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Endocrine Disorders that Cause Diabetes

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A R T I C L E I N F O

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A B S T R A C T

Endocrine disorders are a scientific group of conditions that affect the day-to-day functioning of the endocrine system, which is responsible for producing and regulating hormones in the body. Many endocrine problems can lead to the development of diabetes, a metabolic disorder characterized by persistently high blood sugar levels. Excess cortisol can cause insulin resistance, which causes an increase in blood sugar levels, and eventually leads to diabetes. Another disease is acromegaly which is caused by an overproduction of increased hormones. An extended hormone boom stage can lead to insulin resistance in the long term, contributing to an increase in diabetes. Polycystic ovary syndrome (PCOS) is an endocrine disease commonly associated with insulin resistance and diabetes. PCOS is characterized by an imbalance of hormones, especially androgens. This imbalance can impair insulin signaling, especially insulin resistance, and the subsequent development of diabetes. Hypothyroidism, which is characterized by low thyroid hormone levels, can lead to insulin resistance and impaired insulin secretion. In contrast, hyperthyroidism, which is characterized by overproduction of thyroid hormone, can increase glucose metabolism and lead to diabetes in susceptible individuals. In addition, tumors of the endocrine system, including insulinomas and glucagonomas, can cause atypical insulin production and release, leading to hypoglycemia and hyperglycemia, respectively.

INTRODUCTION

The primary focus of this study was on endocrine disorders that cause hyperglycemia and where effective treatment of endocrinopathy can be expected to normalize the blood glucose concentration. These conditions mostly reflect the excessive secretion of "counter-regulatory" hormones, the metabolicactions of which oppose those of insulin by inhibiting its secretion, action, orboth.

Acromegaly

Etiology, Incidence and Clinical Features of an Acromegaly

Acromegaly comprises a constellation of symptoms and signs caused by excessive growth hormone (GH) secretion that leads to bony and soft tissue overgrowth accompanied by cardiovascular and metabolic pathology (Figure 1 a; Table 1) [1]. It affects approximately 60 people per million [2] and, in 99% of cases, is caused by a pituitary adenoma, most commonly larger than 1 cm in diameter (" macro adenoma "; Figure 1 b). A small minority of cases are caused by excessive secretion of GH-releasing hormone (GHRH) from a hypothalamic gangliocytoma or carcinoid tumor of the lung or pancreas [1]. A small percentage of acromegaly occurs within the wider endocrine syndrome of multiple endocrine neoplasia type 1 (MEN1) caused by mutations in the tumor suppressor gene MENIN [3]. MEN1 can also include glucagonomas and somatostatinomas, both of which are separately capable of causing secondary diabetes. Commonly, acromegaly is present for a decade before diagnosis [4]. This long-standing hypersecretion of GH provides the time necessary for the characteristic external features of the disorder (Figure 1).

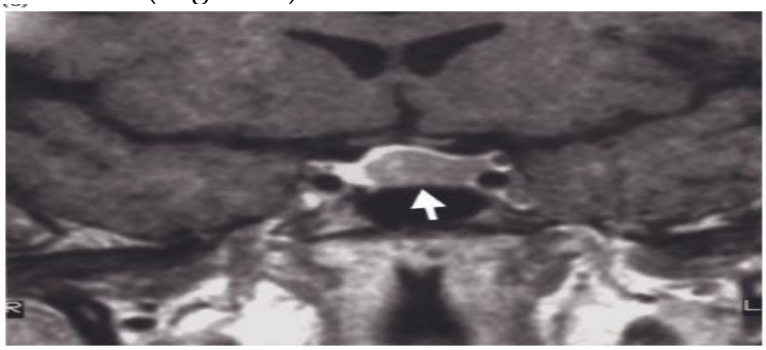

Figure 1. Acromegaly in a Patient

Acromegaly in a patient found to have a random blood glucose level of 13 mmol/L during preparation for sinus surgery. Features included: (a) thecharacteristic facial appearance; (b) a large adenoma (arrow) extending up to but notin contact with the optic chiasm demonstrated by magnetic resonance imaging (R,right; L, left). Following successful trans - sphenoidal removal of the tumor, glucosetolerance returned to normal.

Features of disturbance to glucose tolerance in an acromegaly. Glucose intolerance or overt diabetes is common in acromegaly because of the direct hyperglycemic effects of excess GH (Figure 2).

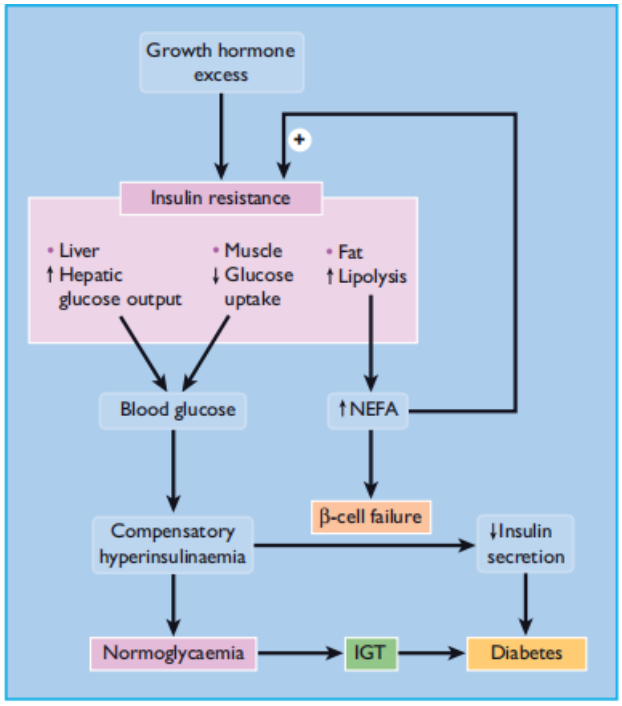

Figure 2. Mechanisms of Hyperglycemia and Diabetes in Acromegaly

Diabetes develops if β - cells fail to compensate for the increased demand for insulin. IGT, impaired glucose tolerance; NEFA, non - esterified fatty acid.

Overt diabetes has been reported in a range of 19–56% of patients with acromegaly, while impaired glucose intolerance (IGT) affects 16–46% [5–8]. Diabetes is most frequent in patients and higher GH levels [9,10]. There was also a correlation between serum insulin-like growth factor I (IGF - I) and both fasting and postprandial glucose levels. Placing age-adjusted IGF - I value into rising quartiles correlated very accurately with decreasing Insulin sensitivity, such that the serum IGF - I level could predict insulin sensitivity more accurately than either random GH levels or the nadir value following glucose tolerance testing [11]. Clinically, diabetes in acromegaly usually resembles type 2 form (T2DM), with most patients not needing insulin therapy, but maintained with oral hypoglycemic agents or diet alone [9]. GH can induce insulin resistance when infused into normal subjects [12,13],

Table 1. Treatment of Acromegaly (Adapted from Holt and Hanley[130])

Advantages	Disadvantages
Trans-sphenoidal surgery	
Rapid effect	Invasive and requires general anesthetic
Can restore vision in optic nerve compression	Non-curative for large extrasellar tumors
Might be curative if complete resection	
Somatostatin analog drugs	
Non-invasive	Monthly intramuscular injection
May shrink tumor	Expensive
Decreases GH in ~60% of patients	Gastrointestinal side effects (commonly diarrhea)
	Unlikely to be curative (i.e. continuous therapy needed)
Pegvisomant	
Non-invasive	Expensive
Blocks GH action	GH concentrations remain elevated
Radiotherapy	
Non-invasive	Slow to act – may take up to 10 years
Likely to shrink tumor	Standard external three-beam radiotherapy likely to cause hypopituitarism by destroying other pituitary cell types
Likely to reduce GH levels	
Might be curative	

GH, growth hormone.

And insulin resistance is a consistent features of individuals with acromegaly [14,15]. Insulin action is impaired in both the liver and extrahepatic tissues, with decreases in the suppression of hepatic glucose production and insulin-dependent glucose disposal [13,15]. For instance, impairment of insulin-mediated activation of glycogen synthase has been demonstrated in skeletal muscles [16 – 18]. Insulin resistance may also be exacerbated by the lipolytic action of GH, generating non-esterified fatty acids (NEFAs) that act on the liver to increase glucose production and in muscle to inhibit glucose utilization (via the "glucose–fatty acid " cycle) (Table 1). Where pancreatic compensation is adequate, exaggerated insulin secretory. The response to hyperinsulinemia can counterbalance insulin resistance and maintain euglycemia. Similar to the natural history of deteriorating blood glucose control in T2DM, β-cell compensation eventually fails, the insulin response is impaired, and hyperglycemia ensues [14]. This has been termed the Starling for the pancreas. Diagnosis and treatment of ana cromegaly GH release is normally pulsatile with intervening periods of low level or undetectable hormones, whereas secretion from pituitary adenomas is autonomous. Therefore, the diagnosis can be deduced from a series of random serum measurements in which GH is consistently detected. An alternative, better diagnostic test takes advantage of the negative feedback of GH secretion by glucose. Failure of serum GH to suppress to below 2mU/L (approximately 1 µg/L) within 3 h of 75 g oral glucose is diagnostic of acromegaly. A further option, particularly suited as the initial screening test of outpatients, is a measurement of serum IGF - I, If raised above, sex - and age-matched controls are diagnostic of acromegaly unless there is a possibility of GH abuse [1]. It is noteworthy that acromegaly can be difficult to diagnose in patients with type 1 diabetes mellitus (T1DM), where GH hypersecretion is observed. Whereas this might compromise the use of Serum GH as a diagnostic biomarker of somatotroph adenoma, IGF - I value tends to be low in poorly controlled T1DM,

indicative of the state of GH resistance. Thus, increased serum IGF-I value remains a reliable predictor for the diagnosis of acromegaly in patients with T1DM. Having been diagnosed with acromegaly, magnetic resonance imaging (MRI) of the anterior pituitary defines the extent of the adenoma (Figure 1 b). Based on this investigation, symptoms, patient wishes, comorbidity, and GH levels, treatment can be surgical, medical, or radiotherapy (Table 1) [1,19]. When the tumor is a macro adenoma, especially if it extends beyond the pituitary fossa, curative surgery becomes unlikely or impossible; however, surgery can be useful for " debulking " and rapid lowering of serum GH levels in patients who are highly symptomatic or where the tumor has encroached upon the optic chiasm and affected visual fields. The standard approach is trans-sphenoidal, either via the nostril or from behind the upper lip. Once the sphenoid sinus has been traversed and midline access to the sellaturcica gained, the tumor is removed from the anteroinferior aspect causing the residual tissue to drop back down into or towards the pituitary fossa. Tumors beyond the fossa in locations such as the cavernous sinus cannot be approached directly; hence, surgery for large tumors is not anticipated to be curative [19]. Conversely, a cure is commonly achieved for over 50% of micro adenomas (< 1 cm in diameter). The reported ranges vary widely, according to experts. Medical therapy, most commonly using somatostatin analogs, is effective at lowering GH levels and shrinking tumor volume [1,20,21]. Approximately 60% of patients respond to somatostatin analogs because of the presence of predominantly type 2 and type 5 somatostatin receptors on the tumor cell surface [1,21]. The analogs can be administered subcutaneously; however, Once it is clear that they are tolerated, the most common formulation is a month-long intramuscular depot preparation. They can be used either before surgery, to operate on a shrunken tumor, on a long-term basis in place of surgery, or post -surgery, in which GH levels were not normalized. Some GH-releasing adenomas that co-express dopamine receptors are more characteristic of prolactinomas [21]. Indeed, 25% of acromegaly cases show increased levels of both prolactin and GH, possibly indicating a tumor cell phenotype that is more consistent with the somatomammotroph from which it is thought that somatotrophs (GH secretion) and lactotrophs (prolactin secretion) terminally differentiate. In these instances, dopamine agonists, as used in hyperprolactinemia, can be useful, especially as they can be administered orally, and allow a reduction in the dosage of the more expensive intramuscular depot somatostatin analogs.

The opportunity to use lower doses of somatostatin analogs may also lessen their side effects, such as gastrointestinal disturbances (most commonly diarrhea) and gallstones. However, it has recently been questioned whether commonly used ergot alkaloid-derived dopamine agonists, such as cabergoline, cause fibrotic side effects, especially involving the heart valves [22,23]. Despite concerns from regulatory agencies, the prevailing view from endocrinologists is that the doses of these agents are used to treat endocrine disorders (compared to therapeutic regimens for Parkinson's disease) are not problematic. Alternative non-ergot-derived agents such as quinagolide are available. Bromocriptine is less commonly used because of its inevitable side effects of nausea. Responsiveness

to both dopamine and somatostatin analog therapy can be easily assessed at the start of treatment by hourly measurement of serum GH over 8 hours following the administration of a test dose of each agent administered sequentially on two consecutive days. The last decade has witnessed the appearance of a new clinical agent that blocks GH action. GH induces signal transduction by binding to its receptor as a dimer. Pegvisomant has been developed as a GH antagonist to prevent dimerization and thus inhibit GH action. This leaves elevated GH levels from the somatotroph adenoma, but pegvisomant is effective at reversing the clinical features of acromegaly [1,24]. The major problem with its use in many countries is its prohibitive costs. Concern over tumor growth due to the loss of negative feedback (a scenario akin to Nelson syndrome following bilateral adrenalectomy in Cushing's disease) seems unfounded [1,24]. Radiation therapy is the most commonly administered as conventional 3 - field external beam radiotherapy [1]. It is effective at lowering GH and IGF - I level [25]. This approach delivers approximately 4500 Gy to the pituitary region with the total dose calculated such that the optic chiasm received less than 8 Gy. Stereotactic radiotherapy (also known as γ-knife therapy or radiosurgery) uses more sources to focus a higher concentration of radiation on a defined area of the tumor. Whereas the latter modality allows greater preservation of adjacent everyday pituitary tissue, the former approach is a greater all-encompassing approach to ensure tumor destruction, albeit with a better post-therapy incidence of Hypopituitarism. The selection is essential as there may be evidence that pituitary radiotherapy is associated with improved morbidity and mortality from next cerebrovascular sickness, meaning that repeat therapy is not always undertaken lightly [26] The outcome of an acromegaly and d disturbance to glucose tolerance Unless there are cogent reasons for this, attempts should be made to normalize GH excess in acromegaly patients to decrease the morbidity and mortality associated with the disorder [1,26]. Curative treatment is best defined by a nadir serum GH level of less than 2 mU/L after a 75 g oral glucose challenge. Glucose tolerance improves and insulin levels decrease after successful treatment with pituitary surgery and irradiation [27,28]. Hyperglycemia may worsen in a few patients, presumably those with a stronger underlying tendency to T2DM when treated with somatostatin analogs because these drugs also suppress insulin secretion [29,30]. In the long term, somatostatin analogs tend to improve glucose tolerance [31,32]. Insulin sensitivity is also improved with pegvisomant therapy in patients with both glucose intolerance and diabetes [33–36]. If hyperglycemia persists after serum GH levels have normalized, then the patient should be considered to have T2DM. One caveat is the possibility of GH deficiency as part of hypopituitarism post-surgery or radiotherapy[14].GH deficiency causes centripetal fat deposition, which causes or accentuates insulin resistance and potential loss of euglycemia. Diabetic complications of acromegaly are rare. Nevertheless, it is worth considering GH action in the context of both macro vascular and Microvascular Diabetic Complications. Untreated GH excess increases cardiovascular morbidity and mortality and, potentially, abnormalities in glucose metabolism occurring in acromegaly could contribute to hypertension, which affects over 50% of patients

with acromegaly [5]. GH has been linked to proliferative diabetic retinopathy since the resolution of diabetic retinopathy was noted in a woman who developed rapid-onset pan-Hypopituitarism [37,38], so much so that hypophysectomy was used as treatment before the advent of laser photocoagulation [38]. This view is supported by the observation that patients with diabetes who are GH-deficient rarely develop retinopathy [39], and an experimental study in mice demonstrated that inhibition of GH secretion ameliorated diabetic retinopathy [40]. However, patients with acromegalic diabetes do not show an increased incidence of diabetic retinopathy [41,42]. Data on the progression of diabetic retinopathy treated with either pegvisomant or somatostatin analogs are contradictory, and the outcomes of larger trials are awaited [38].

Effects of Diabetes on GH–IGF Axis

Dysregulation of the GH–IGF–I axis has been well documented in patients with T1DM. The main disturbances include increased GH secretion , which is paradoxically associated with decreased serum IGF-I levels [43]. GH secretory pulses are larger and more frequent and total 24-hour serum and urinary GH levels are elevated. High circulating GH levels are most obvious during periods of poor diabetic control and return to normal with improved control. Pulses of GH secretion during sleep in the early hours of the morning lead to insulin resistance, which manifests itself.

Before breakfast and is largely responsible for the " dawn phenomenon" of fasting hyperglycemia [44]. This physiological effect, along with that caused by exercise and GHRH, is exaggerated in patients with T1DM, especially in those who are poorly controlled. GH secretion accounts for much of the decreased insulin sensitivity observed during normal puberty as well as the deterioration in glycemic control at this time in adolescents with T1DM. Despite GH hypersecretion, levels of IGF - I, the principal mediator of GH activity, are inappropriately low, indicating a state of GH resistance (Figure 17.4).

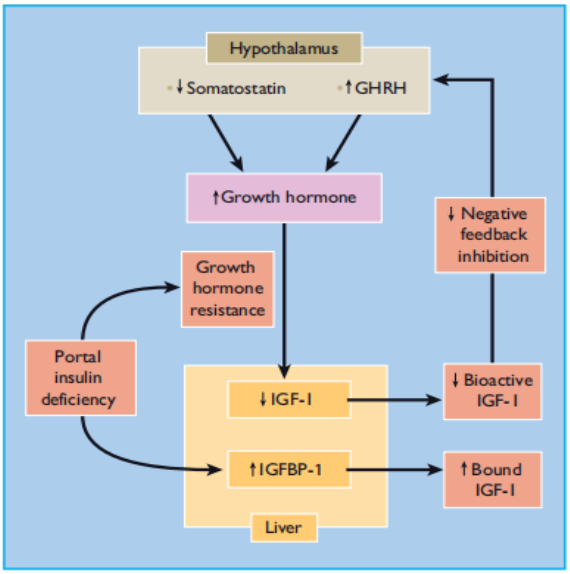

Figure 4. Mechanisms of Growth Hormone (GH) Hypersecretion in Diabetes

Insulin - like growth factor 1 binding protein 1 (IGFBP - 1) binds and reduces the bioavailability of insulin - like growth factor I (IGF - I), which normally decreases GH secretion by negative feedback inhibition on the hypothalamus and pituitary; IGFBP - 1 expression is inhibited by insulin.

Hepatic resistance to GH has been attributed both to decreased number of GH receptors and post-receptor defects [43]. Circulating levels of GH-binding protein (GHBP) are also decreased in T1DM. Administration of recombinant human IGF - I (rhIGF - I) as an adjunct to insulin has been demonstrated to reverse GH hypersecretion and improve glycemic control, while reducing insulin requirements. Co-administration of IGF - binding protein 3 (IGFBP - 3) with IGF - I have similar beneficial effects on carbohydrate metabolism, and also avoids side effects of IGF - I, notably edema, Headache, retinal edema, and jaw pain [45]. Recombinant IGF - I have also been used to treat states of severe insulin resistance in which the insulin receptor is functionally impaired, such as the spectrum from Donohue to Rabson–Mendenhall syndrome (see Chapter 15). In such patients, rhIGF - can be used to treat ketoacidosis, which is the major cause of death and may fail to respond even for massive doses of insulin.

Abnormalities in IGFBP may also alter the regulation of the GH–IGF - I axis in diabetes (Figure 17.4). Six IGFBPs have been identified in humans, the two most relevant being IGFBP - 1 (molecular weight 25 kDa), whose synthesis by hepatocytes is inhibited by insulin but independent of GH, and IGFBP - 3 (molecular weight 44 kDa), which is GH dependent. IGFBP - 1 levels are increased in T1DM as a result of portal and hepatic insulin deficiency , and increase with worsening insulin deficiency and rising HbA 1c concentrations. Increased IGFBP - 1 level have been shown to inhibit IGF - I bioactivity. Portal insulin deficiency in T1DM can thus account for GH resistance through the down regulation of hepatic GH receptors and increased IGFBP - 1 level, both reducing IGF - I production and bioactivity. Decreased IGF - levels in turn cause GH Hypersecretion via reduced negative feedback at the hypothalamus and pituitary exacerbates insulin resistance, thus establishing a vicious circle of increased GH and poor glycemic control.

Another consequence of IGF - I deficiency is impaired growth at puberty. Paradoxically, children with new-onset diabetes tend to be taller, especially if the disease develops several years before puberty, and increased GH and insulin levels during the preclinical evolution of the disease are possible explanations. Once Diabetes is established, and growth may slow, particularly before the age of 10 years, and if glycemia is poorly controlled . The pubertal growth spurt may be blunted and/or delayed, especially in girls, which may lead to a reduction in final height. Growth failure in adolescents with T1DM is rare nowadays, possibly because of the improved management and monitoring of diabetes. Indeed, intensified insulin treatment has been shown to raise IGF - I levels, in parallel with an increase in growth velocity. Finally, growth failure may be associated with truncal obesity, hepatomegaly (secondary to glycogen and/or triglyceride deposition), and sexual infantilism in Mauriac syndrome [49]. This condition has been reported in children with poor glycemic control and excessively high insulin dosages but is now rare.

Cushing Syndrome Etiology, Incidence and Clinical Features of Cushing's Syndrome

Cushing syndrome comprises a constellation of symptoms and signs caused by excessive glucocorticoid levels that lead to a characteristic appearance accompanied by metabolic and cardiovascular pathology. It occurs most commonly as a side effect of synthetic glucocorticoids administered exogenously for conditions such as rheumatoid arthritis or reversible airway diseases. Endogenous Cushing's syndrome arises in approximately two-thirds of cases from adrenocorticotropin (ACTH) secreting corticotroph adenomas of the anterior pituitary which affects 5–10 individuals per million. In one-fifth of cases, the cause is a glucocorticoid-secreting tumor of the adrenal cortex, and in one-tenth of cases is secondary to syndromes of ectopic ACTH secretion, most commonly from small-cell carcinoma of the lung or, more rarely, carcinoid tumors. Cushing’s syndrome is more common in women than in men, with a greater predilection for corticotroph adenomas as the underlying pathology. Prolonged excessive levels of cortisol, the major glucocorticoid in humans, either directly from an adrenocortical tumor or excessive ACTH causing bilateral hyper-functional adrenal cortices, cause the characteristic external features of the disorder to develop, resulting in excess cardiovascular morbidity and mortality.

Features of Disturbance to Glucose Tolerance in Cushing's Syndrome

Impairment of glucose tolerance is observed in 30–60% of cases. Overt diabetes occurs in 20–50%, arguably in patients predisposed to diabetes (e.g., those with a family history of the disorder). This resembles T2DM, because.glucocorticoid excess causes hyperglycemia primarily by inducing insulin resistance,as reflected by hyperinsulinemia [53]. Insulin-stimulated glucose uptake and utilization by peripheral tissues are both reduced, while hepatic glucose production is greatly increased through the stimulation of gluconeogenesis. This results from direct activation of hepatic gluconeogenic enzymes phosphoenolpyruvate carboxykinase (PEPCK), and an increasing supply of glycogenic substrates (amino acids and glycerol) generated by muscle proteolysis and Peripheral adipose tissue lipolysis (Figure 17.8). Glucocorticoids were also present.permissive effects on the gluconeogenesis induced by epinephrine (adrenaline) and glucagon. Besides enhancing hepatic gluconeogenesis, glucocorticoids also increase hepatic glycogen storage [55]. With endogenous causes of Cushing's syndrome, hyperglycemia can sometimes be effectively treated with sulfonylureas, but many cases require insulin therapy. Cushing's syndrome is caused by.exogenous drugs, treatment can be tailored from knowledge of the timing and half-life of the glucocorticoid drug as a predictable period of hyperglycemia follows. For instance, prednisolone administered for reversible airway disease at breakfast will generate elevated glucocorticoid levels throughout the remainder of the day with levels falling in the evening. This profile chooses intermediate-acting insulin.administered at breakfast for appropriate.

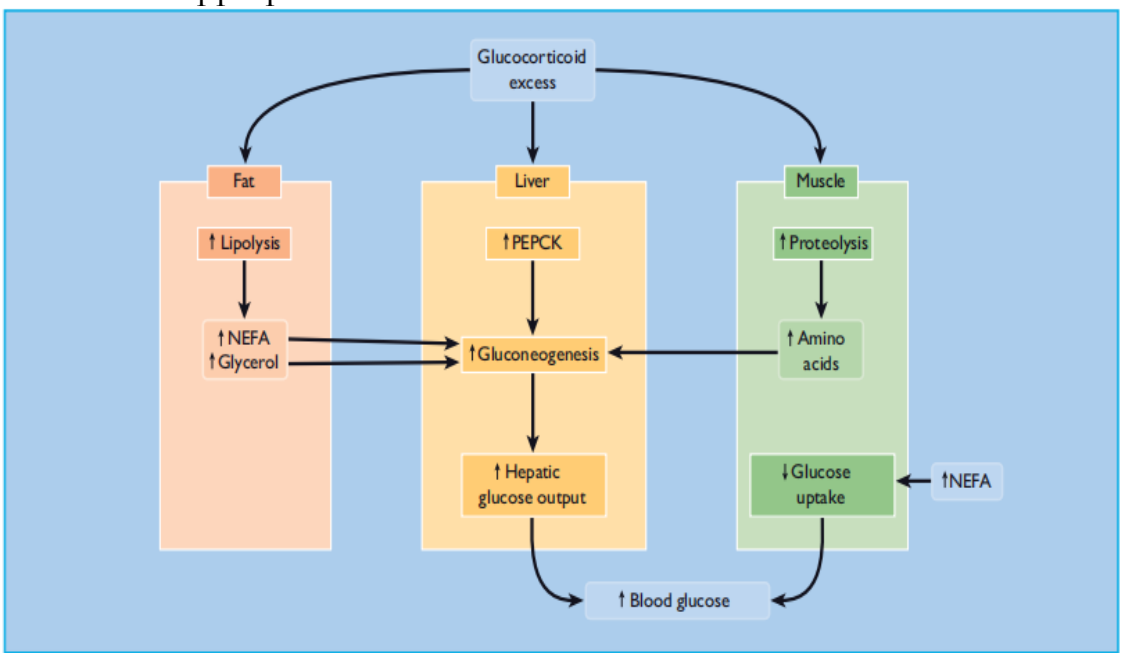

Figure 5. Mechanisms of Hyperglycemia and Diabetes in Cushing Syndrome

NEFA, non - esterified ed fatty acids; PEPCK, phosphoenolpyruvate carboxykinas.

Diagnosis and Treatment of Cushing's Syndrome

For exogenously administered glucocorticoids, the diagnosis and treatment of Cushing's syndrome are straightforward: wherever possible, remove or reduce the offending medication. The major challenge in diagnosing Cushing's syndrome resulting from endogenous causes is frequently one of simply considering the condition as the underlying cause of otherwise very common symptoms, such as tiredness and weight gain. Avoiding this pitfall is aided by thorough clinical examination when more specific signs may be detected, for instance, violaceous stretch marks (called " striae "; or proximal myopathy. This issue may be particularly pertinent to the T2DM clinic, with some evidencethatoccultCushingsyndromemayaffect2% of patients.

The first goal is to establish the presence of either autonomous secretion or excessive levels of cortisol. Several screening tests with high sensitivity have been designed . Circulating cortisol is relatively high during the day and low at bedtime. Maintained daytime levels at night indicate excess. This can be tested by measuring midnight serum cortisol, although this requires prior acclimatization of inpatients for at least 24 hours and quiet surroundings as cortisol levels rise with minimal stress. Where assays have been validated, bedtime salivary cortisol measurement can be very useful as patients can post samples to the laboratory from home. Levels are approximately 10% of those in serum, so care must be taken to avoid contamination with blood (e.g. from brushing teeth). The " low dose " dexamethasone suppression tests interrogate the potential loss of physiologic negative feedback at the cortical trophy, leading to autonomous ACTH secretion. The formal 48-hour test is marginally more specific, however, it is also more inconvenient to perform in the outpatient setting compared with the overnight 1 mg suppression test. Caution needs to be exercised in patients in whom dexamethasone metabolism is enhanced (e.g., by antiepileptic medication), as this can lead to: false-positive results. An alternative screening test examines the total excretion of cortisol in a 24-hour urine collection, commonly on several occasions, as an integrated assessment of adrenocortical function in one day. It is usual for endocrinologists to apply more than one of these various screening tests, which, if failed, provides proof of excess glucocorticoids and a diagnosis of Cushing syndrome. To distinguish between anterior pituitary and ectopic sources of ACTH causes Cushing's syndrome. Corticotroph adenomas, in particular intrasellar adenomas, generally maintain a partial capability for terrible comments; the " high dose " dexamethasone suppression test, administered at 8 2 mg doses every 6 hours, can be anticipated to reduce cortisol stages by at least 50%. As this purpose underlies the authentic description of the sickness via Harvey Cushing in 1912; pituitary-pushed glucocorticoid extra is known as Cushing's disease. Extra pituitary tumors secreting ectopic ACTH much less typically show this diploma of negative feedback, such that ACTH stages and therefore cortisol levels are possible by higher. Although these tumors can be enormously indolent carcinoids, they may more commonly be competitive carcinomas of the bronchus, characterized by the rapid onset of signs within a few months, marked hypokalemia, and weight loss. A high degree of POMC gene expression and dysregulated submit-translational

processing also result in large melanocytes-stimulating hormone (MSH) secretion, resulting in skin pigmentation.

A venous sampling of the bilateral inferior petrosal sinuses can be used to distinguish between ectopic and anterior pituitary sources of excessive ACTH. For pituitary belongings, a gradient in ACTH degrees of at least 2: 1 (or three: 1 after the injection of 100 μ g corticotropin liberating hormone [CRH] intravenously) must be determined for crucial and peripheral samples, respectively. Although it can be very beneficial, bilateral inferior petrosal sinus sampling (BIPSS) has a chance of thrombosis in approximately 1% of instances, which means that its use by endocrinologists is not continually taken into consideration. That is especially genuine in that the preceding biochemical checks were conclusive and MRI indicates clear radiologic proof of a tumor. where biochemistry is supportive of a pituitary supply of ACTH excess, but the MRI is equivocal, even after gadolinium enhancement, BIPSS can help to lateralize a corticotroph adenoma by detecting a clean gradient a number of the right and left sinuses or vice versa. assets of ectopic ACTH, the maximum normally within the chest, can be imaged with fine lesson automated tomography (CT), MRI, or by using way of the use of isotope-classified scintigraphy to locate somatostatin receptors present on about - thirds of ectopic ACTH - secreting carcinoid tumors. self-sustaining cortisol-secreting tumors of the adrenal The cortex may be imaged satisfactorily via CT or MRI, while it can be viable to assess functionality consistent with the lipid content material; capabilities of high lipid content imply a tumor with active steroidogenesis. Wherever viable, healing approaches are undertaken to normalize cortisol secretion, as Cushing's syndrome includes excessive morbidity and markedly increases mortality from cardiovascular motives. For adrenocortical properties, unilateral adrenalectomy was performed. For ectopic ACTH-secreting tumors, the excision of carcinoids is curative, whereas the herbal records of carcinoma of the bronchus with ectopic hormone secretion normally make palliative care more appropriate. The clinical treatment for corticotroph adenomas remains disappointing. Excessive-dose peroxisome proliferator-activated receptor γ (PPAR-γ) agonists have received some excitement; however, large trials have been disappointing. Pituitary tumors are treated with the aid of either trans-sphenoidal surgical procedures or radiotherapy, even when the signs, symptoms, and complications are largely similar to those defined in the acromegaly section. The fact that ACTH-secreting adenomas are normally micro adenomas can increase opportunities for healing surgery, even though this remains closely operator-structured. If surgical treatment is not always on time, suppressants of adrenocortical steroidogenesis, which consist of ketoconazole or metyrapone, may be used quickly, where sufferers are quite symptomatic. In extreme cases, bilateral adrenalectomy presents a fast decision for immoderate cortisol secretion, even though the full loss of terrible remarks to a corticotroph adenoma can bring about a risky pituitary tumor that is refractory to a similar remedy, a state of affairs called Nelson’s syndrome. In sufferers wherein ACTH levels keep to rise Concomitant radiotherapy to the anterior pituitary can help reduce the risk of this problem. The outcome of Cushing's syndrome and

disturbance to glucose tolerance After successful surgery, the patient is reliant on external glucocorticoid administered as oral hydrocortisone, but a return of cortisol secretion from the adrenal gland(s) can be anticipated over ensuing weeks. Commonly, a physiological return of diurnal rhythm is never achieved postoperatively. For some, the extensiveness of anterior pituitary surgery or the long-term suppression of either normal corticotrophs (pituitary or ectopic ACTH-secreting tumors) or normal adrenocortical cells (cortisol-secreting tumors) causes a permanent state of hypocortisolism because of the interactivity of the remaining tissue. This requires continued hydrocortisone administration in patients with Addison's disease, except that mineralocorticoid replacement is not required. With the successful treatment of Cushing's syndrome , glucose intolerance may resolve. In such instances, when the patient might be entirely dependent on replacement doses of hydrocortisone, care needs to be taken to avoid hypoglycemia with continued anti-diabetes medication. By contrast, persisting abnormalities are relatively common and most likely associated with persistent visceral obesity and metabolic syndrome. On close analysis in one case series, there was a marked persistence of visceral obesity and glucose intolerance in approximately 60% of patients who fulfilled the criteria for remission of Cushing's syndrome.

Effects of Diabetes on Hypothalamic – Anterior Pituitary – an Adrenal Cortex Axis

Evidence of over-activity of the hypothalamic-pituitary-adrenal (HPA) axis has been reported in children, adolescents, and adults with diabetes, including moderate increases in urinary-free cortisol excretion, plasma cortisol, and ACTH concentrations. These abnormalities have been related to the duration of diabetes and diabetic neuropathy. Serum cortisol levels decrease as metabolic control improves.

Pheochromocytoma

Etiology, Incidence, and Clinical Features of Pheochromocytoma

Pheochromocytomas are catecholamine-secreting tumors arising from the chromaffin cells of the adrenal medulla. Approximately 10% of cases lie in extra-adrenal sites (paragangliomas) along the sympathetic chain in the para-aortic or chest regions, and approximately 10% are bilateral. Although most pheochromocytomas are sporadic, advances in molecular Genetic studies have demonstrated that a hereditary basis underlies approximately one-fifth to one-quarter of diagnoses, not just in well-known syndromes such as MEN2, von Recklinghausen neurofibromatosis, and von Hippel-Lindau disease. Such Advances have also associated particular genetic defects with tumor type. For instance, succinate dehydrogenase subunit B (SDHB) and succinate dehydrogenase subunit D (SDHD) mutations are more frequent in extra-adrenal tumors. Mutations in SDHB are commonly associated with malignant phenotype. The risk of malignancy also increases with the tumor size. The clinical manifestations of pheochromocytoma are largely caused by hypersecretion of catecholamines, classically as a triad of symptoms including headaches, sweating, and tachycardia [69]. Hypertension is the most common clinical finding, occurring in 80–90% of cases. They can be paroxysmal or

sustained. The latter occurs, especially in children and noradrenaline-secreting tumors. Other symptoms may be secondary to the co-secretion of various peptide hormones, such as vasoactive intestinal peptide (VIP), substance P, atrial natriuretic factor, endothelin - 1, CRH, and GHRH. The normal adrenal medulla predominantly secretes epinephrine, which is converted from a non-repine phone via methylation. This reaction is governed by the enzyme phenyl ethanolamine-N-methyltransferase (PNMT), the expression of which is dependent on high concentrations of cortisol draining centripetally from the outer adrenal cortex towards the adrenal vein. For this reason, larger tumors with more Marked disturbance of the normal anatomy or extra-adrenal pheochromocytomas are notable for predominantly secreting norepinephrine, as conversion to epinephrine is compromised. Features of disturbance in glucose tolerance in pheochromocytoma hyperglycemia occur in up to approximately 50% of patients with pheochromocytoma. The prevalence of diabetes is approximately 35% Its presence in a young, hypertensive person with normal body weight should raise the suspicion of pheochromocytoma. The predominant mechanism is a catecholamine-mediated reduction in insulin sensitivity and secretion, predominantly caused by epinephrine rather than norepinephrine. Epinephrine inhibits β-cell insulin secretion by stimulation α2 - adrenergic receptors In the liver, the spine cell activates β2 - adrenoceptor to enhance glycogenolysis transiently and gluconeogenesis in a sustained manner This hepatic gluconeogenesis is fueled by the precursor's lactate, alanine, and glycerol, generated by β2 - adrenergic stimulation of muscle glycolysis and adipose tissue lipolysis. Lipolysis in the adipose tissue is also stimulated by β1 - and β3 - adrenoceptors. In addition, epinephrine can impair glucose utilization in the muscles through direct β2 - adrenergic effects. The predominance of these β2 - adrenergic effects probably explains why epinephrine, with its higher affinity for β2 - receptors, is more potent than repine pride in inducing hyperglycemia. All these effects are potent mechanisms that raise blood glucose, explaining why epinephrine release is an important component in correcting hypoglycemia after inhibition of insulin and increased glucagon secretion in the hierarchy of counter-regulatory responses.

Diagnosis and Treatment of Pheochromocytoma

Pheochromocytomas are recognized by the presence of circulating catecholamines [66–68]. As a proxy marker, This could be done through several 24-hour urine collections measuring catecholamines, consisting of epinephrine, norepinephrine, and their metabolites. Evaluation of the metabolite vanylmandelic acid is insufficient because it has an excessive false-negative rate. In which specific occasions dictate, for instance, in screening those with a genetic predisposition to pheochromocytoma, or in which urinary outcomes are equivocal, serum measurement of normetanephrine and metanephrine could be very sensitive and precise markers of pheochromocytoma (normetanephrine is the more sensitive). Imaging of the tumor can be done by using both MRI and CT. The remedy is the surgical elimination of the tumor as adrenalectomy, which is increasingly performed laparoscopically unless malignancy is suspected [66–68]. Preoperative guidance must be meticulous to prevent hypertensive crises at

some stage during the manipulation of the tumor and cardiovascular collapse after its elimination. that is completed by a preliminary α- receptor blockade accompanied by the use of a beta-blocker. The order of implementation is vital to prevent a hypertensive disaster from unopposed α- adrenoceptor stimulation. Preoperative α- adrenergic blockade often controls high blood pressure but has much less effect on glucose intolerance. In malignant pheochromocytoma, in which surgery is not feasible, adrenolytic pills, including mitotane, can be used palliatively. The outcome of pheochromocytoma and disturbance to glucose tolerance: removal of the tumor corrects metabolic abnormalities. If presentation, diagnosis, and treatment occur without undue delay, hypertension can be resolved hypertension. Although practice varies, a greater understanding of the molecular genetics of pheochromocytoma makes clinical genetics input advisable. Some laboratories now undertake germ line mutation analyses of seemingly isolated tumors. It is also straightforward to exclude hyperparathyroidism by measuring serum calcium levels, as this simple test, if normal, goes a long way to exclude MEN1. Some clinics offer annual follow-up screening for chromocytomas using 24-hour urine collection. Patients with chromocytomas caused by identified genetic disorders should be followed-up at least annually in dedicated clinical genetics endocrinology clinics.

Effects of Diabetes on an Adrenal Medulla Function

The function of the adrenal medulla may be selectively impaired in patients with long-standing diabetes and hypoglycemia unawareness, and attenuation of the epinephrine response to hypoglycemia can delay the restoration of normal serum glucose levels. Epinephrine responses can remain normal to other stimuli, indicating failure of sympathetic activation at a specific, possibly hypothalamic, level Other endocrine conditions causing disturbance of glucose tolerance Glucagonoma Glucagonoma is a rare tumor of the pancreatic islet α-cells. The first clear-cut case was reported in 1942, but the "glucagonoma syndrome " (in a series of nine patients with similar symptoms) was not described until 1974. It may form part of MEN1 is caused by mutations in the tumor suppressor gene MENIN. In a series of 21 patients [83], the syndrome's most striking clinical features were weight loss (71%), necrolytic migratory erythema (67%) diabetes (38%),cheilosis or stomatitis (29%) and diarrhea (29%). In this report, patients with the combination of necrolytic migratory erythema and diabetes mellitus were diagnosed more rapidly (after a mean of 7 months), but some cases remain undetected for years. Glucagonoma should always be considered in patients with diabetes, unexplained weight loss, or chronic skin rash.

Necrolytic migratory erythema was described in detail in this study. It usually involves the buttocks, groin, thighs, and distal extremities, and characteristically remits and relapses [80,81]. Hyperglucagonemia may contribute to the rash, as may hypoaminoacidemia, through glucagon's enhancement of amino acid uptake by the liver and zinc deficiency. Glucagonoma syndrome is also characterized by normochromic normocytic anemia, a tendency toward thrombosis (pulmonary embolism is a common cause of death), and neuropsychiatric disturbances [80]. Reporting of the prevalence of

diabetes in glucagonoma has is variable, but it probably affects approximately three-quarters of the individuals [80]. In patients with this detection rate, hyperglycemia is most commonly mild and may respond to oral hypoglycemic agents. In studies with lower rates of diagnosis, 75% of patients required insulin [80]. Hyperglycemia is largely caused by the effects of glucagon on stimulating hepatic gluconeogenesis and glycogenolysis in inadequately fed individuals The diagnosis is suggested by finding a pancreatic mass and high fasting plasma glucagon concentration in the absence of other causes of Hyperglucagonemia (e.g. severe stress, hepatic and Renal failure, poorly controlled diabetes, small bowel malabsorption, and synthetic androgenic drugs). Surgical removal of the tumor is the treatment of choice, but 50% of the tumors have metastasized to the liver at the time of diagnosis. Treatment can then be completed by hepatic artery embolization and/or chemotherapy, and somatostatin analogs can also suppress glucagon secretion. The rash may respond to the normalization of glucagon levels following the removal of the tumor or the use of somatostatin analogs; the administration of zinc, a high-protein diet, and the control of diabetes with insulin may also help.

Somatostatinoma

Somatostatinomas are extremely rare tumors bobbing up in 1 in 40 million people from δ - cells of the pancreatic islet or enteroendocrine cells of the duodenum and ampulla of Vater. They may be sporadic or a part of genetic syndromes such as MEN1. The two primary somatostatinomas have been found at some stage during cholecystectomy , but a subsequent case has been reported. identified preoperatively and has been considerably investigated . The prognosis turned into advised via the triad of diabetes, steatorrhea and gallstones, related to a tumor of the duodenum these capabilities, together with hypochlorhydria, are a result of the large inhibitory outcomes of somatostatin in endocrine and exocrine secretions. Constant to the inhibition of both insulin and glucagon by somatostatin, hyperglycemia is slight, non-ketotic, and satisfactorily controlled without insulin. diagnosis is made by way of scientific presentation, measuring multiplied Fasting tiers of circulating somatostatin and imaging using CT or MRI. Octreotide scintigraphy can also be used to localize tumors. Surgical resection is the treatment of choice and may lead to healing. Tumors that are massive and malignant with metastases at the time of prognosis, debulking, embolization, and chemotherapy (consisting of radiolabeled somatostatin analogs) are appropriate.

VIPoma

The first VIP, a secreting tumor, was recognized by Verner and Morrison in 1958. Classic features are caused by zpokalemia, and achlorhydria. Hypercalcemia and glucose intolerance occur in half of the patients; however, overt diabetes is unusual, and hyperglycemia is probably secondary to the glycogenolytic effect of VIP and/or hypokalemia, which can impair both insulin secretion and insulin sensitivity. The diagnosis is aided by serum assays for fasting VIP levels. Tumors are usually large and metastasized from the pancreatic tail at the time of diagnosis. Debulking surgery is the mainstay of treatment, with a 10-year survival rate of approximately 40%.

Hyperthyroidism

Hyperthyroidism is defined as the overproduction of thyroid hormones. Hyperthyroidism leads to thyrotoxicosis, manifesting as increased circulating thyroid hormone levels (Table 17.5). Ignoring the association between autoimmune hyperthyroidism (Graves' disease) and T1DM, thyrotoxicosis can disturb glucose tolerance in approximately one-third of individuals, with diabetes occurring in a further 8% of patients There is evidence that insulin resistance is the primary defect , especially in overweight , although insulin secretion may also be impaired. Glucose production and expression of the hepatocyte glucose transporter 2 (GLUT - 2) protein are enhanced by excess thyroid hormones. Insulin resistance improves with the restoration of euthyroidism, even if body mass index (BMI) increases. When hyperthyroidism develops in insulin-treated patients with diabetes, glucose control deteriorates and insulin requirements increase in approximately half of the patients; these changes are reversed following hyperthyroidism treatment [96]. In addition to these alterations in insulin secretion and action, the response to oral glucose tolerance testing is also altered in hyperthyroidism because of faster intestinal absorption.

Primary Hyperaldosteronism

Primary hyperaldosteronism was originally described by Conn in 1955 in a patient with hypertension, hypokalemia, and neuro muscular symptoms associated with adrenocortical adenoma secreting aldosterone. A benign adenoma is the most common primary cause (65%), with bilateral hyperplasia accounting for 30% of the cases. A handful of cases are caused by a genetic recombination event between genes encoding two closely related steroidogenic enzymes. This causes aldosterone secretion under the regulation of ACTH, which is suppressed by glucocorticoids. Although the debate is active over whether a more subtle normokalemic aldosterone excess is a wider cause of hypertension, the relevance of primary hyperaldosteronism to glucose tolerance relies largely on hypokalemia, which is part of the classic Conn syndrome, as low serum potassium levels impair insulin secretion. Other researchers have questioned whether aldosterone might exert other diabetogenic effects on glucose metabolism, although this remains unclear. Glucose intolerance has been reported in approximately 50% of patients. This condition is generally mild and overt diabetes is unusual. Defective insulin release has been implicated in delayed or reduced insulin response following an oral glucose challenge. Removal of aldosterone or potassium loading can correct these defects.

Primary Hyperparathyroidism

Primary hyperparathyroidism is secondary to parathyroid hormone (PTH) hypersecretion, usually by a parathyroid adenoma and less commonly by parathyroid hyperplasia [100]. The prevalence of diabetes in primary hyperparathyroidism is approximately three-fold higher than that in the general population, with some cases requiring insulin therapy. Insulin resistance with hyperinsulinemia is generally held responsible, with increased intracellular calcium limiting cellular glucose uptake. Whether parathyroidectomy for primary hyperparathyroidism improves glucose homeostasis is debated. Some reports argue that it is beneficial for both diabetes and impaired glucose tolerance, while others have found less of an effect. Possibly this was related to the duration and severity of calcium disturbance. With the widespread availability of serum biochemistry, hyperparathyroidism is shifting from a symptomatic to an asymptomatic disorder, where serum calcium tends to be only marginally elevated. In the latter scenario, glucose tolerance appears less affected [108].

Hypopituitarism with Growth Hormone Deficiency

In children, lack of GH increases insulin sensitivity, such that Young GH - defi client children tend to develop fasting and readily provoke hypoglycemia [109,110]. Using insulin tolerance tests, GH - deficient children were more insulin-sensitive than short Children with normal GH secretion [109]. This exaggerated insulin sensitivity attenuates with age and puberty, possibly following increased gonadal steroid production [109] such that adults with GH deficiency demonstrate insulin resistance [12]. Given that GH excess is diabetogenic and acute, GH administration increases fasting glucose and fasting insulin levels and reduces insulin sensitivity [14,17]. The value of GH replacement in improving glucose tolerance is likely to be physiologically related to physiological administration.

Given this challenge, it is not surprising that the long-term results of GH replacement are somewhat conflicting: a 30 - month study showed a deterioration in glucose tolerance and insulin sensitivity despite an increase in lean body tissue and a reduction of fat mass ; another study of 6 months duration reported increases in fasting glucose and HbA 1c without effects on peripheral or hepatic sensitivity. However, a 5 - year trial concluded that GH replacement decreased HbA 1c levels. Another study, evaluating the impact of GH therapy on GH - deficient patients during the transition from childhood to adulthood showed that the beneficial effects of chronic treatment on body composition did not overcome the direct antagonistic effects of insulin action. Insulin secretion may also deteriorate during GH administration. Thus, the replacement of GH in hypo pituitary patients with diabetes is contentious: long-term treatment with GH may improve insulin sensitivity via improvements in body composition; however, such patients need to be monitored regularly and over treatment that might lead to the development of diabetes should be avoided.

Endocrine Disorders that an Associated with Diabetes

Several endocrine disorders are associated with T1DM because of their common etiology and similar pathology (e.g., autoimmune adrenalitis [Addison's disease] or autoimmune thyroid disease). Attention should be paid to these disorders for the onset of new autoimmune pathologies. In patients with T1DM, screening can be justified to exclude hyperthyroidism or hypothyroidism by measuring the serum thyroid-stimulating hormone (TSH) level annually. The development of Addison's disease in patients with T1DM markedly increases insulin sensitivity, such that unanticipated hypoglycemic reactions occur as dose requirements decrease. Addison's disease can cause hypoglycemia, especially in children, even in the absence of diabetes and insulin therapy. Rare conditions resembling T1DM with associated endocrinopathies, such as autoimmune poly glandular syndrome or POEMS syndrome, may occur. Monogenic causes of diabetes that affect other endocrine organs are covered Examples (and their respective endocrine disorder) include the various types of hemochromatosis (primary hypogonadism), Wolfram syndrome (diabetes insipidus) and Kearns–Sayre syndrome (hypoparathyroidism, hypogonadism, and Hypopituitarism). Polycystic ovarian syndrome (PCOS) is a complex endocrine disorder characterized by insulin resistance. The hormonal alterations in PCOS share relevance with some of the mechanisms underlying glucose homeostasis in pregnancy and obesity and covered, respectively.

Polycystic Ovarian Syndrome

PCOS is defined as clinical or biochemical hyperandrogenism with oligo - or anovulation; other defi noble causes have been excluded [116–120]. Some definitions incorporate the detection of multiple ovarian cysts into the diagnosis [119,120], although these occur in approximately half of the patients with Cushing syndrome and are nondiscriminatory (Figure 17.12). PCOS occurs in 5–10% of women of reproductive age and is primarily characterized by insulin resistance, although there is also evidence of β-cell dysfunction. Impaired glucose tolerance and T2DM are present in nearly 40% and 7.5–10% of patients with PCOS, respectively, with the former tending to progress to T2DM and being associated with an approximately threefold higher risk of gestational diabetes. These data are confounded to some degree by the effect of obesity, but the incidence of PCOS remains high across ethnicities, whereas obesity rates vary. Indeed, it can be argued that PCOS in women with a normal BMI represents the most severe form of the disorder, where genetic screening programs are most likely to identify PCOS susceptibility genes. The source of androgens is the adrenal cortex and ovary. Increased insulin levels can stimulate androgen production in the ovaries and interfere with other aspects of ovarian function. Within the adrenal cortex, where insulin receptors are expressed in the zona fasciculata of the adrenal cortex , there is some evidence that insulin can influence glucocorticoid versus sex steroid precursor production[124] The diagnosis of PCOS is one of the exclusion criteria, meaning that the clinical and biochemical findings are only supportive of the condition. Serum estradiol is detectable and usually > 200pmol/L. Endocrine abnormalities include increases in serum luteinizing hormone (LH), leading to a raised LH: FSH (follicle stimulating

hormone), androstenedione, and testosterone. Serum sex hormone-binding globulin (SHBG) levels are typically low. Ovarian ultrasound is useful to exclude the presence of a tumor underlying androgen excess. Further evidence that the condition is caused by insulin resistance comes from its amelioration with exercise and agents that improve insulin sensitivity, such as metformin and thiazolidinediones [126]. In addition to lowering blood glucose levels, these agents improve menstrual regularity and increase the chances of ovulatory cycles.

LITERATUR REVIEW

Acromegaly

Etiology, Incidence and Clinical Features of an Acromegaly

Acromegaly comprises a constellation of symptoms and signs caused by excessive growth hormone (GH) secretion that leads to bony and soft tissue overgrowth accompanied by cardiovascular and metabolic pathology (Figure 1 a; Table 1) [1]. It affects approximately 60 people per million [2] and, in 99% of cases, is caused by a pituitary adenoma, most commonly larger than 1 cm in diameter (" macro adenoma "; Figure 17.1 b). A small minority of cases are caused by excessive secretion of GH-releasing hormone (GHRH) from a hypothalamic gangliocytoma or carcinoid tumor of the lung or pancreas [1]. A small percentage of acromegaly occurs within the wider endocrine syndrome of multiple endocrine neoplasia type 1 (MEN1) caused by mutations in the tumor suppressor gene MENIN [3]. MEN1 can also include glucagonomas and somatostatinomas, both of which are separately capable of causing secondary diabetes. Commonly, acromegaly is present for a decade before diagnosis [4]. This long-standing hypersecretion of GH provides the time necessary for the characteristic external features of the disorder (Figure 1).

Acromegaly in a patient found to have a random blood glucose level of 13 mmol/L during preparation for sinus surgery. Features included: (a) thecharacteristic facial appearance; (b) a large adenoma (arrow) extending up to but notin contact with the optic chiasm demonstrated by magnetic resonance imaging (R,right; L, left). Following successful trans - sphenoidal removal of the tumor, glucosetolerance returned to normal. Features of disturbance to glucose tolerance in an acromegaly. Glucose intolerance or overt diabetes is common in acromegaly because of the direct hyperglycemic effects of excess GH (Figure 2).

METHODOLOGY

A systematic assessment of the present literature was performed to accumulate relevant statistics on endocrine disorders related to diabetes. PubMed, Google Student, and different authentic databases were searched for suitable key phrases, together with "endocrine problems," "diabetes," and "endocrine issues causing diabetes." The Handiest research posted during the closing decade was covered to ensure the relevance and foreign money of the findings.

RESULTS

The review of the literature identified several endocrine issues that have beenfound to boom the threat of diabetes. those problems consist of Cushing's Syndrome Cushing's syndrome, characterized by extra manufacturing of cortisol, can result in insulin resistance and impaired glucose metabolism in the long run, contributing to the development of diabetes.

Acromegaly

Acromegaly, as a result of an overproduction of increased hormone (GH), can cause insulin resistance and impaired insulin secretion, thereby growing the hazard of diabetes.

Pheochromocytoma

Pheochromocytoma, a tumor of the adrenal glands, can increase catecholamine levels, which can impair glucose metabolism and lead to diabetes.

DISCUSSION

The underlying mechanisms by which these endocrine disorders contribute to the improvement of diabetes include numerous hormonal imbalances and metabolic disturbances. In Cushing's syndrome, multiple cortisol stages promote insulin resistance by inhibiting insulin signaling pathways and promoting gluconeogenesis. Acromegaly-brought on extra GH leads to insulin resistance and impaired insulin secretion through the suppression of insulin receptors and alterations in glucose transporters. Pheochromocytoma-associated catecholamines interfere with insulin secretion and impair glucose metabolism.

CONCLUSIONS

This study highlights the association between certain endocrine problems and the improvement of diabetes. Healthcare specialists should be aware of these relationships to facilitate early detection and management. Patients with endocrine disorders, Cushing's syndrome, acromegaly, or pheochromocytoma should be carefully monitored for diabetes development. Early intervention and appropriate treatment can assist prevent or minimize the danger of diabetes in those individuals with endocrine problems and diabetes and discover potential preventive and therapeutic techniques. through spotting and addressing the Underlying endocrine issues and healthcare carriers can improve patient results and improve the overall control of diabetes.

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Declaration of Interest

I, at this second, declare that: I haven't any pecuniary or another private hobby, direct or oblique, in any dependence that raises or can also boost a war with my duties as a supervisor of my workplace control.

Conflicts of Interest

The authors declare that they have no conflicts of interest. Financial support and sponsorship No Funding was received to assist with the preparation of this manuscript

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