

تأثير المفعول طويل المدى لهرمون التستستيرون وهرمون  
الجوناد وترويين الكوريونى البشرى على نشاط الجهاز التناسلى  
فى ذكور الأرناب

٢ - التغييرات الهستومورفولوجية للغلغة وغدها

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أجريت هذه الدراسة على <sup>عدد</sup> ٣٣ من ذكور الأرناب البوسكات ، قسمت الى خمسة  
مجموعات ، واعتبرت المجموعة الاولى كضابط ، ثم حقنت المجموعات الاخرى بجرعات  
مختلفة من هرمون التستستيرون وهرمون الجوناد وترويين الكوريونى البشرى .  
تم فى هذا البحث تميز نوعين من الغدد فى غلغة ذكور الأرناب ، احدهما  
دهنية والاخرى أنبوية .

لوحظ أن هرمون التستستيرون قد أحدث زيادة ملحوظة فى كل من سمك الطبقة  
القرنية والانقسام الميتوزى للخلايا القاعدية فى بشرة الغلغة .

وقد دلت الدراسات القياسية على أن هناك زيادة معنوية فى قطر النهايات  
المفرزة للغدد الانبوية ، زيادة فى ارتفاع الخلايا المبطنة فى هذه الغدد وزيادة  
فى قطر أنوبيتها ، وتدل هذه النتائج على وجود علاقة طرد يقين نشاط هذه الغدد  
مع زيادة جرعة هرمون التستستيرون . كما لوحظ أيضا هذه العلاقة الطردية وتأثيرها  
على حجم ونشاط الغدد الدهنية للغلغة .

ومن الجدير بالذكر أنه لم يلاحظ أى تغييرهستومورفولوجى على الغلغة وغدها  
فى ذكور الأرناب بعد حقنها بهرمون الجوناد وترويين الكوريونى البشرى .

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**THE EFFECT OF LONG-TERM TP OR HCG ADMINISTRATION  
ON REPRODUCTIVE FUNCTIONS IN ADULT MALE RABBITS\***  
**II. Histomorphological Changes in the Prepuce and Preputial Glands**  
(With 1 Table & 8 Figs.)

By  
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**SUMMARY**

The effect of long-term treatment with various doses of TP or hCG on the prepuce and preputial glands was studied on 33 male rabbits of pure Bouscat breed. The preputial epidermis, sebaceous and tubular glands exhibited a significant dose-related increase in activity in rabbits treated with various doses of testosterone propionate (TP) other than those treated with human chorionic gonadotropins (hCG). In the preputial epidermis, the stratum corneum was greatly increased in thickness, while the stratum basale showed aggravated mitotic activity. Also the sebaceous glands were enlarged and activated. Moreover, the tubular glands presented a significant increment in the diameter of their secretory end pieces as well as in the height of the glandular epithelium.

**INTRODUCTION**

NICKEL, *et al.* (1981) stated that the preputial glands are present in the prepuce of all domestic mammals. Generally, these glands are composed of hair-follicle glands, free sebaceous glands (Smegma glands), alveolar and tubular scent glands. The different types of glands occur in various number and combination in the different mammals. However, HOLTZ and FOOTE (1978) mentioned that the preputial glands in rabbits are rather inconspicuous sebaceous glands and embedded in the dermis of the prepuce near its orifice.

MONTAGNA and KENYON (1949) studied the influences of androgen on the growth and secretion of the sebaceous glands of rabbit. Further investigation on the cutaneous activity of the scrotum of rabbit after long-term TP and hCG administration has been carried out by FATH EL-BAB, *et al.* (1982). There are various opinions about the function of the preputial glands; the old concept have considered these glands to be rudimentary organs, but recent studies suggested that the secretory material of the preputial glands produces individually-specific olfactory signals which make the lair and act as a record of possession of the mate. Consequently, the present work was performed to study the histomorphological features of the prepuce and

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the preputial glands in rabbits and to determine the effect of long-term administration of testosterone propionate or human chorionic gonadotropins as contraceptives on these organs.

### MATERIAL and METHODS

The findings presented here were made in the course of experiments which were conducted in an attempt to determine the impaired testicular activity of androgen-treated rabbits. Testosterone propionate (TP) and human chorionic gonadotropins (hCG) were administered until minimal testicular activity was observed in a trial to determine the effectiveness of these substance as contraceptives.

Thirty three adult male rabbits (9 months old, approximately 2.5 kgs weight) of pure Bouscat breed were divided into 6 groups and treated as follows:

Group	Number of rabbits	Treatment
Control	6	Untreated
Low TP	6	5 mg TP/Kg/day
High TP	5	10 mg TP/Kg/day
Low hCG	5	200 I.U.hCG/day
Medium hCG	6	400 I.U.hCG/day
High hCG	5	800 I.U.hCG/day

Drug application was by deep intramuscular injection into the anterior aspect of the thigh muscle.

Animals were sacrificed during the 16<sup>th</sup> week after the commencement of the treatment. Specimens from the prepuce and preputial glands of the control and treated rabbits were fixed in 10% neutral formalin and in Bouin's fluid. Serial horizontal and vertical paraffin sections of 8-10  $\mu$ m thickness as well as frozen sections were made. Haematoxylin and Eosin, Mallory's trichrome, Periodic acid Schiff's technique, Alcian blue and Sudan black-B stains were adopted.

### RESULTS

The prepuce of the adult rabbit consist of an external layer which reflected inward at the preputial orifice to form the internal layer. The preputial epidermis (Fig. 1) was thin and folded, while the dermis was relatively thick and contained a mass of adipose tissue in its deepest layer. The hair follicles were arranged in groups and were found in the external layer of the prepuce. Two types of preputial glands could be recognized; Sebaceous and tubular glands.

#### A- Sebaceous glands:

It were of the compound alveolar variety. Several alveoli opened into common excretory ducts which in turn opened into a main large duct lined with stratified cornified epithelium.

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This main duct drained its content into a large reservoir which was formed by the distal portion of a hair follicle and opened near the preputial orifice (Fig. 2). Each glandular alveolus was composed of basal, intermediate and central cell layers and bounded peripherally by a distinct basement membrane. The basal cells were small in size and flattened in shape, with a basophilic cytoplasm and small darkly stained nuclei. Few mitotic figures has been recognized. The intermediate cells were arranged into 3-4 polyhedral cell layers of variable sizes. The cytoplasm contained fine acidophilic granules and few vacuoles. The nuclei were large rounded, eccentric, lightly stained and contained one or two nucleoli. The central cells were larger than those of the other layers and contained deeply stained nuclei with indistinct nucleoli. Their cytoplasm was vacuolated. Near the lumen the cells showed progressively various signs of disintegration, however the lumen contained cellular debris and keratin.

### B- Tubular glands:

These glands were enclosed within a connective tissue capsule. Trabeculae were detached from the capsule dividing the gland into several lobules. The secretory cells were low columnar or cuboidal cells with rounded basally located nuclei (Fig. 3). The apical portion of the cytoplasm was granular and deeply stained. These cells contained faintly PAS-positive materials. Slight Sudanophilia was also observed within these cells. The average diameter of the secretory tubules was 75  $\mu$ m. The epithelial thickness and the nuclear diameter were also measured (Table 1). Luminal bleb-like projections from the columnar epithelium lining the intralobular, interlobular and secretory tubules were observed. The interlobular ducts were joined together to form a large excretory duct which was lined with stratified squamous epithelium and opened into the inner surface of the prepuce near the preputial orifice (Fig. 4).

### Testosterone Propionate (TP):

The effect of low dose of TP induced a moderately increase in the epidermal thickness. The stratum basale presented an increased mitotic activity. The interlobular connective tissue was reduced. The tubular glands were lined by tall columnar cells with large rounded basally located nuclei. The average diameter of the secretory tubules was about 87.50 $\mu$ m. However the height of the epithelium and the nuclear diameter were 22.50 and 7.36 respectively. The sebaceous gland did not show any remarkable changes than in the control animals.

The effect of high dose of TP persuaded a noticeably increase in the epidermal thickness (Fig. 5) particularly in the stratum corneum. The mitotic activity of the basal cell layer was also aggravated. In the external preputial layer, most of the hair follicles were increased in thickness and extended deeper in the dermis. The sebaceous glands were enlarged and activated. The peripheral cell layer showed numerous mitotic figures (Fig. 6), while the intermediate cells contained abundant lipid droplets and the central cells were greatly hypertrophied, vacuolated and fragmented (Fig. 7). The tubular glands were greatly stimulated and showed a significant increment in the average diameter of the secretory tubules, height of the glandular epithelium and their nuclear diameter (Fig. 8a). Moreover, numerous bleb-like protrusions from the apical border of the glandular cells were clearly observed (Fig. 8b).

### Human Chorionic Gonadotropins(hCG):

Administration of various doses of human chorionic gonadotropins did not provoke any significant histomorphological changes in the preputial epidermis, tubular glands and sebaceous glands.

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### DISCUSSION

The present investigation revealed two types of glands embedded within the dermis of the prepuce of the rabbits. The first type was multilobulated sebaceous glands which opened into a large reservoir formed by the distal portion of a hair follicle. The second type was lobulated tubular glands which opened into the inner surface of the prepuce by a large excretory duct. However, HOLTZ and FOOTE (1978) gave a brief description for the first type of the preputial gland in rabbits and considered the lobulated tubular glands to be perineal or inguinal gland.

Our findings are in consistent with MONTAGNA and NOBACK (1946) who described two types of preputial glands embedded within the dermis of the prepuce of the rats and open onto the surface by a large excretory duct.

The present investigation showed an increment in the mitotic activity of the basal cell layer and in the thickness of the cornified layer of the preputial epidermis after TP administration. Similar results were observed by FATH EL-BAB, *et al.* (1982) in the scrotum of rabbits. This phenomenon might be due to the fact that both prepuce and scrotum arose from a common anlage in the urogenital ridge and each of these organs developed in response to androgenic stimuli. Hence steroidogenesis, which play an essential role in the process of epidermal maturation and keratinization, could be significantly accelerated by testosterone therapy (PARKER, 1981). It seems likely that long-term injection of TP stimulates the steroid metabolism in the preputial epidermis and concomitantly causes thickening of the stratum corneum and increasing mitotic activity of the stratum basale. These findings greatly support the previous studies of BURKICK and CAMON (1941); BULLOUGH and VAN OORDT (1950) and ALLEN (1957, 1958) on the mitogenic action and the influence of testosterone propionate on the preputial gland, the epidermis and the cell division in mouse, respectively.

In accordance with the data in the available literature the work herein showed a dose-related increase in the activity of the preputial sebaceous glands. However, the sebaceous glands at the face, back and chest (PARKER, 1981) and in the prepuce (NICKEL, *et al.* 1981) are dependant upon androgenic stimulation for both their development and secretory activity. Seemingly, the sebaceous glands at the prepuce of male rabbits are exquisitely sensitive to small amounts of androgens. It was observed in the present study that, TP causes a more profound and significant increase in the tubular gland-activity than HCG. In broad outlines, the mechanism of TP action on the tubular gland-epithelium is probably through the binding of the TP with the intracellular protein and then an interaction with its initiation sites on the nuclear chromatin which results in a striking increase in nuclear metabolism with a subsequent increase in the protein metabolism. There is no doubt that the preputial tubular and sebaceous glands in rabbits are cutaneous scent glands, the secretion it produces may disseminate into the environment by the urine, which then acts as a mode of communication between sexual partners or between members of the same species. The secretions produced by the cutaneous scent glands contain one or more pheromones (BRUCE, 1969; McDONALD, 1980 and NICKEL, *et al.* 1981). The term, pheromone, is applied to chemical substances secreted by one animal that arouse either behavioral or hormonal changes in another individual or the same species (PARKER, 1981). So, it should be emphasized that TP may accelerate pheromone production in adult male rabbits.

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## LEGEND OF THE FIGURES

- Fig. (1):** The skin of the internal layer of the prepuce. (Hx & E. X 250).
- Fig. (2):** L.S. in the main secretory duct of the preputial sebaceous gland. (Hx & E. X 43).
- Fig. (3):** Section in the preputial tubular gland of control male rabbits. (Hx & E. X 250).
- Fig. (4):** L.S. in the main secretory duct of the preputial tubular gland. (PAS. Hx. X 43).
- Fig. (5):** Section in the skin of the prepuce after TP administration showing an increase in the thickness of the stratum corneum. (Hx & E. X 100).
- Fig. (6):** Section in the preputial sebaceous gland after TP administration showing mitosis (arrow) in the stratum basale. (Hx & E. X 400).
- Fig. (7):** Section in the preputial sebaceous gland after TP administration showing mitosis (arrow) in the peripheral cells and hypertrophied central cells. (Hx & E. X 400).
- Fig. (8 a,b):** a, Section in the preputial tubular gland after TP administration (PAS. Hx. X 250).  
b, Higher magnification of the glandular cells showing the secretory droplets that protruded from the cell apex. (PAS. Hx. X 400).

Table (I)  
 The diameter of the secretory end-piece; hight of the glandular epithelium  
 and its nuclear diameter of the preputial gland in the control and treated rabbits

	Control	TPL	TPH	CGL	CGM	CGH
Diam. of gland. end-piece (Um)	75.0 $\pm$ 0.9	87.5 $\pm$ 0.9*	93.7 $\pm$ 0.9*	76.0 $\pm$ 0.9	77.5 $\pm$ 0.9	75.2 $\pm$ 0.9
High of gland epith. (Um)	18.6 $\pm$ 0.5	22.5 $\pm$ 0.5*	26.9 $\pm$ 0.5*	20.1 $\pm$ 0.5	20.1 $\pm$ 0.5	20.2 $\pm$ 0.5
Nuclear dian. of gland. epith. (Um)	5.7 $\pm$ 0.3	7.3 $\pm$ 0.3*	7.5 $\pm$ 0.3*	6.1 $\pm$ 0.3	5.7 $\pm$ 0.3	5.7 $\pm$ 0.7

$\pm$  : Standard deviation.

\* : Highly significant.









