GENERAL INTRODUCTION
The anatomy of the adrenal glands was described almost 450 years back by Eustachi (1563). A functional role of the adrenal glands was not accurately defined until the pioneering work of Thomas Addison who described the clinical and autopsy findings in 11 cases of "Addison's disease" in his classical monograph in 1855. Brown-Sequard (1856) described that the adrenal glands are "organs essential for life" based on his findings in adrenalectomized (ADX) dogs, cats and guinea pigs.

In mammals a pair of adrenal glands are present one on the top of each kidney. It is an important endocrine gland secreting hormones that are essential for life. They are concerned with carbohydrate metabolism (Blair et al., 1996; Voice et al., 1997; Casadevall, 1999), balance of electrolytes in the blood (Bia and De fronzo, 1981; Bhaskar et al., 1989), maintenance of the volume of circulatory blood (Addison, 1849; Weiner et al., 1967; Stith et al., 1989; Bhaskar et al., 1989), normal modulation of renal water excretion and regulation of extracellular fluid (ECF) volume (Skoreck and Brenner, 1981; Reilly and Ellison, 2000) and controls sexual maturity (Biagini et al., 1995; Gao et al., 1997).

During the stress or emergency conditions the adrenal medulla becomes highly active leading to the release of the said hormones that bring drastic metabolic changes like increased arterial pressure, increased blood flow to active muscles, increased cellular metabolism, increased glucose concentration and glycolysis. The medullary hormones are responsible for alarm reaction;
hence the adrenal gland is frequently called as fight, fright and flight hormonal gland or emergency hormonal gland. Besides its functions, medulla however, is not essential for the survival of an organism (Stryer, 1995; Murry et al., 1997; Guyton and Hall, 2000).

Anatomically adrenal gland is distinctively two parts, adrenal cortex and adrenal medulla (Cuvier, 1805). According to Neelson (1977) and Murry et al., (1997) adrenal gland possesses three independent biologically active zones, which differ functionally and structurally. The medulla is centrally located and the cortex is around the medulla. The adrenal cortex is mesodermal in origin and produces a number of potent hormones, all of which are steroid derivatives having a characteristic cyclopentanoperhydrophenanthrene nucleus with alcohol side chains (Lehninger, 1995; Gamong, 1995). It consists of inner reticularis and middle fasciculate zones and a thin outer layer of glomerulosa zone beneath the adrenal capsule (Majumdar, 1980). The cells of zona glomerulosa secrete the mineralo corticoids, aldosterone; the cells of the zona fasciculata secretes cortisol, cortisone and glucocorticoid, the derivatives of C-19 keto steroids, and the inner layer zona reticularis secretes mainly the sex steroids (Harper, 1983; Guyton and Hall, 1996). Edelman (1975) reported that biosynthesis of steroid hormones takes place in the adrenal cortex from acetyl co-A or from cholesterol. About 50 steroids have been isolated from adrenal cortex but only few are known to possess physiological activity. The important adrenocortical
hormones reported by several investigators are cortisone, hydrocortisone (cortisol), aldosterone, anthrostenodione and dehydro-epiandrosterone. Among these cortisol is identified as the major free circulating adreno-cortisol hormone in humans and fishes, whereas corticosterone is the most important hormone in rodents. According to Haltmeyer et al., (1966) the newborn rat is capable of increasing the rate of adrenal corticosterone production in response to severe stress.

The inner portion of the adrenal gland is adrenal medulla, which is ectodermal in origin and is a derivative of the sympathetic portion of the autonomic nervous system (Mace Hadley, 2000). Studies on chromatin cells of adrenal medulla revealed that they secrete, store and synthesize the catecholamines namely adrenaline or epinephrine and noradrenaline or norepinephrine with different functions (Eranko, 1960). Several investigators reported that chromatin cells contain granules or subcellular particles, which are composed of proteins and phospholipids in relatively high proportions as well as amines (De Robertis, 1964). These subcellular particles are also rich in ATP and ATPase activity (Hillarp, 1958; Hillarp and Thieme, 1959). Type-II glucocorticoid receptors are found on the chromaffin cells. Their activation produces a stimulation of the enzyme adrenal phenylethanolamine-N-methyl transferase (PNMT), which is used in adrenaline synthesis (Kennedy and Ziegler, 2000). Catecholamines also affect on the pituitary secretion of prolactin and growth hormone (Danef and Baes, 1982; Perkins et al., 1983).
Studies on Adrenal Hormones:

Three main types of hormones are produced by the adrenal cortex; they are glucocorticoids (cortisol, corticosterone), mineralocorticoids (aldosterone, deoxycorticosterone (DOC)) and sex steroids. All steroid hormones are derived from the cyclopentanoperhydrophenanthrene structure i.e., three cyclohexane rings and a single cyclo-pentane ring. Glucocorticoids are among the hormones that maintain blood glucose levels, facilitating stress responses requiring rapid and intense physical exertion such as the encounter of prey and predator. From the standpoint of evolution, that may be their main role in metabolism (Sapolsky et al., 2000). In addition, glucocorticoids interact with insulin during feeding and fasting in complex ways that not only maintain blood glucose level but also influence on appetite, feeding patterns, disposal of food stuffs and body composition (Cryer et al., 1986).

Several studies revealed that among adrenal cortical hormones, the corticoids, both glucocorticoids and mineralocorticoids, have a broad spectrum with diverse individual functions i.e., regulation of carbohydrate metabolism (Blair et al., 1994; Holmang et al., 1995; Cipres et al., 1995; Takahashi et al., 1996) and balancing of electrolytes in the body fluids (Imms and Neame, 1974; Bia and Defronzo, 1981; Souness et al., 1995). Glucocorticoids induce gluconeogenesis (Weber, 1968; Voice et al., 1997), lipolysis (Vocharov et al., 1995; Świerczynski et al., 1996; Deshaies et al., 1997), and catabolic break down of amino acids (Beck and Mc Garry, 1962; Almon and Dubois, 1985).
and nitrogen excretion (Tanz, 1962; Schmidt and Thews, 1983; Murry et al., 1997). Selye (1956) proved that an increase in glucocorticoid secretion accompanies external stimuli that cause emotional responses such as extreme cold or heat, hypoxia, trauma and loud sound. Glucocorticoids modulate ACTH secretion (Olefsky, 1975; Speigel et al., 1979), maintenance of inotropy of cardiac muscle (Lefer, 1968), modulate vascular response to the β-agonists (Rodan and Rodan, 1986) and antagonize insulin action (Livingstone and Lockwood, 1975; Olefsky, 1975). Glucocorticoids also regulate appetite (Saxena and Paul, 1991; Arora et al., 1993), energy retention and its utilization (Woodward and Emergy, 1989).

Glucose uptake by muscles is inhibited in the organisms treated with glucocorticoids (Riddick et al., 1962). This action is apparently indirect via the glucose-fatty acid cycle (Munck, 1971). Glucocorticoids appear to be capable of completely protecting against the adverse circulatory effects during adrenal insufficiency (Weiner et al., 1967). Increase in plasma glucocorticoid level (Orr and Mann, 1992) may suppress testicular steroidogenesis (Mann et al., 1982). Most of the enzymes whose activity increases after glucocorticoid treatment are involved in the glucose and aminoacid metabolism.

Several studies revealed the influence of steroid hormones including corticosterone, on the mitochondrial oxidation and oxidative phosphorylation by direct action upon the NAD-Flavo protein region of electron transport chain (Fazekos and Sandor, 1971). Cortisone induces increased gluconeogenesis and
imposes a negative nitrogen balance by enhancing transamination reaction (Gavosto et al., 1957). Noall et al., (1957) reported enhanced uptake of amino acids by liver on cortisol administration. Adrenalectomized animals showed the increased activity of enzymes such as alanine transaminase, tyrosine transaminase (Lin and Knox, 1957) and threonine dehydrase (Goldstein et al., 1962) on cortisol treatment. An alteration of the activity of alanine amino transferase (AlAT) in the testis of ADX rats was reported (Devendra Naidu, 2000), along with the decrease in the enzymes of urea cycle (Schimke, 1963) and aspartate ketoglutarate transaminase in the liver (Gavosto et al., 1957).

Physical stress induces an increase in adrenocorticotrophic hormone (ACTH) and cortisol secretion under the influence of central nervous system mediated by corticotrophic releasing hormone (CRH) and arginine vasopressin (AVP). The very long duration of exercise can also cause an elevation of blood glucocorticoid level (Viru, 1983). Cortisol secretion rises in response to fever, surgery (Udelsman et al., 1987), burns (Vaughan et al., 1982), hypoglycemia (Fish et al., 1986), hypotension and exercise (Luger et al., 1987) due to a normal counter regulatory response to the insult. Numerous observations showed that treatment with glucocorticoids slightly increases the RNA content of liver of rats (Desrache et al., 1959). Glucocorticoids (GC) regulate the change in the protein mass of muscles (Almon and Dubois, 1985), cell differentiation and milk production (Couto et al., 1998) in rats. Deshaies et al., (1997) reported that the corticosterone is essential for global energy balance,
and closely integrate the adaptations of lipid metabolism in ovariectomized (OVX) rats. Hypothalamic glucocorticoid receptor (GR) mRNA levels may change in response to maternal adrenalectomy. In addition, maternal corticosterone is essential for fetal developmental processes including the differentiation of the adrenal medulla (Mace Hadley, 2000). Adrenal deprivation during gestation can greatly influence on fetal adrenal gland with alterations in the activity of steroidogenic enzymes (Machin et al., 1995) and plasma catecholamine levels (Bohn et al., 1987).

Many studies on mineralocorticoids revealed that aldosterone regulates the plasma concentration (Ballard et al., 1960; Imms and Naeme, 1974; Bia and Defronzo, 1981), elevates blood pressure in the rat (Gomez-Sanchez et al., 1990) and also regulate the excretion of electrolytes. Aldosterone increases the active transport of sodium into the cell membranes (Dustan et al., 1973) and regulates potassium concentration in extra cellular fluids (Solomon et al., 1959; Ballard et al., 1960; Tanz, 1960; Bia and Defronzo, 1981). Swierczynski et al., (1996) reported that oral administration of dehydroepiandrosterone causes an increase in NADPH-dependent lipid peroxidation in microsomes of rat liver and kidney. Aldosterone acts rapidly to activate the Na⁺-K⁺, -2Cl⁻ cotransporter in the cardiac myocytes of rabbits, thus enhances Na⁺ influx and secondarily stimulates the Na⁺/ K⁺ pump (Milhailidou et al., 1998). Minute quantities of sex hormones such as testosterone, estrogens are derived from the sex steroids. Testosterone and follicular stimulating hormone (FSH) are
required for the initiation of spermatogenesis during sexual maturation. Estrogen has an important role in maintaining pregnancy and preparing the reproductive tract for parturition.

The hormones of the adrenal medulla are structurally related to catechols (the aromatic nucleus is similar to that of 1,2-dihydroxybenzene) but the amine group is attached to aliphatic side chain. 80% of medullary activity is attributable to epinephrine (α, 3,4-dihydroxy phenyl, β-methyl amino ethanol, L-isomer) and remaining to the norepinephrine ((α, 3,4-dihydroxy phenyl-amino ethanol). Guyton (1983) and Murry et al., (1997) reported that the secretion of epinephrine and norepinephrine is regulated by external stimuli transmitted by the nervous system and they are almost similar in their function. Under various stress conditions i.e., cold, heat, pain etc., adrenal medulla is very active in secreting hormones to compensate fight and flight situations or emergency conditions (Lehninger, 1995; Gamong, 1995; Guyton and Hall, 1996).

Adrenal medullary catecholamines and peripheral adrenaline and noradrenaline factors are involved in the inhibition of gonadotrophin secretion during chronic stress (Ariznavarreeta et al., 1989). Plasma epinephrine levels decreased in adrenal medullectomized (MED) female rats and resulted adverse alterations in pituitary and ovarian activity (Aguado and Ojeda, 1984). Kvetnansky et al., (1993) reported that glucocorticoids inhibit catecholamine synthesis and their release decreases in rats during rest and immobilization.
stress. During exercise both norepinephrine and epinephrine increase in their plasma levels depending upon the duration and intensity of work (Loucks and Horvath, 1984).

Epinephrine is supposed to induce an increase in blood pressure, heart beat rate and glycogen break down in the muscle and liver tissues (Guyton and Hall, 1996). Epinephrine causes an increase in the synthesis of fatty acids in plasma by enhancing lipolysis in adipose tissue regulating the rapid release of fatty acids and glycerol (Murry et al., 1997). Adrenal medullary hormones are catabolic in action that is antagonistic to the anabolic functions of insulin (Schmidt and Thews, 1983) and are secreted in response to low blood glucose level i.e., hypoglycemia in ADX rats (Cannon et al., 1957).

SEX HORMONES

Adrenal gonadal interaction appears to depend upon overlapping function of the steroid hormones, relationship between reproductive function, stress and a variety of other mechanisms (Bambino and Hsueh, 1981; Cumming et al., 1983; Goncharov et al., 1984). The sexual steroid hormones are derived from cholesterol and perform important role in determining and regulating the pattern of sexual behaviour (Young et al., 1964; Phoenix et al., 1968). The female sex steroid hormones have been implicated in the regulation of normal cardiovascular function and in the pathophysiology of hypertensions and cardiovascular diseases (Henry and Norman, 2003). The ovary secretes two main types of female hormones, the estrogen and progesterone. Of these,
the estrogen plays a central role in controlling multiple reproductive processes (Mangelsdorf et al., 1995). The biosynthesis of estrogens during pregnancy involves a complex interplay between the placenta and the fetal adrenal glands. The placenta is capable of carrying out the terminal steps in estrogen synthesis but is incapable of producing androgens because it does not express P-450c 17 (17α-hydroxylase, 17, 20-lyase). Thus, the immediate androgen precursors of placental estrogens are provided mainly by the fetal adrenal cortex. The action of ACTH on the fetal adrenal glands is mediated by insulin growth factor (IGF)-II and adenylate cyclase, which promote cell proliferation and steroidogenesis respectively (Mesiano et al., 1993). The immunoreactivity of estrogen receptor mRNA has been demonstrated in the rat intestinal mucosal cells (Thomas et al., 1993) and it has also been shown that the cells respond to estrogen with enhanced calcium transport (Arjamandi et al., 1994). Estrogen also increases expression of vitamin D receptors (VDR) and bioresponse in rat duodenal mucosa (Liel et al., 1999). However, evidences suggest that estrogen itself act direct upon the intestinal cells to stimulate calcium absorption rather than through calcitriol (Arjamandi et al., 1993). Serum calcitriol levels increase after estrogen (E₂) treatment in postmenopausal women (Gallagher et al., 1980).

Estrogens have been postulated to have a number of important functions in maintaining pregnancy and preparing reproductive tract for parturition and also regulate uterine blood flow in nonpregnant and pregnant animals (Pepe
and Albrecht, 1995). Estrogen suppresses the development and growth of hormone dependent breast tumours (James and Reed, 1980). *In vitro* studies show that the ovaries of the androgen-sterilized rats produce several times more testosterone, estrone and estradiol than the ovaries of untreated rat (Weisz and Loyd, 1965). In the lower animals, the estrogenic hormones induce at estrus phase a series of changes in the female reproductive system associated with ovulation. These changes may be detected by the histological appearance of the vaginal smear. Estrogens are effective in maintenance of female secondary sexual characteristics, acting antagonistically to testosterone (Harper, 1983).

The principal male hormone, testosterone is synthesized by the interstitial (Leydig) cells of the testis from cholesterol, under the control of pituitary FSH, LH and prolactin at least partially through activation of adenylate cyclase. Increased testosterone levels cause feed back inhibition of LH secretion and reduce blood testosterone during surgical or emotional stress (Harper, 1983). Testosterone increases the thickness of the skin over the entire body and increases the ruggedness of the subcutaneous tissues (Guyton and Hall, 2000) and greatly increase the strength of the entire pelvis for load bearing. In the absence of testosterone, the male pelvis develops into a pelvis that is similar to that of the female (Mc Lachlan *et al.*, 1996).

The development of testis and other sex organs were closely dependent on the optimum level of testosterone secreted by the leydig cells under the
influence of pituitary hormones (Smith and Conti, 1996). During maturation the concentration of serum testosterone increases along with a dramatic increase in prolactin secretion (Bittas and Bittar, 1998). Glucocorticoids reduce the number of LH receptors on the leydig cells (Mann et al, 1982; Stahl et al, 1984) by acting the glucocorticoid receptors on them (Stalker et al, 1989; Griffin et al, 1992). Decline in testosterone is mediated by the action of glucocorticoids on the testis (Orr and Mann, 1992).

STUDIES ON ADRENALECTOMY

Adrenal insufficiency is the first clinical disorder that was linked unequivocally to pathologic changes in an endocrine organ. The recognition of this disease by Addison is generally accepted as the beginning of clinical endocrinology. The Addison’s disease (primary adrenal insufficiency) is reported in humans worldwide. Tuberculosis causes adrenal insufficiency by replacing the adrenal cortex with cesating granulomas. Initially enlarged in most cases, the adrenal glands eventually fibrose and shrink, calcifying in 50% of cases (Vita et al, 1985). The most common cause of adrenal deficiency in the industrialized West is Idiopathic adrenal insufficiency also known as autoimmune adrenal insufficiency or the poly endocrine deficiency syndrome. There are evidences of both cell mediated and humoral immune activity directed degeneration against all layers of adrenal cortex. About 50% of the patients show evidence of other autoimmune endocrine disorder. The symptoms of the syndrome is hypoparathyroidism (Neufeld et al, 1981) and
other disease such as autosomal recessive pattern in Sibships (Eisenbarth and Jackson, 1992) and dominant pattern appearing in multiple generations of an affected family (Eisenbarth et al., 1978). The hyper function of adrenal glands leads to Cushing’s syndrome (Cushing, 1932) due to a primary pituitary abnormality. The symptoms of this disease are obesity, reproductive dysfunction, depression, moon face, osteoporosis etc.

Since the time of Addison (1849) there were reports on adrenalectomy. Many investigators reported various changes in the anatomy and physiology of different animals like dog, rat, cat and pig on adrenalectomy (Lefer, 1968; Rovetto et al., 1970). Funder et al., (1973) and Coutard et al., (1978) were reported death of animals due to impairment of circulatory system on adrenalectomy. Several other investigators also supported the same and showed various causes such as alterations in capillary permeability (Zweifach et al., 1953), changes in vasomotor function (Fritz and Levine, 1951), impairment of myocardial function (Reiden-berg et al., 1963; Hofmann and Sobel, 1964), decreased myocardial contractility, arterial blood pressure, cardiac out put (Lefer, 1968; Rovetto et al., 1970) and decreased rate of heart beat in cats and rats (Weiner et al., 1967).

Bilateral removal of the adrenals produces a series of metabolic disturbances which are identical with those appearing in patients with Addison’s disease such as extreme muscular weakness, a variable degree of hypoglycemia, gastrointestinal disturbances, reduced blood pressure and body
temperature, ceased growth in young animals, lose of body weight (Haynes et al., 1985; Joseph et al., 1991; Stryer, 1995; Gamong, 1995; Guyton and Hall, 1996; Murry et al., 1997) and back pain (Jain et al., 1990; Siu et al., 1990; Chin, 1991; De GRoot and Jameson, 2001). Rarely patients may recover from malfunctioning of adrenal gland (Feurstein and Streiten, 1991). Adrenalectomized animals are unable to tolerate stress of any type such as exposure to trauma, cold, heat, toxins, infections, fasting and forced exercise etc., (Turner and Baganara, 1976). Adrenalectomized rats exhibited a decreased strength of muscles, decreased gonadotrophins (Calderon et al., 1986; Lopez-calderon et al., 1987). Primary adrenal insufficiency includes amyloidosis (Arik et al., 1990), congenital unresponsiveness to ACTH (Migeon et al., 1968), congenital adrenal hypoplasia (Wise et al., 1987) and familiar glucocorticoid insufficiency (Moshang et al., 1973). In addition, scenarios include sepsis, trauma and hypertension (Dahlberg et al., 1990) and increase in plasma levels of ACTH (Rees et al., 1971; Mims, 1973; De Souza and Vanloon, 1983; Taylor et al., 1998) in ADX rats. Increased zinc concentration is observed in the tissues of testis (Nair et al., 1987), liver (Nair et al., 1988), intestine (Nair et al., 1989) and in hepatic tissues (Gregoriadis and Sourkes, 1970; Fields et al., 1991) of adrenalectomized rats. Adrenalectomized rats exhibit nearly normal potassium (K+) balance while maintained on saline and glucocorticoids in the form of dexamethasone, although the adrenalectomized animals have a slight elevation in plasma K+,
renal $K^+$ excretion ($U_{K^+}$) (De Fronzo et al., 1980; Bia et al., 1982). Adrenal insufficiency results in metastasates in patients with disseminated breast or lungs, stomach and colon cancers (Ihde et al., 1990; Hasan et al., 1991). Acquired immuno deficiency syndrome (AIDS) can be associated with adrenal insufficiency in its late stages (De GRoot and Jameson, 2001). The adrenals are involved with infection or tumor in well over of the autopsy cases, although less than 50% of the adrenal gland is destroyed in 97% of cases (Glasgow et al., 1985).

Adrenalectomy or administration of the glucocorticoid antagonist RU486 enhance the response to inflammatory agents, showing that endogenous glucocorticoids control inflammation, loss of neurons of the denate gyrus and pyramidal neurons in ADX animals (Flower et al., 1986; Sapolsky et al., 1991). Adrenalectomy can alter nutritional status through appetite loss (Fletcher, 1988), which can be stimulated by glucocorticoid administration (Saxena and Paul, 1991). Yadav-veena et al., (1997) reported that the ADX rats showed decreased glycogenesis and increased glycogenolysis. A decrease in $\alpha$-galactosidase, but an increase in $\beta$-glucosidase were reported in ADX ovary intact rats (Gladson et al., 1998).

Patients with adrenal insufficiency have reduced free water clearance and increased plasma vasopressin (VP) levels, probably due to increased rate of transcription of VPmRNA (Davies et al., 1986). The increased levels of sodium and decreased levels of potassium have been reported in plasma of
adrenalectomized animals (Bia and Defronzo, 1981) and also electrolyte imbalance and attenuated weight gain (Roy et al., 1990). Ma Ehlen and Torvik (1990) suggested that the same process occur in humans in that granule cell necrosis was noted in an individual with a case of progressive adrenocortical insufficiency due to Addison's disease. In earlier reports an increase in Inter-Leukine-I (IL-I) gene expression in rats was noticed after ADX (Goshen et al., 2003).

In adrenalectomized animals there is a progressive reduction in pituitary corticotrophin (CRH) binding capacity and CRH-stimulated c-AMP production, which is sustained for at least 9 weeks after surgery (De Souza et al., 1985; Wynn et al., 1985; Aguilera et al., 1986). Upon adrenalectomy a number of liver enzymes were reported to alter their activity showing a similarity with metabolic or physical stress (Weber, 1968). Blair et al., (1996) reported reduced body weight and decrease in liver glycogen content of gold thioglucone (GTG) obese mice on adrenalectomy. Reidenberg et al., (1963) and Rovetto et al., (1970) were reported prevailing of hypertension and tachycardia in adrenalectomized rat and cat.

The above reports clearly indicate the impact of loss of adrenal glands on various metabolic activities of different groups of mammals. These reports, however, are specific on certain aspects of study. Hence, in order to understand more comprehensively the physiological and biochemical implications of the patients of Addison's disease, the present investigation has
been taken up to study precisely the effects of adrenalectomy on certain aspects of carbohydrate and protein metabolisms of the rats, in addition to haematology, hormones and histology. In order to identify and compare the varying effects of adrenalectomy on the two sex groups of rats, the study is made in both males and females separately. As the reproductive organs appear to be more sensitive in matured beings to adrenalectomy and as studies are on these organs are very limited, the reproductive organs like testis, epididymis and penis in males and uterus, vagina and ovary in females are chosen for study along with the liver in both the sex groups as it is the main metabolic centre of the body. Haematological and hormonal studies are made in blood.

MALE REPRODUCTIVE TISSUES:

The process of reproduction is a complicated and intricately synchronized phenomenon. The organs that take part in this mechanism will function perfectly in co-ordination with each other. The existing literature indicates that ADX have influence on the hormonal integration of the body involving changes in the blood constituents and also tissue constituents. The changes witnessed in the hormonal and biochemical profiles of the serum during adrenalectomy might exhibit changes in the reproductive system and reproductive performance of animals. The male reproductive system consists of a number of individual organs acting together to produce functional spermatozoa and to deliver them into the female reproductive tract. The main organs of it, however, are testis, epididymis and penis.
Testis:

Testis is the central part of the male reproductive system. It is the organ, which generates the haploid germ cells by the process of spermatogenesis and also a site of androgen production. The whole system of reproductive activity is known to be triggered and maintained by three tiered systems of neurohormononal mechanisms in which the hypothalamus, hypophysis and gonads involve (Gamong, 1995; Guyton and Hall, 1996; Murry et al., 1997).

The two major functions of the adult testis are to provide an environment for spermatogenesis and secrete testosterone to regulate a variety of functions related to male reproductive function (Mace Hadley, 2000). The control of these diverse functions requires the coordinated activity of a number of pituitary hormones that are in turn regulated by a complex of neurohumoral inputs from the hypothalamus.

Glucocorticoids seem to modulate testis activity in a complex way. They stimulate gonadal testosterone secretion, but this effect is short living and testosterone levels decline consistently after few hours of glucocorticoid administration (Orr and Mann, 1992). Evidence for a direct inhibition of testosterone synthesis after persistent glucocorticoid exposure was obtained by in vivo (Bambino and Hsueh, 1981; Sapolsky, 1985) and in vitro experiments (Orr and Mann, 1992). Decline in cortisone levels cause pathological changes in the seminiferous tubules and a reduced libido (Mc Kenna et al., 1979; Mac Admas et al., 1986). Reproductive functions are affected by stress (Rabin et
The stress response involves the activation of neural and hormonal networks, which lead to an increase of catecholamines and glucocorticoid secretions. Catecholamines augment testosterone plasma levels by increasing local blood flow in the testis or stimulating directly on the Leydig cells (Eiknesk, 1977; Sapolsky, 1986). Intensive exercise can result in dysfunction of the male reproductive system (Hackney, 1996; Manna et al., 2003). A few research findings in this area have shown that chronic exercise training lower the levels of testosterone along with other reproductive hormonal activities (Raastand et al., 2000), degenerative changes are reported in testis of ADX rats (Nair et al., 1995; Devendra Naidu, 2000).

**Epididymis:**

The epididymis is a heavy cord like structure formed from highly coiled ducts, which closely adheres to the surface of the testis. It is an important organ in the male reproductive system. Spermatozoa acquire progressive motility only during their epididymis transit (Robaire and Hermo, 1988). Epididymis contributes to the physiological maturation of the spermatozoa through secretion of several proteins, glycoproteins and modifying some of the surface proteins with which spermatozoa reach the ductus epididymis (Cooper, 1992, 1995). The maturation of spermatozoa and the acquisition of motility and fertilizing ability do not result from a passive journey of spermatozoa but as a result of exposure and active interaction with the luminal content of different epididymal regions (Jervis and Robaire, 2001).
maturational events take place due to the microenvironment formed by the luminal contents of the epididymal duct (Hinton and Pallandino, 1995). A deficiency of glycosidases and glycosyltransferases (Tulsiani et al., 1998) has been shown to be responsible for male infertility (Corrales et al., 2000).

Epididymis provides conducive microenvironment by rapidly eliminating the harmful metabolic byproducts and free radicals (Hinton et al., 1996). It also protects spermatozoa by blood epididymis barrier provided by tight junctions between the principal cells. This barrier not only protects the spermatozoa from external non-conducive environment but also prevents the access to the immune system (Pollanen and Cooper, 1994). Epididymal spermatozoa are extremely vulnerable to oxidative stress. To overcome this problem epididymis has a rich source of an antioxidant enzyme that scavenges any excess reactive oxygen metabolite released by spermatozoa during epididymal transit (Dacheux et al., 2003).

Number of clinical evidences shown the correlation between abnormalities or disturbances in the epididymal secretions and infertility due to malfunction of the epididymis (Blaguier et al., 1987; Lunde et al., 1990; Fichorova and Nakov, 1993; Fichorova et al., 1995). Principal cells have been shown to be actively involved in the physiological functions of the epididymis involving in endocytosis (Hermo et al., 1998), secretion (Legare et al., 1999) and degenerative changes in epididymis of ADX rats (Nair et al., 2002).
Penis:

All mammals have a single intermittent or copulatory organ, the penis for transfer of semen from male to female. In humans, erectile dysfunction is considered to be a disease state and is referred to as the condition of "impotence". This condition shows impact on the quality of life of the male patients as well as their partners (Impotens, 1992). Excretion is a haemodynamic phenomenon involving the tissue of the corpora cavernosa as well as the corpus spongiosum in the penis (Martin Burchardt et al., 1999). Penile vascular insufficiency is believed to be a very common pathomechanism of erectile dysfunction (Christ, 1995) and which is associated with substantial pathological changes in the erectile tissue leading to reduction in vascular smooth muscle cells and increase in collagen and fibrosis (Nehra et al., 1995; Aydos et al., 1996; Karadeniz et al., 1996; Nehra et al., 1996). Vascular endothelial growth factor (VEGF) is to play a key role in embryonic vasculogenesis (Breier et al., 1992), maintenance of vascular structures and formation of new blood vessels in the adult in response to ischemia and other pathological states. During ejaculation decrease of the parasympathetic stimuli and increase of the sympathetic stimuli were observed and after castration it has been found to decrease substantially the erectile responses (Meisel and Sachs, 1994; Mills et al., 1996). Hence, androgen has major stimulatory influence on several aspects of male sexual behaviour including penile erections. In contrast, androgen suppression decreases the secretion of
testosterone or dihydroepiandrosterone in ADX rats (Chamness et al., 1995; Penson et al., 1996).

FEMALE REPRODUCTIVE TISSUES:

The female reproductive system also consists of a number of organs acting together to produce fertile ovum, of which ovary, uterus and vagina are most important.

Ovary:

The ovaries are paired organs suspended from the body wall by a mesovarium. The ovary has two functional roles that are distinct with intertwined. The first is hormonogenesis and the second is gametogenesis (Irianni and Hodgen, 1992). The mesenchymal tissue differentiates into interstitial tissue, which is the primary source of estrogen production by the ovary. The epithelial tissue becomes closely associated with the germinal elements of the ovary and in addition providing a nutritive environment for the oocytes (Mace Hadley, 2000).

Adrenalectomized rats showed lower birth rate (Angervall, 1962; Thoman et al., 1970), fetal wastage (Mayer and Dulue, 1955) and failure of lactation (Vander schoot and De Greef, 1983). Arora et al., (1994) reported that the compensatory changes in corpus luteum (CL) volume and ovarian \(^5\) \(3\beta\)-HSD activity show significant increase only on day 3 post coitum after adrenalectomy. However, the extent of corpus luteum (CL) volume or ovarian steroidogenesis suppression is indicated by reduction \(^5\) \(3\beta\)-HSD activity after
adrenalectomy (Arora et al., 1994). Shupnik et al., (1989) revealed that gonadotrophin slightly up regulate ERα-mRNA and decreases ERβ-mRNA levels (Shughrue et al., 1998) in endometrium of ovariectomized (OVX) rats. In the ovary, ERβ-mRNA is highly expressive in larger follicles because of the ability of gonadotrophins to down regulate ERβ gene expression (Kuiper et al., 1996; Byers et al., 1997).

**Uterus:**

The uterus is a thick walled, highly muscular, pear shaped hollow organ somewhat flattened dorsoventrally at its anterior end and acts as endocrine organ during pregnancy. It has three openings two anteriolateral, each leading to the fallopian tube and one posterior leading to the vagina. The uterus is an estrogen-dependent organ and its structure and function dramatically changes with estrogen (Clark et al., 1978). It plays an important role in regulation of ovarian function and maintenance of normal reproductive cyclicity. These processes involve systematic biochemical, physiological and morphological changes in both endometrial and myometrial tissues by ovarian hormones. Uterine macrophages and lymphocytes serve as an important line of defense against infectious microorganisms that gain access to the uterine environment. During the menstrual cycle, the uterus undergoes drastic structural and functional changes in response to estrogen with thickening of the endometrium and proliferation of uterine glands in preparation of embryo implantation (Ikeda et al., 2004). Exogenously administered estrogen rapidly increases the
microvascular permeability, edema and increases in weight of the rodent uterus (Cullinan-Bove and Koos, 1993). As this uterotrophic response is very sensitive and rapid, it has been used as a bioassay for a variety of estrogenic compounds. Uterine weight decreased in ADX rats (Venkata Reddy, 2002) and administration of adrenomedullin (ADM) to immature rats led to increased uterine weight (Ikeda et al., 2004).

**Vagina:**

The vagina is a canal extending from the vestibule to the cervix, in which semen is generally deposited. The levels of total carbohydrates, glycogen and glucose markedly decrease in the vagina during diestrus over the estrus phase (Manohar Reddy, 1985). During the proliferative phases of the menstrual cycle, when estrogen levels rise, the superficial epithelial cells become large and flattened, the nuclei become pyknotic, the cytoplasm shows increased acidophilia and glycogen accumulates in the cytoplasm. During the secretory phase of the cycle estrogen levels decrease, the epithelial thickness decreases due to sloughing of surface cells, glycogen is less abundant within the cells; hence the pH of vaginal fluid increases with increased chances of infections. Vasoactive intestinal polypeptide (VIP) is present in high content in the vagina, which increases the rate of vaginal fluid production and blood flow during sexual arousal. The normal flora of the vagina includes the bacteria *Lactobacillus acidophilus*, which is responsible for the production of lactic acid from glycogen and maintenance of the proper pH of the vagina; this helps
in protection of the vagina from most other infectious bacteria (Knobil and Neill, 1998). Ovarian hormones also profoundly influence the vagina and metabolic changes are found in vaginal histology during estrous cycle (Martin and Claringbold, 1960; Kapshikar, 1979). Mukherjee et al., (1986) reported that the utilization of lipid content in female body depends on the estrogen level, as the estrogen level decreases under stress condition (Riggs et al., 1968; Dale et al., 1979). Adrenalectomy also induces stress condition which might be responsible for the decreased estrogen level and in turn utilization of lipids leading to elevated lipids, decreased water content, TSI, organ weight in vagina of ADX rats (Venkata Reddy, 2002).

The above account on the reproductive tissues of male and female rats provide evidence of their importance, hence it will be interesting to trace out the effect of adrenalectomy on the carbohydrate and protein metabolisms and histology of those tissues.

Liver:

The liver is the largest gland of the body and is located in the upper and right part of the abdominal cavity immediately below the diaphragm. The components of liver include the hepatocytes, hepatic venule, portal veins and sinusoids. The liver performs a number of important functions like the production of bile juice and bile pigments, synthesis of urea as a byproduct of protein metabolism and conversion of lipids and amino acids into glucose through gluconeogenesis. The key function, however, is the maintenance of
normal blood glucose concentration, which is an immediate energy source. Reports reveal that the total carbohydrate levels decrease were in the liver tissue of ADX rats (Madhuri, 2001). It suggested the alterations in the basic functions of the liver in the absence of adrenal hormones. Since all the biochemical and physiological activities of the liver are concerned with the majority of the metabolic systems of the body which anticipates more possibility of changes in liver carbohydrate metabolism on ADX. Hence, this tissue is also taken for the present study to understand the changes in the carbohydrate and protein metabolisms of it on adrenalectomy in addition to the changes in histology.