The testicular parenchyma is enclosed by a capsule composed of three distinct layers. The outer layer is a serous membrane, the visceral portion of the tunica vaginalis; the middle layer is the tunica albuginea and the third and innermost layer is the tunica vasculosa (Leeson and Adamson, 1962; Holstein and Weiss, 1967; see Davis and Langford, 1970).

The testicular parenchyma is composed of seminiferous tubules and interstitial tissue. The seminiferous tubules show a complex pattern of convolution. Basically they form loops that empty at both ends into the rete testis, a structure connected with the epididymis via the ductuli efferentia (Johnson, 1934; Liang, 1966). The interstitium is rich in Leydig cells and forms an irregular meshwork of loose connective tissue filling the space between seminiferous tubules (Von Leydig, 1850; Lacy and Pettitt, 1969).

The fine structure of the Leydig cell has been described in detail in rats (Christensen and Desautel, 1973), mouse (Mori et al., 1982), monkeys (see Dym, 1979) and man (see Christensen, 1970). The Leydig cell is polygonal in form and is about 15-20 μm in diameter. It is surrounded by a typical plasma membrane, frequently thrown into folds or microvilli. It has abundant smooth endoplasmic reticulum.
(SER), scattered patches of rough endoplasmic reticulum (RER), moderate sized mitochondria and well developed Golgi complex. The cytoplasm also contains lipid droplets, Reinke crystals, micro tubules and microfilaments. The nucleus is large, usually more or less round or oval, with one or two prominent nucleoli (see Christensen, 1970). Leydig cells are the principal sites of testicular steroidogenesis, as enzymes, coenzymes and cofactors necessary for steroidogenesis are abundant in this cell type (Bouin and Ancel, 1903; Baillie and Mack, 1966).

The seminiferous tubules encompass Sertoli cells (Sertoli, 1865) and germinal cells (Von La Valetta, 1876). The lining of the seminiferous tubules consists of non proliferating Sertoli cells and a proliferating population of germ cells that move slowly upward in the epithelium as they progress from spermatogonia at the base to spermatozoa at the free surface (see Fawcett, 1975). Each spermatocyte is supported by several neighbouring Sertoli cells (Elftman, 1950). Sertoli cells act as supporting matrix for the division and maturation of germ cells (Clermont, 1963), and regulate the process of spermatogenesis (Means et al., 1976; Orth and Christensen, 1977; Jutte et al., 1982).

Sertoli cells are columnar cells extending
from the basal lamina of seminiferous epithelium to the tubular lumen (see Steinberger and Steinberger, 1975). The nucleus of the Sertoli cell is infolded to some extent in all species. The mitochondria are numerous, more slender than those of the germ cells and often very long. The Golgi complex comprises of multiple separate Golgi elements scattered through the basal cytoplasm. Both rough-surfaced and smooth-surfaced types of endoplasmic reticulum are present in the Sertoli cell. It also contains lipids, glycogen and as age advances, lipid, glycogen and ascorbic acid accumulation increases due to decline in spermatogenesis (Lynch and Scott, 1950).

The Sertoli cell is involved in the synthesis of a protein called androgen binding protein (ABP) (see Steinberger et al., 1974; Hansson et al., 1976). FSH stimulates production of androgen binding protein by Sertoli cells which is essential to achieve intratubular concentrations of androgens required for spermatogenesis (French and Ritzen, 1973; Hansson et al., 1973). The ABP synthesized by Sertoli cells helps in the transport of androgen to their target organ, the epididymis (see French et al., 1974).

The pituitary gonadotropins, leutinizing hormone (LH) and follicle stimulating hormone (FSH) are the major
regulators of testicular structure and function. The release of LH and FSH from the anterior pituitary is stimulated by the leutinising hormone releasing hormone (LHRH) produced by the hypothalamus (Schally et al., 1973, 1976). Testosterone production in adult mammalian testes is largely under the control of leutinizing hormone (Catt et al., 1980; Purvis et al., 1981). LH binds with receptors in the Leydig cell membrane (Dufau, 1971; Catt and Dufau, 1973), and initiates a cascade of biochemical events which lead ultimately to increased testosterone synthesis and secretion (de Kretser et al., 1971; Rommerts et al., 1974; see Eik-Nes, 1975). Withdrawal of LH by hypophysectomy (Morat, 1977) causes changes in Leydig cell structure and function.

3β-hydroxy steroid dehydrogenase (3β HSD) is a key enzyme for testicular androgen biosynthesis and a marker for the Leydig cells. This enzyme catalyses the formation of Δ4-3β-ketosteroids from Δ5-3β hydroxy steroids in all steroidogenic tissues (Samuels et al., 1951; Levy et al., 1959; Philpott and Peron, 1971; Van der Vusse et al., 1974). In the testis, 3β-HSD has been localised exclusively in the Leydig cells (Levy et al., 1959; Van der Vusse et al., 1974; Wiebe, 1976; Orth and
Weisz, 1980), and LH/hCG appears to regulate the enzyme activity (Samuels et al., 1951; Hafiez et al., 1971; Shaw et al., 1979; Blanco et al., 1981).

Studies on testicular cells from adult hypophysectomised rats demonstrate that the steroidogenic activity of the Leydig cells may be regulated by an ultra short loop negative feedback mechanism (Chen et al., 1977; Purvis et al., 1979; Adashi and Hsueh, 1981; Ruiz de Galarreta et al., 1983; Centol et al., 1988) via the androgenic secretory products (Ewing et al., 1976; Darney and Ewing, 1981; Centol et al., 1988). Leydig cell responsiveness to gonadotropins is modulated by intratesticular factors (Clermont, 1972; Sharpe et al., 1981; Bergh, 1983; Pintar et al., 1984). Testicular testosterone production is the result of an exquisite cooperation between seminiferous tubules and adjacent interstitial cells for which the requirement of local factors may be important. Testicular estrogens (Hsueh et al., 1978) and androgens (Adashi and Hsueh, 1981) are among those proposed as local regulators to control both Sertoli and Leydig cell functions (Tahka, 1986). The inhibitory effect of androgens on testicular steroidogenesis has been reported to be exerted at the 3β HSD enzyme level.
(Ruiz de Galaretta et al., 1983; Centol et al., 1988). The exact mechanism by which androgens regulate testosterone bio-synthesis remains unclear. Specific receptors for androgens have been found in Sertoli and interstitial cells (Verhoeven, 1980; Nakhla et al., 1984; Isomaa et al., 1985). Therefore, it supports the hypothesis that androgens bind to specific receptors in one of the cell types and promote genomic events leading to synthesis of factors, which in turn results in autocrine and/or paracrine regulation of steroidogenesis (Centol et al., 1988).

Estradiol, in microgram quantities, also is capable of suppressing both LH and FSH (Kulin and Santner, 1977). Several authors have suggested that either testosterone (Purvis et al., 1979) or estrogen (Wang et al., 1980; see Gooren et al., 1980) exert a direct inhibitory effect on Leydig cell production of testosterone. Estradiol is thought to induce its antifertility and anti-androgenic effects in males by directly affecting the testicular structural and functional integrity (Chinoy et al., 1984; Rao and Chinoy, 1984).

The initiation of spermatogenesis in mammalian testes is dependent on the presence of follicle stimulating
hormone (FSH) and testosterone, and maintenance of spermatogenesis is largely obtained in the presence of testosterone (Steinberger, 1971; see Kelch et al., 1972; Lee et al., 1974, 1976; see Fritz, 1978). Administration of FSH alone to immature or mature hypophysectomised rats, does not result in the formation of germinal cells more advanced than pachytene primary spermatocytes (Lostroh, 1963; Lostroh et al., 1963). Since 1965, the Sertoli cell has been implicated as a primary target for FSH and is known to initiate a variety of biochemical events in the rat testis (Murphy, 1965; Mancini et al., 1967; Castro et al., 1970).

The rate of aerobic glucose utilization and production of lactate in vitro by Sertoli cells, from immature rats, is found to be increased during incubation in the presence of FSH (Jutte et al., 1982; Mita et al., 1982). The rate of pyruvate and lactate production by Sertoli cells may be involved in the hormonal regulation of spermatogenesis (Jutte et al., 1983). The main action of FSH on the Sertoli cell involves the stimulation of ABP production (see Fritz et al., 1974; see Tindall et al., 1974; Fakunding et al., 1975; see Steinberger and Steinberger, 1975). Steinberger and Steinberger (1977)
suggested that the effect of FSH on spermiogenesis may be mediated by the creation of high androgen concentration in the vicinity of the germ cells. In rats, high intratesticular testosterone concentration is essential for completion of meiotic divisions of the spermatocyte (Steinberger and Duckett, 1967).

Energy for the normal steroidogenic and spermatogenic functions of the testes is supplied by lipids and carbohydrates. A major portion of the total lipid content of the testis is in the form of phospholipids (Wislocki, 1949; George and Ambedkar, 1963; see Johnson, 1970). The lipid content of Sertoli cells is highly variable from species to species. In the rat, lipid droplets are abundant in stages IX-I of the spermatogenic cycle and droplets are larger immediately after sperm release (Lacy, 1967). Germ cells also contain cytoplasmic lipid droplets (Montagna and Hamilton, 1951). FSH, LH and testosterone are the most effective hormones in maintaining lipid concentration in rat testis (Gambal and Ackerman, 1967). Glucose is a main energy source in the testis and is essential for normal testicular functioning (Waites and Setchell, 1964; see Free, 1970; Zysk et al., 1975). In vitro cultures of seminiferous
tubules in the absence of glucose lead to death of pachytene spermatocytes and round spermatids within 24 hours (Jutte et al., 1961). Glucose and acetate are taken up from the blood, by the testis (Annison et al., 1963).

The first phosphorylating enzyme of the glycolytic pathway, hexokinase (HK), is present in the seminiferous tubules, and its activity is low in the spermatogenic stages up to meiosis, rises during spermatid maturation and is maintained until just after spermiation (Brown et al., 1966; Blackshaw, 1976). The circadian rhythm of rat testicular hexokinase and pyruvate kinase may be indirectly or directly regulated by the gonadotropins, through stimulation of testosterone synthesis (Sosa et al., 1972). Phosphofructokinase and glucose-6-phosphate dehydrogenase (G-6-PDH), two other enzymes of the glycolytic pathway, are also located in the rat testis (Blackshaw, 1976). The function of G-6-PDH in the interstitial cells has been suggested to be to provide the NADPH required in lipogenesis and hormonal steroid synthesis (Ito, 1966; see Blackshaw, 1970; Blackshaw and Elkington, 1970). The G-6-PDH of germinal cells is presumed to mainly function
as a glycolytic enzyme. G-6-PDH was stimulated \textit{in vivo} in rat testis by human chorionic gonadotropin (hCG) (Schor \textit{et al.}, 1963).

Testis has a considerable ability for lactate formation from glucose in the absence of oxygen (Dickens, \textit{et al.}, 1929, 1932; Ewing \textit{et al.}, 1966; Robinson and Fritz, 1981). A specific LDH isozyme, called LDH\textsubscript{X} has been identified in the testis (Blanco and Zinkham, 1963), which is associated with advanced germinal cells (Blackshaw and Samisoni, 1966) and spermatozoa (Goldberg, 1963) only. A possible nutritive role for Sertoli cell in germ cell development was supported by its capacity to produce lactate at high rate (Jutte \textit{et al.}, 1981). The rate of aerobic glucose utilization and production of lactate by Sertoli cells from immature rats were found to be increased when incubated with FSH (Jutte \textit{et al.}, 1982; Mita and Hall, 1982). Lactate and pyruvate are important energy substrates for germ cells (Jutte \textit{et al.}, 1981, Santiemma \textit{et al.}, 1989). Leydig cells appear to be the major site of total LDH enzyme activity in the testis of dog, cat, goat and pig (Wrobel and Kuhnel, 1968) and human (Koudstaal \textit{et al.}, 1967). LDH isozymes with H subunits are predominant in the testis and epididymis (Valenta \textit{et al.}, 1976). FSH stimulation of
lactate production by Sertoli cells may be mediated by cAMP (Steinberger et al., 1978; Mita and Hall, 1982). The Sertoli cells of rat show an active ATPase in plasma membranes (Muffly et al., 1985).

Besides testosterone and gonadotrophins, other hormones also play a role in testicular function. Prolactin has receptors in testicular interstitial cells (Aragona et al., 1977; Charreau et al., 1977) and it acts synergistically with FSH to promote testicular sensitivity to LH. Prolactin probably acts directly on the Leydig cells to increase androgen production (Bartke and Lloyd, 1970; Bartke et al., 1977). Prolactin also facilitates LH action by enhancing binding of LH to its receptors in Leydig cells (Bex and Bartke, 1977; Zipf et al., 1978; Bartke, 1980) and by increasing the number of LH receptors in Leydig cells (Purvis et al., 1979). In hypophysectomised rats, LH, in the presence of prolactin, induced a greater production of androgens than in the absence of prolactin (Bartke, 1971; Hafiez et al., 1972; Bartke and Dalterio, 1976). Prolonged suppression of prolactin in immature male rats inhibits the spermatocyte-spermatid conversion process and alters Leydig cell morphology (Nag et al., 1981).
Thyroid hormones also have a major role to play in male reproduction. Hypothyroidism in human has been generally associated with hypogonadism (Peake et al., 1977). Hypothyroidism in male rats resulted in slight retardation of testicular and epididymal growth (Hammet, 1923) and decreased testicular androgen production (Smelser, 1939; Karkun and Mukherjee, 1967). Reduced FSH (Aruldhas et al., 1982b) or unaltered gonadotropins (Kalland et al., 1978) have also been reported in hypothyroid rats. In human males, thyrotoxicosis was found to be associated with loss of libido, impairment of spermatogenesis, low sperm count and gynaecomastia (Clyde et al., 1976; Kidd et al., 1979). Decreased levels of FSH and LH have been reported in hyperthyroid rats (Aruldhas et al., 1982a).

In addition, altered status of thyroid hormones have been shown to impair testicular carbohydrate and lipid metabolism in rats (Aruldhas, 1981; Aruldhas et al., 1982b; Aruldhas et al., 1986).

Similar to hyperthyroidism, serum cortisol excess was also found to cause hypospermatogenesis, loss of libido, impotency and abnormal pattern of hormone secretion in human males (Sobel et al., 1951; Wilkins and Cara, 1954 and Schoen et al., 1961). In prepubertal rats, dexamethasone reduced the plasma testosterone levels and LH
receptors in Leydig cells. It also inhibited DNA and protein synthesis in Leydig cells (Saez et al., 1977). Corticosterone treatment also decreased the testosterone synthesis in adult rats (Desjardins and Ewing, 1971). Kumar and Rao (1976) reported that administration of cortisol acetate reduced the number of type B spermatogonia, pachytene spermatocytes and spermatids. Unlike serum corticosterone excess, adrenalectomy or corticosterone deficiency was found to have no appreciable influence on serum gonadotropins and testosterone (Valivullah, 1981; Balasubramanian et al., 1983). Kolena et al. (1980) observed no change in labelled hCG binding to its receptors in the testis and plasma testosterone concentration after adrenalectomy. Testicular carbohydrate and lipid metabolism in rat has been shown to be modulated by altered levels of serum glucocorticoids (Valivullah, 1981; Valivullah et al., 1983).

Besides prolactin, thyroid hormones and glucocorticoids, insulin has also been shown to modulate testicular function (Adashi et al., 1982; Blanco et al., 1981).

Clinical diabetes mellitus is a metabolic disease involving altered ability to metabolize glucose. The most common defect associated with diabetes is an inability to
secrete insulin in response to elevated blood glucose levels or an inability of the tissues to appropriately respond to endogenous insulin (see Robbins, 1974; see Stowers, 1975). Traditionally, diabetes has been classified according to the patient's age at the onset of symptoms (Juvenile-onset versus adult-onset). In 1979, the National Institute of Health (NIH) diabetes data group (U.S.A.) recommended that diabetes mellitus be classified into one of 2 major types according to dependence on exogenous insulin. Most patients with diabetes fall into one of 2 major categories: insulin dependent (Type I) or insulin independent (Type II) diabetes mellitus.

Recent studies with morphometric techniques (Rahier et al., 1983; Foulis and Stewart, 1984) have shown that Type I diabetes in man is associated with a specific loss of the pancreatic B cells. The existence of islet cell surface antibodies (ICA) suggests that B cell function may be inhibited by the binding of these antibodies to their antigen on the B cell surface and contribute to the development of type I diabetes (Lernmark et al., 1978).

In experimental animals, diabetes can be successfully induced using chemicals like alloxan (Dunn et al., 1943; Mordes and Rossini, 1981) or streptozotocin (see Dulin et al., 1982) both of which induce a diabetic state.
by causing severe B cell necrosis (Rakieten, 1963; see Dulin and Soret, 1978). The damage to islet tissue is confined to insulin secreting pancreatic B-cells (Dunn et al., 1943), through a direct effect (Hellman and Diderholm, 1955), the A-cells being resistant to alloxan (Dunn et al., 1944). Thus, alloxan proved to be a suitable compound for inducing experimental diabetes in animals. Alloxan inhibits glucose induced insulin secretion (Lazarow, 1949; Rerup, 1970) by inhibiting glucokinase in pancreatic B-cells (Meglasson and Matschinsky, 1984; Lenzen et al., 1987).

The alloxan-diabetes in animals presents like diabetes mellitus in man, with the typical symptoms such as body weight loss, polyuria, glycosuria, Ketonuria, hyperglycemia and Ketonemia (see Lenzen and Panten, 1988). Lundquist and Rerup (1967) explained that there are three phases of alloxan-diabetes development, mainly due to insulin deficiency, insulin surplus, then insulin lack. The initial hyperglycemic phase following alloxan injection was accompanied by a significant decrease in plasma insulin and liver glycogen levels (5 minutes after injection). The subsequent hypoglycemic phase was accompanied by a marked rise in plasma insulin levels. Liver glycogen levels also increased towards normal values (2 hours after injection).
During the development of the permanent hyperglycemic phase (24 and 48 hours after injection), plasma insulin levels decreased gradually to subnormal.

A common secondary effect of diabetes is reproductive dysfunction (Rodriguez-Rigau, 1980). Sexual disturbances such as impotence, (Rubin and Babbott, 1958; Schoffling et al., 1963; Irisawa et al., 1966; Kolodny et al., 1974; Morley and Melmed, 1979), decreased libido (Klebanow and MacLeod, 1960) and decreased semen quality (Irisawa et al., 1966; Bartak et al., 1975) are frequently observed in diabetic patients. Diabetes is seen to cause a reduction in testicular and accessory sex gland weights (Foglia et al., 1969; Oksanen, 1975; Howland and Zebrowski, 1976; Hutson et al., 1983), testicular tubular degeneration, reduced spermatogenesis (Rosenmann et al., 1974), decreased serum androgen levels (Tesone et al., 1976; Paz et al., 1978; Murray et al., 1981; Centol et al., 1968), and a reduced capacity of the Leydig cells to synthesize androgens (Calvo et al., 1979; Paz et al., 1979). It has been reported that diabetic patients, as a group, showed impaired nocturnal penile tumescence as evidenced by decreased total penile tumescent time, diminished duration and frequency of full erections and a reduction in the maximum increase in penile circumference (Karacan et al., 1977; 1978; Fisher et al., 1979). In most descriptions of diabetic impotence, sexual
appetite is said to remain intact despite the profound impairment of erectile function (Rubin and Babbott, 1958; Cooper, 1972; Kolodny et al., 1974). However, recent studies have found a reduction in sexual appetite in over a quarter of their samples (Jensen et al., 1979, McCulloch et al., 1980). Decreased release of FSH and LH after the administration of GnRH in diabetic patients has been reported (Distiller et al., 1975). However, Rastogi et al. (1974) reported no attenuation in pituitary response to GnRH in diabetic patients.

It has been postulated that the reproductive disturbances in the diabetic rat could be due, at least in part, to alteration in the secretion or production of hypophyseal gonadotropins (Foglia et al., 1969; Calvo et al., 1984). In 21-day-old alloxan-diabetic rats, the serum LH levels tend to be diminished while the hypophyseal values augmented, whereas serum FSH levels are normal and the hypophyseal levels are increased (Howland and Zebrowsky, 1976). In streptozotocin diabetic rats, low circulating levels of LH (Howland and Zebrowsky, 1976) and prolactin (Smith et al., 1977) were observed. Howland and Zebrowsky (1980) suggested that GnRH secretion by the hypothalamus of the diabetic rat might be deficient. Further, it is suggested
that deficiency of both LH and insulin affects the activity of at least one of the regulatory enzymes 3-B-hydroxy steroid dehydrogenase (3B-HSD) of the biochemical pathway leading from cholesterol to androgens (see Eik-Nes, 1970; Ruiz de Galarreta et al., 1980; Blanco et al., 1981).

The testis has been regarded as an insulin independent organ (Fritz, 1972), but recently, insulin receptors are demonstrated in the testis (Saucier et al., 1981). Insulin has been shown to enhance the production of ABP (Karl & Griswold, 1980), and metabolism of glucose (Borland and Hall, 1983) by cultured Sertoli cells. Ruiz de Galarreta et al. (1980) have shown that streptozotocin-diabetes inhibits the oxidation of glucose by rat seminiferous tubules.

At the testicular level, the number of LH receptors is reduced in diabetic rats (Charreau et al., 197b). It has been suggested that reduced testicular steroidogenesis in the diabetic male rat may represent a direct consequence of insulin deficiency at the hypothalamic and/or pituitary levels (Adashi et al., 1981; Benitez and Diaz, 1985). On the other hand, other reports show that insulin may play a direct role in the rat testis (Adashi et al., 1982).

A careful perusal of the foregoing literature
reveals that glucose is a main energy source in the testis and is essential for normal testicular functioning. Diabetes mellitus has been shown to cause various reproductive dysfunctions, like impotence, decreased libido, decreased testicular weights and impaired testicular functioning. Although some amount of work has been carried out to show the alterations in testicular steroidogenesis and serum hormonal profiles due to diabetes, no work has been done so far to study the impact of diabetes on testicular metabolism. Since the glycolytic enzymes are essential to maintain the normal supply of substrates and coenzymes necessary for protein and lipid synthesis, it was felt that the study of these enzymes would give a better understanding to the diabetes - induced functional changes in the testis. The response of ATPases has also been considered under diabetic conditions.

It is thought that the present investigation may throw light on certain metabolic changes brought about in the testis due to diabetes.