this challenging condition, ultimately reducing the associated morbidity and mortality.

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متلازمة كوشينغ: مراجعة شاملة للفيزيولوجيا المرضية، التشخيص، والاعراض.

الملخص:

الخلفية :تحدث متلازمة كوشينغ نتيجة التعرض المطول لمستويات مرتفعة من الجلوكوكورتيكويدات، مما يؤدي إلى زيادة كبيرة في الممراضة والوفيات. على الرغم من التعرف عليها تاريخيًا منذ أكثر من قرن، إلا أن التحديات لا تزال قائمة في تشخيص وعلاج هذه الحالة بسبب أعراضها غير المحددة والآليات الكامنة المعقدة.

الهدف :تهدف هذه المراجعة إلى توضيح الفيزيولوجيا المرضية، وطرق التشخيص، وخيارات العلاج لمتلازمة كوشينغ لتعزيز فهم الأطباء وتحسين نتائج المرضى.

الطرق :تم إجراء مراجعة شاملة للأدبيات، تجمع بين البيانات حول الأسباب، والتصنيف، وعلم الأوبئة لمتلازمة كوشينغ. قامت المراجعة بتصنيف متلازمة كوشينغ إلى أشكال تعتمد على هرمون ACTH وأخرى غير معتمدة عليه، مع تسليط الضوء على التحديات التشخيصية واستراتيجيات العلاج، بما في ذلك الخيارات الجراحية والطبية والإشعاعية.

النتائج :تكشف النتائج أن متلازمة كوشينغ تنشأ بشكل أساسي من عوامل داخلية) مثل، الأورام الغدية النخامية، إنتاج ACTH خارج الموقع (أو استخدام الجلوكوكورتيكويدات الخارجية. تشكل داء كوشينغ المعتمد على ACTH الغالبية العظمى من الحالات، خاصةً في النساء اللواتي تتراوح أعمارهن بين 25-40 عامًا. كما تحدد المراجعة الأدوات التشخيصية الرئيسية، بما في ذلك الاختبارات الكيميائية الحيوية والدراسات التصويرية، وتناقش أهمية التعرف على كل من العروض السريرية الظاهرة والدقيقة.

الخاتمة :تظل متلازمة كوشينغ اضطرابًا غديًا معقدًا يتطلب نهجًا متعدد الأبعاد للتشخيص الدقيق والإدارة الفعالة. هناك حاجة إلى مزيد من البحث لفهم آلياتها الفيزيولوجية المرضية بشكل أفضل وتطوير استراتيجيات علاج محسنة تناسب احتياجات المرضى الفردية.

الكلمات المفتاحية :متلازمة كوشينغ، الجلوكوكورتيكويدات، المعتمدة علىACTH ، غير المعتمدة علىACTH ، التشخيص، خيارات العلاج.