# A STUDY OF EFFECT OF PROGESTERONE ON EPIDIDYMIS IN ALBINO RATS

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## ABSTRACT

Progesterone, an anti androgen compound that recently receiving attention for potential use as male contraceptive and for other medical purposes, such as treatment of prostate diseases. In the present study adult male albino rats were administered the progesterone for 15 & 30 days and the histology and fine structures of the epididymis were studied. After treatments for 15 and 30 days sperms were found to greatly reduce in number from lumen of caput epididymis, middle segment and cauda epididymis, of severely affected specimen. The epithelium was tall and the light cells were large and distended with many dense bodies resembling lysosome (Loving & Flickinger 1976)1. The lumen was filled with scanty sperm and debris, which appears to be derived from germ cells. It is suggested that the light cells of epididymal epithelium may have a role in clearing the lumen in which they are particularly large and numerous.

The aim of present study is to determine the effect of progesterone on the structure of target cells of epididymis normally stimulated by androgens and further correlate the findings in light of previous studies, to draw the significant conclusion. The study showed that the progesterone have intense inhibitory effect on the epididymis. The degenerative histological findings are found in form of reduce number of spermatozoa, debris of cell mass & reduce epithelial cells height. These changes may have an important role in the anti fertility effect of progesterone.

**Key words** Progesterone, contraceptive, epididymis.

## INTRODUCTION

Progesterone is the natural progestin and is derived from cholesterol. It is the natural antagonist of testosterone (Brotherton 1976)[2]. It shows strong feed back action on hypothalmo hypophysial axis and so reduced plasma luteinizing hormone and testosterone level (Aubray & Khosla 1971)[3]. Cyproterone acetate, the anti-androgen, most potent derivative of progesterone, leads to atrophy of accessory sex glands (Dhal & Asmundkjacheim 1974[4], Loving & Flickinger 1976[1]and Hohback 1977[5]). Effects of this in intact animals resemble castrational changes and most noticeable of these is the atrophy of the sex accessory glands. Cyproterone acetate is of medical interest because that causes reversible infertility (Whalen & Luttge 1969)[6] by suppressing androgen dependent organs. They may be useful in the treatment of various diseases; including prostatic neoplasia.The basis of the anti fertility action of progesterone is not clear, however, because several parts of the reproductive tracts are affected by it. The weights of the testis and accessory sex glands of animals treated with cyproterone acetate are reduced (Neumann et al 1970[7]. Ultra structural studies of the prostate and the seminal vesicles of animal treated with cyproterone acetate have shown that there is a large decline in the height of the epithelium and a diminution in the organelles involved in secretion ( Dahl & Tveter 1974[4] and Loving & Flickinger 1976[1]). Information on the structure of testis and epididymis in the presence of cyproterone acetate indicated that spermatogenesis is affected (Neumann et al 1969[7]).and the histology of the epididymal epithelium is altered as well (Prasad et al 1970[8], Rajalakshmi et al 1971[9], Prasad et al 1972[10]). Micro quantities of cyproterone acetate released from subcutaneously implanted Sialistic capsule, cause transient infertility in rats by selectively inhibiting epididymal function. Consequently, sperm motility and viability are lost. The purpose of present study was to study the effects of progesterone on the structure of target cells of epididymis, normally stimulated by androgens, in albino rats and to correlate the findings

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in light of previous studies to draw the significant conclusion. Such data could be useful when this experiment is evaluated in man and it seemed that such a study could aid in understanding the anti fertility action of progesterone by providing more detailed information on the type of alteration in epididymal epithelium and spermatozoa. Therefore, in the present study we examined the histology of the several parts of epididymis of albino rats treated for up to 15 & 30 days.

## MATERIAL AND METHODS

The present study was carried out on 18 sexually mature adult male albino rats weighing 150-200 grams. The rats were kept in airy room in steel cages in separate groups. They had constant access to water and food, and the temperature was maintained. Before the treatment 6 rats were taken as control for normal histological structures and 12 rats were used for progesterone treatment in two groups A, and B.

The group A having 6 rats & was administered progesterone up to 15 days.The group B having 6 rats & was administered progesterone up to 30 days.The drug was administered in dose of 10 mg/day/rat subcutaneously irrespective of body weight, at 10 a.m. daily under aseptic precaution. This constant dose was used, rather than one that was a function of the weight of the animal, so that our results could be correlated with extensive work in the literature that has been carried out using a dose of 10 mg /rat/day ( Neumann et al 1969 7 and Whalen & Luttge 1969 6 ). The animals of control group were scarified before treatment start. The animals of group A and B were scarified at 15 and 30 days of drug administration respectively. After sacrificing the animals on different days of experimentation epididymis have been removed and processed for histology. Sections, cut at 6 microns, were stained with haematoxylin & eosin.

## OBSERVATION OF CONTROL GROUP OF RATS-

The epididymis has an even contour and good vascularity. The lining epithelium of epididymis is composed of two types of cells- Tall columnar (principal) cells and triangular shaped basal cells. Each cells reach to the basement membrane, thus the epithelium is pseudostratified columnar. The columnar (principal) cells of the epididymis are accompanied by 'halo' cells, which are believed to be migrating lymphocytes and by small basal cells. The epididymis also contains significant number of the 'light cells' (Loving C.K. & Flickinger C.J. 1976[1] ).The nature of the light cells indicates that they are absorptive cells ( Flickinger 1977[11]). The columnar cells bear non motile processes (stereocilia) and the cytoplasm of most of the columnar cells contains distinct droplets and granules of various sizes. The nuclei of the cells are elongated and lay some what different levels. The lumens of epididymis are filled with spermatozoa. (Fig.01)

## OBSERVATION OF A GROUP OF RATS (15 DAYS TREATED RATS)

There are no any clear changes seen in shape & size of epididymis but vascularity is slightly reduced. The epididymis of 15 days treated rats shows slightly degenerative histological changes. The lumen of epididymis show scanty number of spermatozoa & the spermatozoa appears to be clumped and often only a few round cells resembling immature germinal cells. Despite this change in luminal content the epithelium remained columnar with slightly reduced cells height. The diameter of epididymis is also decreased. At places epithelium showed the changes in character, as evidenced by reduction in affinity for eosin. Nucleus showed reduced size & morphological deformity at places. The stereo cilia have been also found to be reduced. (Fig.02)

## OBSERVATION OF B GROUP OF RATS (30 DAYS TREATED RATS)-

There is no any clear changes seen in shape of epididymis but size and vascularity is slightly reduced. The epididymis of 30 days treated rats show progressive degenerative histological changes in form of reduce cell height of epithelial lining. The lumen of epididymis show progressive reduced numbers of spermatozoa. The spermatozoa almost loss there morphological features. The lumens of epididymis are filled with masses of cells which appear to be that protein material of spermatozoa, might have been denatured. The diameter of lumen of epididymis has been found to decrease. Nucleus showed reduced size & morphological deformity at places. At some places nucleus also show less affinity for haematoxylin staining. The stereo cilia have been also found to be highly reduced. (Fig.03)

## DISCUSSION

In the epididymis, the numbers of sperm were greatly reduced or absent from the lumen of the severely affected animals. Since epithelium did not appear to be significantly altered in its complement

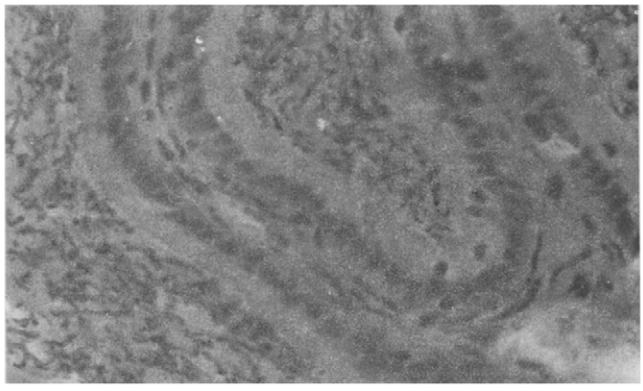

Fig .01-Photomicrograph of epididymis of control rat shows, lumen are full of spermatozoa and epithelium is pseudostratified columnar. H &E. Staining x 600

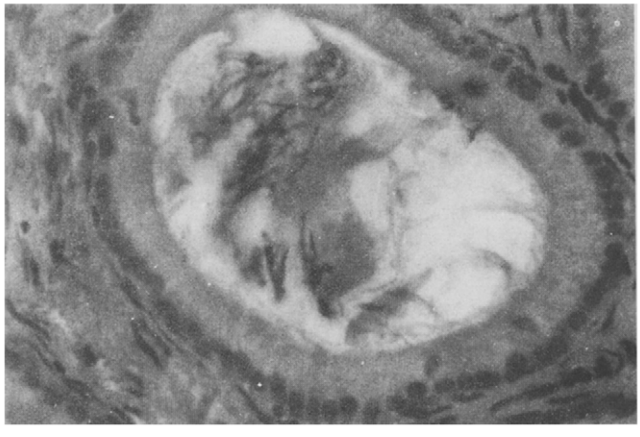

Fig .02-Photomicrograph of epididymis of 15 days treated rat with progesterone, shows reduce number of spermatozoa and presence of cell debris in the lumen.It also shows slightly reduce in the height of principal cells. H &E. Staining x 600

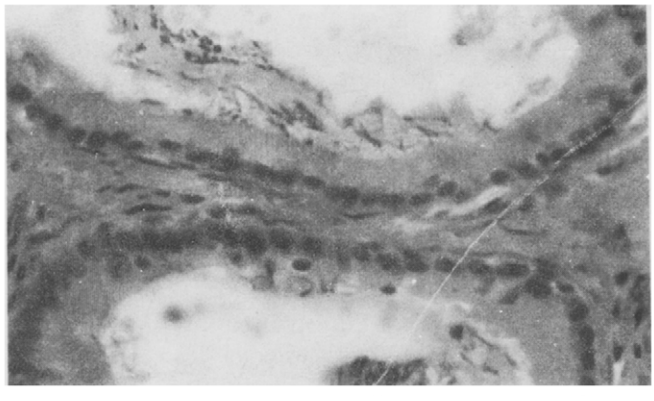

Fig .03-Photomicrograph of epididymis of 30 days treated rat with progesterone, Show reduced numbers of spermatozoa. The spermatozoa almost loss there morphological features. The lumens of epididymis are filled with masses of cells which appear to be that denatured protein material of spermatozoa. H &E. Staining X 600.

of organelles and there were no indications of infiltration of phagocytic cells, the lack of sperm seems most likely due to the decreased production of sperm by the testis and sperm may have to move to more distal parts of the male duct system. This finding is in accord with most of previous light microscopic studies, which indicated that the influence of progestational agents on the testis have yielded important results. Progestin, including progesterone have been reported to suppress spermatogenesis in several species (Kar et al 1967[12], Heller et al 1958[13], Heller et al 195914 and MacLeod 1965[15])

The presence of material in lumen of epididymis on the basis of light microscope observed as exfoliated epithelial cells. Our observations, however suggest that these structures have a different origin. They did not bear a resemblance to the epithelial cells. They have migrated in the lumen. There nature is not definitely established, but they usually were masses of cytoplasm that lacked of the nucleus, and there morphology was reminiscent of that of the residual body of the Reguard which was normally shed by developing sperm in the testis. This, along with occasional presence of parts of sperm tails suggest that these luminal structure consist of germ cell cytoplasm either derived from sperm in epididymis or from remnants of earlier stages of germ cells, shed by seminiferous epithelium following depletion of late spermatids, in the testis. Cyproterone acetate, the anti-androgen, most potent derivative of progesterone, competitively inhibits the action of exogenous or endogenous andr ens by interfering with the uptake of androgen by receptors in such target tissues, as the ventral prostate, seminal vesicle and the epididymis, leads to reduction in weight and secretary function of these structures (Dhal & Tveter 1974 [4], Loving & Flickinger 1976[1] and Hohback 1977[6]).

In present study the epididymis of 15- 30 days treated rats show progressive degenerative histological changes in form of reduce cell height of epithelial lining and reduce diameter of lumen of the epididymis.

## CONCLUSION

Administration of progesterone at the dose used in the present study results in infertility in rats within 15 to 30 days. The results of present study suggest that an important basis for this antifertility

action is an alteration in spermatogenesis (Loving C.K.& Flickinger C.J.1976[1]).Changes in the epididymis may also contribute, however, since the lumen of epididymis appeared to be filling with a mass of cellular debris and degenerating sperm. A very small dose of cyproterone acetate released from implanted Silastic capsules (232 micro grams /day) cause infertility, non motile sperm and alteration in epididymal histology, in the absence of any change in testis, sex accessory glands or libido (Prasad et al 1970[8], Rajalakshmi et al 1971[9], Prasad et al 1972[10],)

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