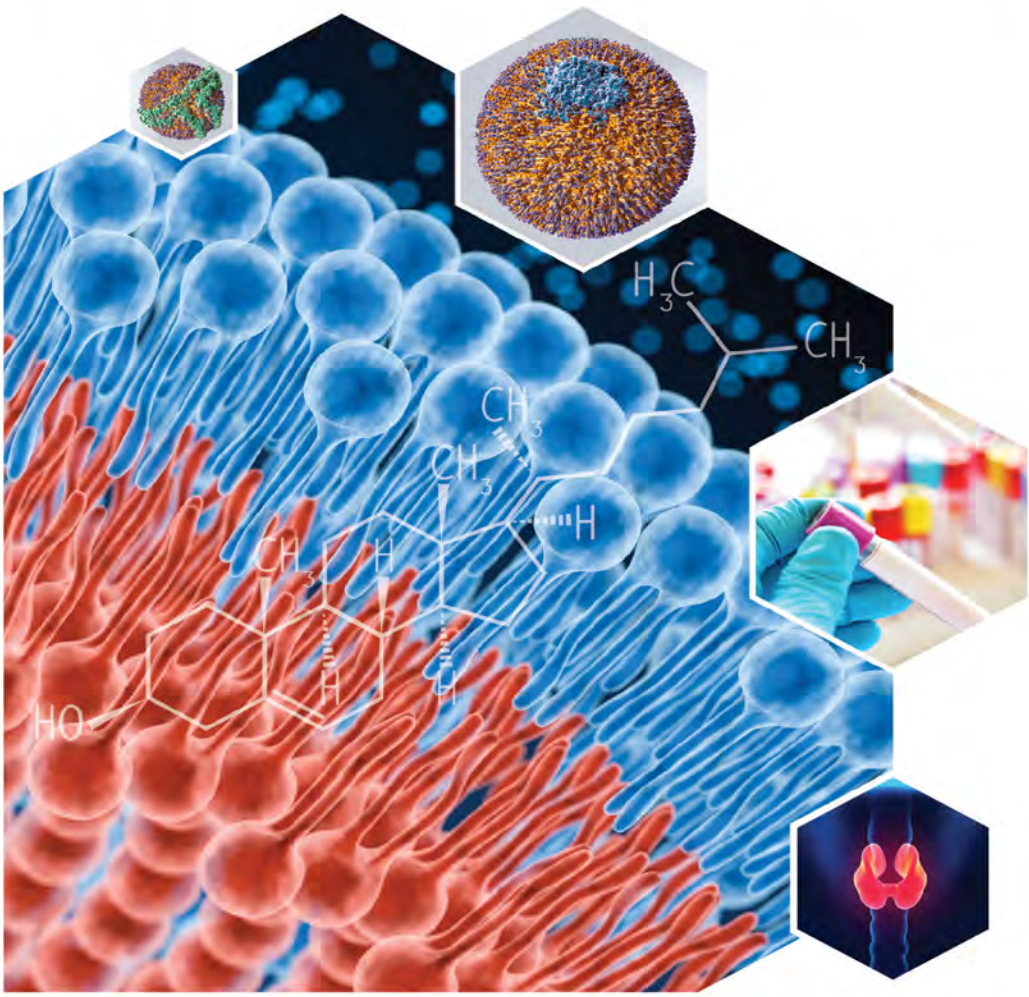
ebsite www.jaypeebrothers.com, for detailed information on endocrinology books, visit our website www.jaypeebrothers.com

Celebrating 50 Years
Passion, Quality and Innovation in Healthcare Publishing

LIPOCRINOLOGY

The Relationship between Lipids and Endocrine Function



Editors
Sanjay Kalra
Gagan Priya

Forewords
Brian Tomlinson
Ashwin B Mehta

JAYPEE

Contents

Section 1 Lipids in Endocrinology

1. **Lipocrinology: Definition and Domains** 3
   Gagan Priya, Sanjay Kalra
2. **Lipo-health and Endocrine System: Thyroid, Parathyroid, and Pituitary** 9
   Parjeet Kaur
3. **Lipo-health and the Endocrine System: Adrenals** 19
   Gagan Priya, Emmy Grewal, Neelam Pandey
4. **Lipo-health and the Endocrine System: Reproductive System** 30
   KVS Hari Kumar
5. **Lipo-health and the Endocrine System: Pancreas** 38
   Arjin P Jacoby, Jubbin J Jacob
6. **Lipid-health as an Aid to Clinical Decision-making in Endocrinology** 50
   Sanjay Kalra, Gagan Priya
7. **Dyslipidemia as a Risk Factor for Atherosclerotic Cardiovascular Disease in Endocrinology** 60
   Subhodik Pramanik, Om J Lakhani

Section 2 Endocrine Aspects of Lipidology

8. **Adipose Tissue as an Endocrine Organ** 73
   Lakshmana P Nandhini, Ankush Desai, Jayaprakash Sahoo
9. **Lipotoxicity and Diabetes Mellitus** 87
   Sameer Aggarwal, Jaikrit Bhutani
10. **The Asian Lipophenotype** 97
    Altamash Shaikh
11. **Lipodystrophies: Endocrine Effects** 109
    Emmy Grewal, Rajat Gupta
12. **Endovigilance in Lipid Disorders** 121
    Sunil K Kota, Sambit Das, Lalit K Meher

Section 3 Management Issues in Lipocrinology

13. **Lipid-lowering Drugs in the Management of Endocrinopathy** 137
Om J Lakhani, Subhodik Pramanik

14. **Lipotropic Effects of Drugs Used in Endocrinology and Diabetes** 146
Gagan Priya

15. **Endocrine Effects of Lipid-lowering Drugs** 160
Yashpal Singh

16. **PCSK-9 Inhibitors: Endocrine Considerations** 172
Sunil K Mishra, Sanjay Kalra, Gagan Priya

Index 183

3

CHAPTER

Lipo-health and the Endocrine System: Adrenals

Gagan Priya, Emmy Grewal, Neelam Pandey

ABSTRACT

The adrenal glands have a high lipid content and cholesterol serves as a precursor for adrenal steroid hormones. At the same time, adrenal hormones regulate adipose tissue function and lipids. Glucocorticoids are key regulators of energy metabolism and affect lipid and lipoprotein metabolism through several mechanisms. Cushing's syndrome is associated with increased visceral and upper body fat, increased lipogenesis as well as increased lipolysis. The resultant changes in serum lipids include increase in total and low-density lipoprotein (LDL) cholesterol and triglycerides. In addition, patients with chronic glucocorticoid excess also have abnormal glucose metabolism, central obesity, hypertension, hypercoagulability, and endothelial dysfunction. Cardiovascular (CV) risk and mortality are significantly elevated, even after remission of hypercortisolism. This calls for aggressive multifactorial risk factor management with therapy targeted at optimization of glycemic control, blood pressure and lipids, and lifestyle modification, in addition to management of Cushing's syndrome. The effect of aldosterone, adrenal androgens, and catecholamines on lipid physiology, however, is not clearly understood. Lipid content of adrenal lesions can provide important clues in differentiating benign adenomas from malignant lesions in radiological imaging studies.

INTRODUCTION

The endocrine and lipid physiology are closely interlinked at several levels. Lipids modulate the function of endocrine organs and act as precursors for steroid hormone synthesis, and as second messengers in hormone signaling pathways. At the same time, endocrine function determines adipose tissue distribution and function, lipid metabolism, and overall metabolic health. Dyslipidemia is often seen associated with disorders of the endocrine system and modulates the risk of long-term cardiovascular (CV) complications that contribute toward morbidity and mortality in endocrine diseases.[1]

The interrelationship between lipo-health and endocrine function is particularly relevant in the context of the adrenal glands. In this chapter, we delineate the role

JAYPEE BROTHERS

of adrenal hormones in the regulation of lipid metabolism and describe the lipid alterations seen in disorders of adrenal function.

ADRENAL GLANDS—PHYSIOLOGY

The adrenals are small endocrine glands situated above the kidneys and are composed of the outer adrenal cortex and inner adrenal medulla. The adrenal cortex and medulla have distinct embryological origins and physiological functions. The adrenal cortex is derived from mesoderm while the medulla is of ectodermal origin. The cortex is further composed of three layers involved in the production of steroid hormones and includes:

1. Zona glomerulosa that primarily secretes mineralocorticoid aldosterone
2. Zona fasciculata that secretes glucocorticoids, including cortisol
3. Zona reticularis that secretes adrenal androgens, including dehydroepiandrosterone (DHEA), DHEA sulfate (DHEAS), and androstenedione.

The function of the adrenal cortex is regulated by the hypothalamus and pituitary via adrenocorticotropic hormone (ACTH). On the other hand, the inner medulla secretes catecholamines, adrenaline and noradrenaline, in response to sympathetic nervous system stimulation.

LIPIDS AS A PRECURSOR OF ADRENAL HORMONES

Lipids have diverse physiological functions, including maintaining structural integrity and fluidity of cell membranes and its role in cell signaling, nerve conduction, and intracellular transport. In addition, cholesterol serves as a precursor for hormones, vitamin D, and bile acids.[2]

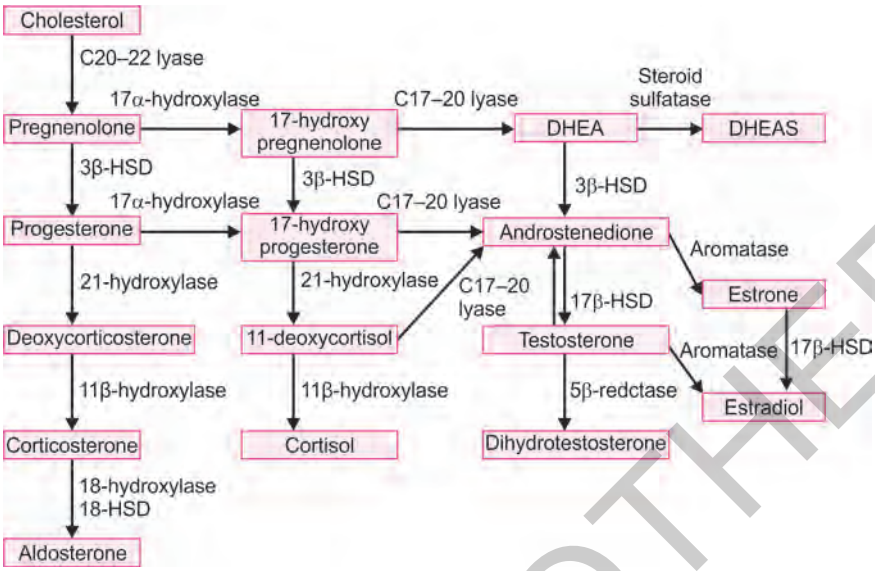
The adrenal cortex has a distinct yellow color due to its extremely high lipid content.[3] The adrenal cortical cells are specialized in steroid biosynthesis, are rich in mitochondria and smooth endoplasmic reticulum, and contain a high content of intracellular lipid droplets that store cholesteryl esters. They readily take up cholesterol, which serves as the common precursor molecule for adrenal cortical hormones, including glucocorticoids, mineralocorticoids, and adrenal androgens. Flowchart 1 depicts the steroid hormone biosynthetic pathway.

The steroidogenic acute regulatory protein (StAR) mediates the transport of cholesterol into inner mitochondrial membrane where it is utilized for hormone synthesis. Deficiency of the StAR protein results in a rare form of lipoid congenital hyperplasia characterized by severe adrenal insufficiency and significantly enlarged adrenal glands.[4]

EFFECTS OF GLUCOCORTICOIDS ON LIPID METABOLISM

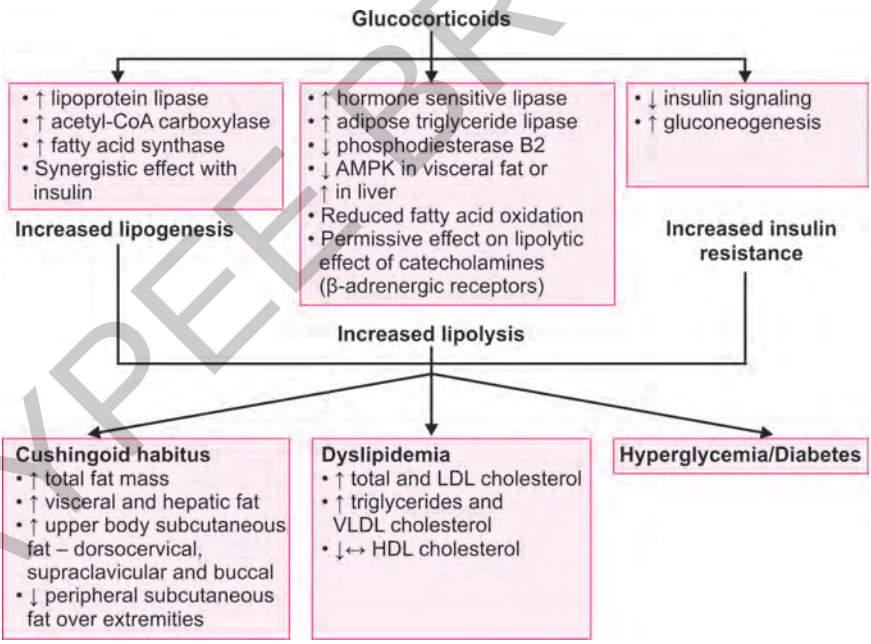
The adrenal steroid hormones, including glucocorticoids, mineralocorticoids, and adrenal androgens regulate lipid and lipoprotein metabolism in several ways. Glucocorticoids play a significant role in energy metabolism and regulate the metabolism of glucose, fat, and protein in conjunction with other hormones such as insulin, glucagon, and thyroid hormones. In fact, it has been shown that glucocorticoids can modulate the expression of almost 10% of human genes.

JAYPEE BROTHERS



HSD, hydroxysteroid dehydrogenase; DHEA, dehydroepiandrosterone; DHEAS, dehydroepiandrosterone sulfate.

FLOWCHART 1: Steroid biosynthesis pathway.



CoA, coenzyme A; LDL, low-density lipoprotein; HDL, high-density lipoprotein; VLDL, very low-density lipoprotein; AMPK, adenosine monophosphate-activated protein kinase.

FLOWCHART 2: Effects of glucocorticoids on adipose tissue and lipid metabolism.

Glucocorticoids regulate adipose tissue distribution and function, and lipid metabolism in several ways and these are depicted in flowchart 2:[5]

JAYPEE BROTHERS

- *Increased adipogenesis:* They increase the differentiation of adipocyte precursors and promote fat deposition, especially visceral and abdominal subcutaneous fat. Other fat depots such as dorsocervical, supraclavicular, and buccal fat pads are also sensitive to the adipogenic effect of glucocorticoids
- *Increased lipogenesis:* They increase the expression and activity of intravascular lipoprotein lipase that hydrolyzes the breakdown of triglycerides into fatty acids and glycerol. The resultant increase in adipose tissue uptake of fatty acids and glycerol promotes lipogenesis and increased fat storage in visceral, abdominal, and upper body subcutaneous depots. Glucocorticoids act synergistically with insulin to stimulate acetyl coenzyme A (CoA) carboxylase and fatty acid synthase to further increase lipogenesis[6]
- *Increased lipolysis:* While lipogenesis is increased, glucocorticoids also increase lipolysis by upregulating the activity of hormone sensitive lipase and adipose triglyceride lipase. On the other hand, they inhibit adenosine monophosphate-activated protein kinase (AMPK) and phosphodiesterase 3B that further contribute to their lipolytic effect.[7] They also have a permissive effect on the lipolytic effects of catecholamines, mediated via β-adrenergic receptors, and growth hormone as well.

Therefore, both lipogenesis and lipolysis are increased. Adipogenesis and lipogenesis are predominantly increased in central fat depots; the peripheral adipose tissue is more sensitive to their lipolytic effect.[5] The effect on hepatic lipid metabolism is less well understood. Lipogenesis is increased, with increased production and secretion of very low-density lipoprotein (VLDL) from the liver. Fatty acid oxidation, on the other hand, is reduced. Among apolipoproteins, glucocorticoids increase the production of apolipoprotein AIV and AI. The net effect action of glucocorticoids is an increase in total body fat and lipid turnover.[7]

In addition, glucocorticoids reduce uncoupling protein 1 (UCP1) activity in brown adipocytes and have been shown to reduce thermogenic activity in rats. Thus, they may reduce thermogenesis and promote shift toward white adipocytes, but the significance in humans in not known.

Glucocorticoids also regulate insulin sensitivity and glucose metabolism by decreasing the peripheral uptake and utilization of glucose and increasing gluconeogenesis. The adipose tissue inflammatory activity is also modulated. They increase the expression of leptin while the secretion of inflammatory cytokines interleukin (IL)-6, IL-8, and tumor necrosis factor-α (TNF-α) is reduced.

The effects of glucocorticoids are primarily mediated via the nuclear receptors—glucocorticoid receptor (GR) and mineralocorticoid receptor (MR). There is local conversion of inactive corticosterone to cortisol in the adipose tissue mediated by 11β-hydroxysteroid dehydrogenase-1 (11β-HSD1) enzyme. Since the local concentration of cortisol in adipose tissue is high, it acts via both GR and MR. While GR activation reduces release of proinflammatory adipocytokines, MR activation has the opposite effect. MR activation is now understood to play a significant role in the pathophysiology of obesity, hypertension, and dysmetabolism.[7] Selective agonist of the GR, dexamethasone, and selective antagonists of the MR, eplerenone, reduce secretion of proinflammatory adipokines.

JAYPEE BROTHERS

Polymorphisms of the GR are associated with variations in glucocorticoid sensitivity. These have been associated with body mass index (BMI), blood pressure, blood glucose, total and LDL cholesterol, and triglycerides. Glucocorticoid resistance is linked to less visceral obesity, lower fasting insulin, lower cholesterol, and a healthier metabolic profile, while greater responsiveness to glucocorticoids is associated with increased CV risk.[8]

CUSHING'S SYNDROME—LIPID PHENOTYPE

Chronic glucocorticoid excess or Cushing's syndrome can result from exogenous systemic glucocorticoid therapy or endogenous causes, including ACTH secreting tumors (pituitary or ectopic) or cortisol hypersecretion from adrenal lesions. Cushing's syndrome is typically associated with increased central and visceral fat deposition but a depletion of peripheral subcutaneous fat in extremities. The central adiposity is accompanied by increased buccal, dorsocervical and supraclavicular fat, which gives rise to the characteristic Cushingoid features that are considered important clinical clues of hypercortisolism.[5]

In addition to weight gain and central adiposity, chronic glucocorticoid excess is also associated with significant insulin resistance, metabolic syndrome, hyperglycemia or diabetes, hypertension, hypercoagulability, and dyslipidemia. Dyslipidemia results from both the direct effects of hypercortisolism on lipid metabolism as well as due to insulin resistance and diabetes. It also contributes to the development of nonalcoholic fatty liver disease. Both exogenous and endogenous Cushing's syndrome have been associated with increased incidence of hepatic steatosis.

Dyslipidemia is Cushing's Syndrome

Chronic glucocorticoid excess can cause secondary dyslipidemia, but the severity of lipid abnormalities is highly variable in both exogenous and endogenous hypercortisolism.[9] Reports of lipid alterations in Cushing's syndrome vary based on patient characteristics and the severity of disease. Patients with endogenous hypercortisolism have elevated total and LDL cholesterol, elevated triglycerides, and VLDL cholesterol, while the high-density lipoprotein (HDL) levels are not significantly altered.[9] Lipoprotein (a) may also be elevated.

Some of the potential mechanisms contributing to the lipid alterations in hypercortisolism include:

- *Low-density lipoprotein cholesterol:* Glucocorticoids decrease the expression of hepatic LDL receptor and decrease LDL clearance. This may contribute to the increased plasma LDL cholesterol levels[9]
- *Triglycerides:* Glucocorticoids increase hepatic acetyl-CoA carboxylase and fatty acid synthase. Triglyceride synthesis in the liver is increased, apo B degradation is reduced and there is increased formation and secretion of VLDL, while VLDL clearance is unaltered.[6] The increased VLDL production results in increase in both serum triglycerides and LDL cholesterol. Glucocorticoid excess also results in increased adipose tissue lipolysis, with increase in circulating free fatty acids.[10] An increased transport of fatty acids from adipose tissue to liver may also contribute

JAYPEE BROTHERS

to increased secretion of VLDL from the liver, but this has not been clearly documented

- *High-density lipoprotein cholesterol*: The synthesis and secretion of apo A1 is increased. In addition, hepatic lipase is inhibited while lecithin–cholesterol acyltransferase (LCAT) is inhibited. This may result in increase in HDL cholesterol.[11] However, significant changes in HDL cholesterol have not been reported.

The total and LDL cholesterol levels seem to correlate with the severity of hypercortisolism and contribute to increase CV risk. While Cushing's syndrome is not associated with low HDL cholesterol, lipid changes in subclinical Cushing's syndrome seem to replicate metabolic syndrome with increased triglycerides and low HDL cholesterol.[12] In individuals with hypopituitarism who were on glucocorticoid replacement, a dose-response relationship was seen between steroid dose and weight, BMI, total and LDL cholesterol, and triglycerides, suggesting that higher doses are associated with greater dyslipidemia. However, in a large survey of 15,004 patients using exogenous glucocorticoids, dyslipidemia was not reported. Exogenous glucocorticoids seem to be associated with dyslipidemia particularly in those individuals who exhibit Cushingoid features.[13]

Insulin resistance and secondary diabetes associated with chronic hypercortisolism further alter the lipid and lipoprotein abnormalities. In addition, Cushing's syndrome may be variably associated with abnormalities in other hormones including growth hormone, prolactin and thyroid hormones, estrogen, or testosterone. These may also modulate lipid parameters.

Cardiovascular Risk in Cushing's Syndrome

Chronic glucocorticoid excess presents a constellation of high CV risk environment with central obesity, insulin resistance, diabetes, hypertension, dyslipidemia, endothelial dysfunction, hypercoagulability, and inflammation. The global CV risk was estimated to be high or very high in almost 80% patients with Cushing's syndrome in a large cohort.[14] Several reports suggest that these patients have higher carotid intima media thickness and coronary artery calcium scores and CV event rates are higher (hazard ratio of 3.7 for myocardial infarction and 2.0 for stroke) and these remain elevated even after treatment of Cushing's syndrome.[12,15] They have a higher mortality rate compared to age and gender-matched controls, largely contributed by CV mortality.[16] The increased risk for atherosclerotic CV disease (ASCVD) and ASCVD-related mortality is multifactorial and is seen even long after achieving remission of hypercortisolism.[17]

Does Treatment of Cushing's Syndrome Improve Dyslipidemia?

Several studies have reported improvements in serum lipids when hypercortisolism is treated, with either medical or surgical management. LDL cholesterol is significantly reduced. However, some reports suggest small to no improvement in lipid profile after achieving remission or cure in Cushing's syndrome. Medical therapies for hypercortisolism such as ketoconazole or mitotane may also impact lipid profile, as discussed in subsequent section. More importantly, the CV risk remains elevated even after achieving remission in Cushing's syndrome patients.[17]

JAYPEE BROTHERS

Impact of Medical Therapy for Cushing's Syndrome on Lipid Parameters

Several drugs may be used to reduce cortisol levels in endogenous Cushing's syndrome, including ketoconazole, mitotane, and metyrapone.

- *Ketoconazole:* Ketoconazole blocks several enzymes in cortisol synthesis pathway and reduces serum cortisol levels. In addition, it also blocks cholesterol biosynthesis by inhibiting the conversion of methyl sterols to cholesterol. In fact, ketoconazole was used for lowering of serum lipids in patients with familial hypercholesterolemia before the advent of statins.[18] Use of ketoconazole may lead to improvement in lipid parameters in patients with Cushing's syndrome
- *Mitotane:* On the other hand, mitotane which is used in adrenocortical carcinoma or refractory cases, increases cholesterol levels by reducing the production of oxysterols in liver and increasing the activity of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase. Thus, it leads to significant increase in total and LDL cholesterol and apo B, while triglycerides, HDL cholesterol and lipoprotein (a) are not affected.[13]

Management of Dyslipidemia in Cushing's Syndrome

There is a lack of specific studies addressing the management of dyslipidemia in Cushing's syndrome and therefore, there is no clear consensus. It is important to note that CV risk is significantly elevated due to multiple factors and persists even after remission of hypercortisolism. Therefore, good clinical sense suggests that these individuals should be assessed for CV risk and they should be considered for aggressive multifactorial management for CV risk factors.[13] This would include optimization of glycemic control, blood pressure control, and use of lipid-lowering drugs. CV risk assessment can guide the use of lipid-lowering drugs. Statins remain the first-choice hypolipidemic drugs.

Safety Concerns with Statins

- Cushing's syndrome patients often have proximal myopathy and may be more susceptible to statin-induced myopathy. However, this has not been clearly documented
- *Drug interactions with ketoconazole:* Ketoconazole inhibits several hepatic P450 enzymes including *CYP3A4*. Since many statins such as atorvastatin, simvastatin, and lovastatin are metabolized by *CYP3A4*, their plasma concentrations may be elevated with resultant increased risk of myopathy. However, there is no interaction with rosuvastatin or pravastatin that is not metabolized via *CYP3A4*.[13]

ROLE OF GLUCOCORTICOIDS IN OBESITY

There exist several similarities in the phenotype of central obesity and Cushing's syndrome. It is hypothesized that abnormal glucocorticoid physiology may be playing a role in pathophysiology of obesity, leading to the description of visceral obesity as "Cushing's disease of the omentum".[5]

Chronic stress and inflammation are associated with increased activity of the hypothalamic–pituitary–adrenal axis and increased cortisol production and turnover.

JAYPEE BROTHERS

However, serum cortisol levels are not increased in obese individuals, though the loss of diurnal variation of serum cortisol is associated with waist hip ratio. Many obese individuals may have inadequately suppressed morning cortisol on overnight dexamethasone suppression test.[5]

In addition, overexpression of 11β-HSD1 that mediates local conversion of cortisone to active cortisol, thus resulting in increased local production of glucocorticoids, has been implicated in obesity, dyslipidemia, and insulin resistance. However, it is unclear if higher 11β-HSD1 activity is a contributing factor to obesity or a compensatory mechanism. Meanwhile, 11β-HSD2 activity also seems to be increased with resultant increase in cortisol turnover. Pharmacological inhibition of 11β-HSD1 may lead to weight loss, improved lipid parameters and increased insulin sensitivity.

LIPID PARAMETERS IN ADRENAL INSUFFICIENCY

Adrenal glucocorticoids are needed for the optimal activity of enzymes that participate in intestinal triglyceride synthesis. Consequently, patients with Addison's disease (adrenocortical inefficiency) may report steatorrhea that improves with steroid replacement. Serum lipid changes have not been documented.

Do Statins Affect Adrenal Function?

Since statins and newer lipid lowering drugs such as proprotein convertase subtilisin/kexin 9 (PCSK9) inhibitors cause significant reductions in cholesterol, a theoretical concern would be their impact on adrenal and gonadal hormogenesis. However, LDL receptor knockout mice do not demonstrate any abnormalities in adrenal or gonadal steroid hormone production.[2] Similarly, most studies with statins or PCSK9 inhibitors do no suggest any adverse effect.[1]

EFFECT OF ADRENAL ANDROGENS ON LIPID PARAMETERS

The role of adrenal androgens in lipid regulation is less clear. The effects of DHEA and DHEAS are mediated via conversion to more potent sex steroids that regulate insulin sensitivity and metabolism. However, studies with DHEA supplementation have failed to report benefits on insulin sensitivity, weight, or lipids; and one study in patients with adrenal insufficiency reported an unfavorable effect on lipids with reduction in HDL cholesterol.[19]

While lipid metabolism may not be affected by congenital adrenal hyperplasia (CAH), most patients are treated with long-term glucocorticoid treatment. Several studies report increased total and LDL cholesterol and triglycerides in CAH patients compared to controls.[20]

EFFECT OF MINERALOCORTICOIDS ON LIPIDS

Aldosterone does not have any direct impact on lipid metabolism, but plays an important role in mediating blood pressure control, endothelial function, insulin sensitivity, and chronic inflammation. Both mineralocorticoids and glucocorticoids act via the MR to increase adipogenesis and inflammatory activity. Primary hyper-

JAYPEE BROTHERS

aldosteronism is associated with hypertension, insulin resistance, and increased CV risk but consistent changes in lipids have not been reported.[21]

ADRENAL MEDULLA—EFFECT ON LIPID METABOLISM

Catecholamines increase thermogenesis in brown adipose tissue via β2-adrenergic receptors and may induce browning of white adipocytes. Agonists of the β2-adrenergic receptors are currently being explored for their role in obesity.

Catecholamines, epinephrine and norepinephrine have a predominant lipolytic effect, by increasing cyclic AMP levels and activity of hormone-sensitive lipase. In addition, they inhibit insulin secretion and decrease insulin sensitivity, which further increases lipolysis. Catecholamine-secreting tumors or pheochromocytomas may be associated with lower body fat, carbohydrate intolerance, elevated free fatty acids, and lower HDL cholesterol, but changes in LDL cholesterol or triglycerides have not been reported. The carbohydrate tolerance and free fatty acid levels return to normal after surgical resection of the tumor.[22]

LIPID CONTENT OF ADRENALS—IMAGING OF ADRENAL TUMORS

Adrenal lesions include adenomas, adrenocortical carcinomas, pheochromocytomas, metastasis, myelolipomas, lymphomas, cysts or pseudocysts, hemorrhage, infections, or nodular hyperplasia. The primary concern on imaging is to distinguish benign adenomas from malignant lesions. Most adrenal adenomas have intracytoplasmic fat, which differentiates them from malignant or metastatic lesions.[23] These can be easily identified in nonenhanced computed tomography (CT) and magnetic resonance imaging (MRI).

On noncontrast CT, most adenomas have a low attenuation, below 10 HU (Hounsfield unit) due to their fat content. But 10–40% adenomas have a higher attenuation and therefore, noncontrast CT may be indeterminate. Contrast-enhanced images may assist as adenomas have significant arterial enhancement and rapid washout of contrast. However, some pheochromocytomas and metastatic lesions have similar characteristics.[24]

Fat can be depicted in routine fat-suppressed MRI that can detect macroscopic fat. However, it may not pick up microscopic intracellular fat that can be demonstrated via the use of chemical shift MRI. The precession frequencies of water and lipid molecules are different and can be easily distinguished during the acquisition sequence of chemical shift MRI. Intracellular fat is detected as a signal drop on opposed-phase images with a darker appearance compared to in-phase images and the microscopic fat content can also be quantified.[23] Therefore, adenomas have a signal drop on chemical shift MRI, which has a high sensitivity and specificity in differentiating them from malignancies or other lesions which are lipid-poor.

Certain adrenal tumors, adrenal myelolipomas, have significant macroscopic fat and are very easily diagnosed on imaging. They appear as lesions with significant fat attenuation on CT and loss of signal on fat-saturated MRI. The differential diagnosis of such lesions includes lipomas, liposarcomas, and pheochromocytomas that have undergone significant fat degeneration.[24]

JAYPEE BROTHERS

CONCLUSION

Glucocorticoids are key regulators of energy metabolism and affect lipid and lipoprotein metabolism through several mechanisms. Cushing's syndrome is associated with increased visceral and upper body fat, increased lipogenesis as well as increased lipolysis. The resultant changes in serum lipids include increase in total and LDL cholesterol and triglycerides. In addition, patients with chronic glucocorticoid excess also have abnormal glucose metabolism, central obesity, hypertension, hypercoagulability, and endothelial dysfunction. Cardiovascular risk and mortality are significantly elevated, even after remission of hypercortisolism. This calls for aggressive multifactorial risk factor management with therapy targeted at optimization of glycemic control, blood pressure and lipids, and lifestyle modification, in addition to management of Cushing's syndrome.

REFERENCES

1. Kalra S, Priya G. Lipocrinology—the relationship between lipids and endocrine function. Drugs Context. 2018;7:212514.
2. Berg JM, Tymoczko JL, Stryer L. Section 26.4, Important Derivatives of Cholesterol Include Bile Salts and Steroid Hormones. In: Berg JM, Tymoczko JL, Stryer L (Eds). Biochemistry, 5th edition. New York: W H Freeman; 2002.
3. Blaschko H, Firemark H, Smith AD, et al. Lipids of the adrenal medulla: Lysolecithin, a characteristic constituent of chromaffin granules. Biochem J. 1967;104(2):545-9.
4. Kim CJ. Congenital lipoid adrenal hyperplasia. Ann Pediatr Endocrinol Metab. 2014;19(4):179-83.
5. Lee MJ, Pramyothin P, Karastergiou K, et al. Deconstructing the roles of glucocorticoids in adipose tissue biology and the development of central obesity. Biochim Biophys Acta. 2014;1842(3):473-81.
6. de Guia RM, Herzig S. How Do Glucocorticoids Regulate Lipid Metabolism? Adv Exp Med Biol. 2015;872:127-44.
7. Macfarlane DP, Forbes S, Walker BR. Glucocorticoids and fatty acid metabolism in humans: fuelling fat redistribution in the metabolic syndrome. J Endocrinol. 2008;197(2):189-204.
8. Yan YX, Dong J, Wu LJ, et al. Associations between polymorphisms in the glucocorticoid-receptor gene and cardiovascular risk factors in a Chinese population. J Epidemiol. 2013;23(5):389-95.
9. Gälman C, Angelin B, Rudling M. Prolonged stimulation of the adrenals by corticotropin suppresses hepatic low-density lipoprotein and high-density lipoprotein receptors and increases plasma cholesterol. Endocrinology. 2002;143(5):1809-16.
10. Peckett AJ, Wright DC, Riddell MC. The effects of glucocorticoids on adipose tissue lipid metabolism. Metabolism. 2011;60(11):1500-10.
11. Feingold K, Brinton EA, Grunfeld C. The effect of endocrine disorders on lipids and lipoproteins. In: De Groot LJ, Chrousos G, Dungan K, et al. (Eds). Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-2017.
12. Arnaldi G, Scandali VM, Trementino L, et al. Pathophysiology of dyslipidemia in Cushing's syndrome. Neuroendocrinology. 2010;92 Suppl 1:86-90.
13. Greenman Y. Management of dyslipidemia in Cushing's syndrome. Neuroendocrinology. 2010;92 Suppl 1:91-5.
14. Mancini T, Kola B, Mantero F, et al. High cardiovascular risk in patients with Cushing's syndrome according to 1999 WHO/ISH guidelines. Clin Endocrinol. 2004;61:768-77.
15. Barahona MJ, Resmini E, Viladés D, et al. Coronary artery disease detected by multislice computed tomography in patients after long-term cure of Cushing's syndrome. J Clin Endocrinol Metab. 2013;98(3):1093-9.
16. Ntali G, Asimakopoulou A, Siamatras T, et al. Mortality in Cushing's syndrome: systematic analysis of a large series with prolonged follow-up. Eur J Endocrinol. 2013;169(5):715-23.

JAYPEE BROTHERS

17. Clayton RN, Jones PW, Reulen RC, et al. Mortality in patients with Cushing's disease more than 10 years after remission: a multicentre, multinational, retrospective cohort study. Lancet Diabetes Endocrinol. 2016;4(7):569-76.
18. Gylling H, Vanhanen H, Miettinen TA. Hypolipidemic effect and mechanism of ketoconazole without and with cholestyramine in familial hypercholesterolemia. Metabolism. 1991;40(1):35-41.
19. Srinivasan M, Irving BA, Dhatariya K, et al. Effect of dehydroepiandrosterone replacement on lipoprotein profile in hypoadrenal women. J Clin Endocrinol Metab. 2009;94(3):761-4.
20. Botero D, Arango A, Danon M, et al. Lipid profile in congenital adrenal hyperplasia. Metabolism. 2000;49(6):790-3.
21. Pimenta E, Calhoun DA. Aldosterone and metabolic dysfunction: an unresolved issue. Hypertension. 2009;53(4):585-6.
22. Okamura T, Nakajima Y, Satoh T, et al. Changes in visceral and subcutaneous fat mass in patients with pheochromocytoma. Metabolism. 2015;64(6):706-12.
23. Adam SZ, Nikolaidis P, Horowitz JM, et al. Chemical Shift MR Imaging of the Adrenal Gland: Principles, Pitfalls, and Applications. Radiographics. 2016;36(2):414-32.
24. Herr K, Muglia VF, Koff WJ, et al. Imaging of the adrenal gland lesions. Radiologia Brasileira. 2014;47(4):228-39.

JAYPEE BROTHERS

detailed information on endocrinology books, visit our website www.jaypeebrothers.com, for detailed information on endoc

LIPOCRINOLOGY

The Relationship between Lipids and Endocrine Function

Key Features

- The novel concept of "Lipocrinology" adds a new dimension to the fields of both lipidology and endocrinology
- Lipocrinology describes the relationship between lipid metabolism and endocrine function in health and disease
- Section 1 explores the impact of endocrine function on lipid health and the clinical utility of lipid parameters in decision-making in endocrine disorders
- Section 2 discusses the impact of adipose tissue and lipid metabolism on endocrine health, and the endocrine aspects of lipidology
- Section 3 focuses on the lipotropic effects of hormone-based therapies in various endocrine disorders including diabetes and describes the endocrine effects of lipid-lowering drugs, including recently introduced PCSK-9 inhibitors
- Written by experts in the field with wide clinical and research experience
- The book is presented in an easy-to-read format
- A must-read book for endocrinologists, lipidologists, cardiologists, internists, clinicians, and postgraduate students

Sanjay Kalra, DM (AIIMS), works at Bharti Hospital, Karnal, Haryana, India. Executive Editor of the Indian Journal Endocrinology Metabolism (IJEM); from 2011 to 2015, he is also Associate Editor, Diabetic Medicine (UK); Section Editor, Diabetes, of the Endocrine Society of India (ESI); Manual of Clinical Endocrinology (1st and 2nd editions); and Section Editor, Endocrinology, of the Association of Physicians of India (API) Textbook of Medicine, 11th edition. Vice-President of South Asian Federation of Endocrine Societies (SAFES), he remains busy in clinical care, patient education, and research and medical writing. He is also a member of Asia Lipid Academy Steering Committee.



Sanjay Kalra

Gagan Priya works as Senior Consultant Endocrinologist at Fortis Hospital and Ivy Hospital Mohali. After completing her MD in Internal Medicine from S.M.S. Medical College, Jaipur, she pursued her DM in Endocrinology from AIIMS, New Delhi, where she was awarded Professor M. M. S. Ahuja award and also underwent training in Pediatric Endocrinology through the Asia Pacific Pediatric Endocrinology Fellowship course. While dealing with challenging endocrinology cases in day-to-day practice, she has also been active in medical writing and has contributed to several national and international publications and book chapters.



Gagan Priya

Available at all medical bookstores or buy online at www.jaypeebrothers.com

JAYPEE BROTHERS
Medical Publishers (P) Ltd.
www.jaypeebrothers.com

Join us on facebook.com/JaypeeMedicalPublishers

Shelving Recommendation
ENDOCRINOLOGY

ISBN 978-93-5270-388-3