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EFFECT OF TYROSINE ON THE PARS DISTALIS OF THE RABBIT'S HYPOPHYSIS

BY

El-GHARBAWY, S. M. NAAR, M. I.;* El-AZAB, A. I.* and ABO-El-ROOS, M. A.*

Department of Cytology and Histology, Fac. of Vet. Med. Cairo University
* Dept of Obstet. Gynaec. and A. I., Fac. of Vet. Med. Zagazig University (Benha branch).

SUMMARY

The present study was conducted on 36 Newzealand white rabbits assigned into three age groups of two, three and four months, 12 rabbits for each group of the same age, there were 6 males and 6 females. For each sex, four rabbits were given orally a single dose of L-tyrosine, 100 mg/kg body weight and the other two rabbits, were left as control.

The treated groups revealed an increase in the amount, size and the secretory activity of somatotrophs, lactotrophs and LH gonadotrophs, in addition to a marked increase in the amount, size and the secretory activity of thyrotrophs, adrenocorticotrophs and FSH gonadotrophs during the second month of age.

From the present results it could be concluded that tyrosine acts as a growth promoting factor and a hormonal inducing factor, it can be used in rabbits for enhancing the puberty of both males and females. It could be recommended that tyrosine can be used on a large scale for regulating the reproductive cycle of males and females in large animals.

INTRODUCTION

Based on the use of some organic substances possessed to improve the reproductive efficiency of the animal, the present study was suggested. One of these substances is the tyrosine (Hammerl and Russe, 1987) as an aromatic amino acid derived in the body from the essential amino acid phenylalanine by the action of an enzyme phenylalanine hydroxylase. It is necessary for the synthesis of catecholamine, (adrenaline, nor adrenaline and dopamine), thyroxine and protein synthesis, in addition to its important role in the citric acid cycle and in building of melanine (Harper et al., 1980).

However, it is difficult to study the changes in activities of the pituitary gland in the mature animal in which the pituitary gland is functioning, therefore, selection of animals just before reaching puberty is helpful to study the effect of tyrosine on the activity of the pituitary gland.

Looking through the available literature, informations concerning the use of tyrosine in rabbits seemed to be lacking. Therefore, reference is made to reviewing the effect of tyrosine on the reproductive performance of other animals.

Scheuermann (1984) studied the effect of tyrosine on development of the reproductive organs of male and female immature rats. Gindele and Koppen (1988) studied the effect of L-tyrosine on the reproductive performance of sows. El-Amrawi et al., (1991) studied the effect of L-tyrosine on the ovarian activity in Egyptian buffaloes.

The present study was designed to give confirmative results on using tyrosine as a growth promoting factor for developing the pituitary gland of immature rabbits, thus early induction of puberty and thence breeding of rabbits could be achieved.

MATERIAL AND METHODS

The present study was conducted on a total number of 18 male and 18 female immature Newzealand white rabbits aged 2-5 months and bred at the Faculty of Veterinary Medicine Moshtohor during the period from January to April, 1991.

The total number of rabbits (36) was assigned according to the actual age at the beginning of the experiment into three equal groups: A, B and C of 2,3 and 4 months old, respectively. Each group contained an equal number of both sexes, 6 males and 6 females. From each sex, within the same age group, four rabbits were treated by the oral administration of 100mg tyrosine*/kg body weight, in a single dose, and the other two rabbits were left as control.

At the end of the experimental period (one month) for each age group, all male and female rabbits were slaughtered. Immediately the pituitary glands were removed and fixed in 10% neutral formaline and Susa fluid, processed and embedded in paraffin and cut in sagital sections 4-6um. These sections were stained as mentioned by Crossmon (1937), Drury and Wallington (1967) with the following stains:

1- Harris Haematoxylin and Eosin stain for general studies.

2- Crossmon's trichrome stain for demonstration of collagenous fibers and smooth muscle fibers.

Based on the composite nature of the different types of cells of pars distalis, different special staining techniques were adopted to differentia between these types of cells as follows:

1- Aldehyde fuchsin-periodic acid Schiff-oran G (AF-PAS-OG) for differentiation of thyr trophs, gonadotrophs, somatotrophs and lact trophs (Elftman, 1959).

2- Aldehyde thionin-periodic acid schiff-orange (Ath-PAS-OG) for differentiation of thyr trophs, FSH gonadotrophs, LH gonadotrop and adrenocorticotrophs (Ezrin and Murra 1963).

3-Azocarmine-anilin blue-orange G (Heidenhain azan modification) for differentiating somat trophs from lactotrophs (Bancroft and Steven 1982).

RESULTS

Two-three months old rabbits:

The cells forming the pars distalis of both ma and female rabbits could be easily identified in chromophobes and chromophils and were a ranged in branching and anastomosing cords an clumps intermingled with numerous vascul channels.

In sections stained with Haematoxylin and Eosi and Crossmon's trichrome stains, the chromo phobic cells were relatively few. The acidophili cells appeared the predominant cell type (Fig.1) These acidophilic cells appeared as orange somat otrophic cells and bright red lactotrophic cells a revealed by Heidenhain azan modification stai (Fig.2).

At the age group of three month old rabbits, th pars distalis of both male and female rabbit was characterized by the presence of numerou somatotrophs and lactotrophs and few LH gonad otrophs after aldehyde fuchsin-periodic aci

Schiff-orange G procedure (Fig.3). Both the somatotrophs ad lactotrophs were found in groups and rarely seen scattered singly. Their cytoplasm contained abundant yellow and orange granules respectively. On the other hand, the LH gonadotrophs were mainly scattered singley. They were small in size and their cytoplasm showed intense magenta red closely packed cytoplasmic granules. At the same age, the gland of both male and female rabbits showed few thyrotrophs, FSH gonadotrophs and adrenocorticotrophs (Fig.4). The cytoplasmic granules of the thyrotrophic cells were stained blue after aldehyde thionin periodic acid Schiff-orange G technique. These granules were dispersed allover the cell and more often predominated around the nucleus. The FSH gonadotrophs were irregular with ill-distinct borders. they showed numerous purple cytoplasmic granules. Moreover, adrenocorticotrophs appeared as pale magenta red cells scattered individually in the clusters.

The pars distalis of both male and female treated animals with tyrosine at either two or three month old was characterized by an increase in the amount and size of somatotrophs, lactotrophs and LH gonadotrophs (Fig.5). The cytoplasm of the lactotrophic cells were predominantly granular, whereas the cytoplasm of the somatotrophic cells and LH gonadotrophic cells appeared granulated or partially degranulated. Golgi apparatus was recognized as a crescent or oval negative image close to one side of the nucleus. In addition there was a marked increase in the amount and size of the thyrotrophs, adrenocorticotrophs and FSH gonadotrophs (Fig. 6&7) especially in the treated female animals.

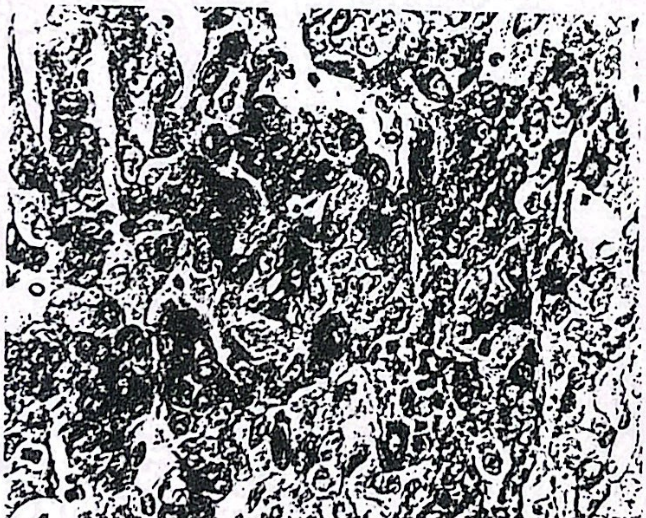

Fig. (1): A section of the pars distalis of two-month-old control male rabbit showing the arrangement of the chromophobes and chromophils in branching and anastomosing cords and clumps intermingled with numerous vascular channels. Fine collagenic fibers form the supporting frame-work of the gland, Notice, the acidophilic cells were the predominant cell type.
Crossmon's trichrome stain, x 410.

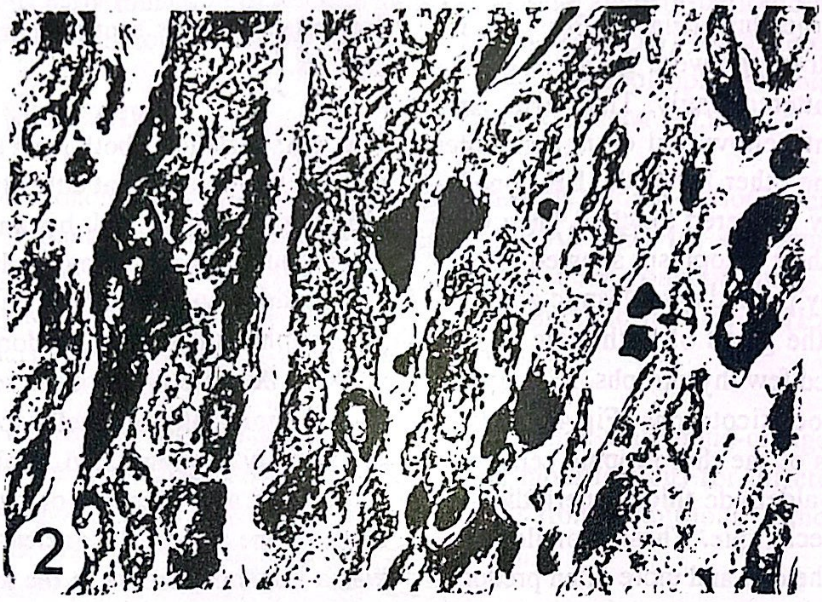

Fig. (2): A section of the pars distalis of two-month-old male rabbit showing numerous somatotrophs (orange) and lactotrophs (bright red). Modified Heidenhain azan stain, x 410.

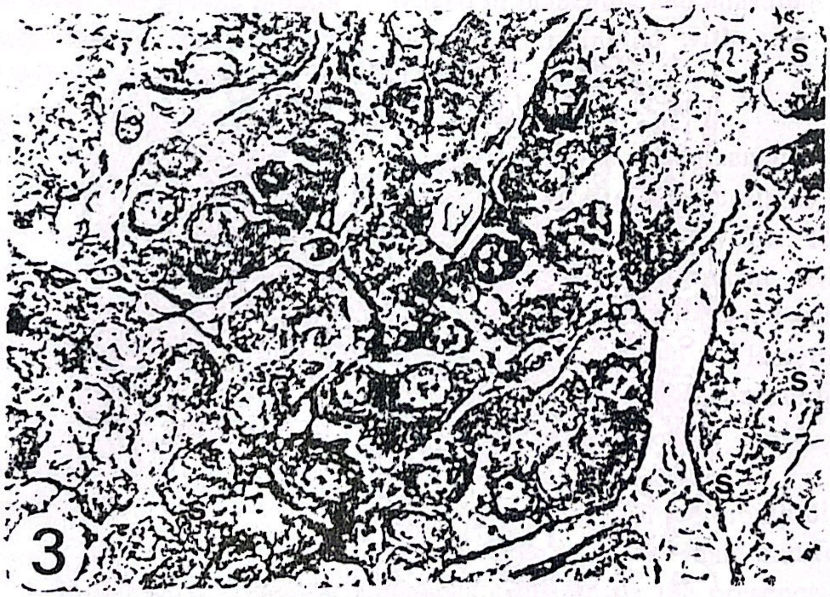

Fig. (3): A section of the pars distalis of three-month-old control male rabbit showing numerous somatotrophs (S) and Lactotrophs (t) and few ISCH gonadotrophs (I). AF-PAS-OG procedure, x800.

Fig. (4): A section of the pars distalis of three-month-old control female rabbit showing few thyrotrophs (T), FSH gonadotrophs (F) and adreno-corticotrophs (A). Ath-PAS-OG procedure, x 800.

Fig. (5): A section of pars distalis of three-month-old treated male rabbit with tyrosine showing an increase in the amount and size of somatotrophs (S), Lactotrophs (t) and ICSH gonadotrophs (I). Notice: clear negative Golgi image (arrows). AF-PAS-OG procedure, x 800.

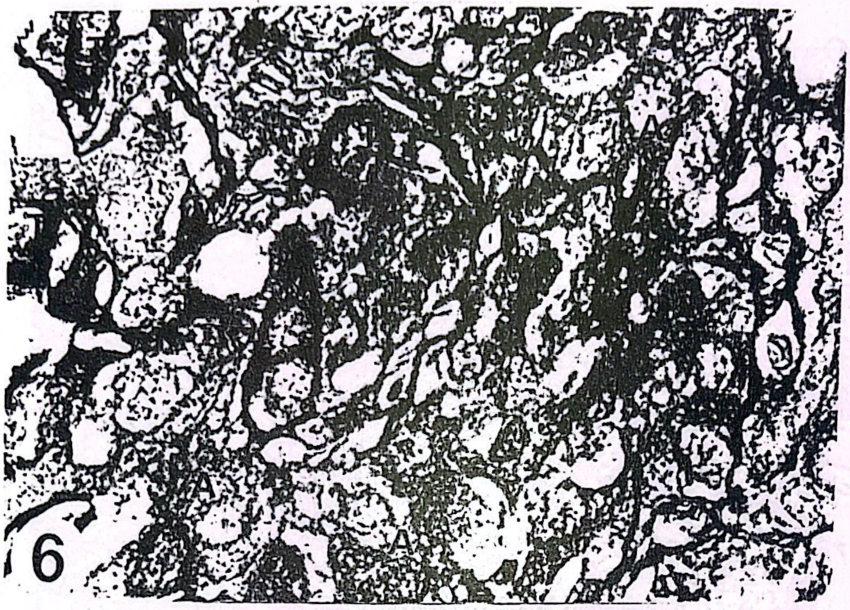

Fig. (6): A section of the pars distalis of three-month-old treated female rabbit with tyrosine showing an increase in amount and size of thyrotrophs (T) and adrenocorticotrophs (A).
Ath-PAS-OG procedure, x 800.

Fig. (7): A section of the pars distalis of three-month-old treated female rabbit with tyrosine showing an increase in amount and size of the FSH gonadotrophs (F)
Ath-PAS-OG procedure, x 800.

Fig. (8): A section of pars distalis of four-month-old control male rabbit showing somatotrophs (S), Lactotrophs (t) and ICSH gonadotrophs (I).
Af-PAS-OG procedure,, x 800.

Fig. (9): A section of pars distalis of four-month-old control male rabbit showing adrenocorticotrophs (A), FSH gonadotrophs (F) and thyrotrophs (T).
Ath-PAS-OG procedure, x 800.

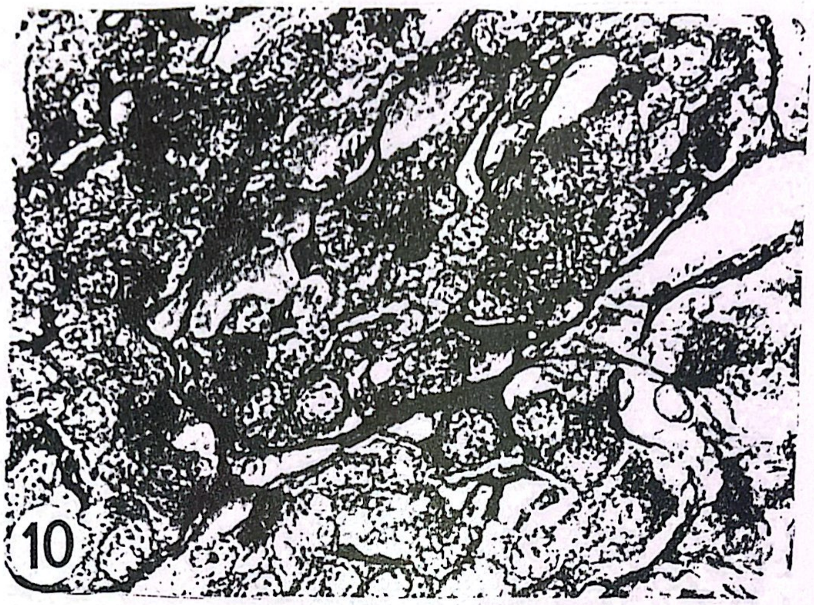

Fig. (10): A section of pars distalis of four-month-old control female rabbit during the follicular phase showing numerous FSH gonadotrophs (F) and thyrotrophs (T). Ath-PAS-OG procedure, x 800.

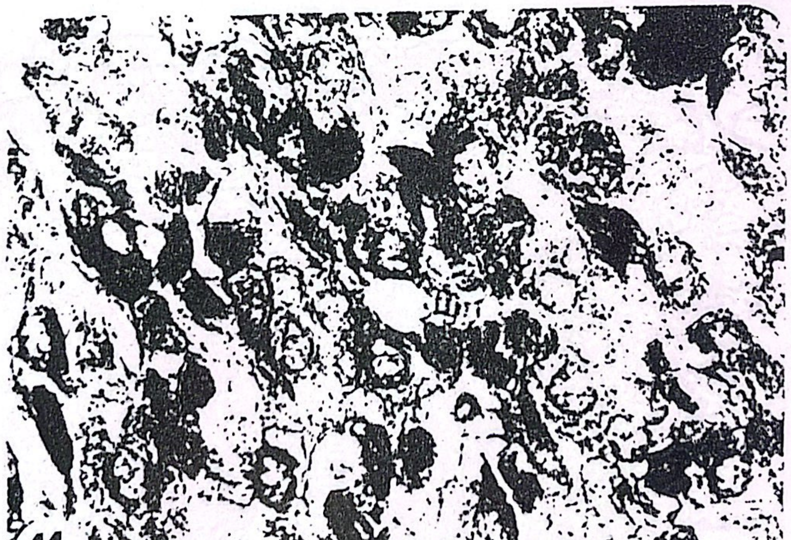

Fig. (11): A section of pars distalis of four-month-old control female rabbit during the luteal phase showing numerous bright red lactotrophs and less orange somatotrophs.
Modified Heidenhain azan stain, x 800.

Fig. (12): A section of pars distalis of four-month-old control female rabbit during the luteal phase showing numerous LH gonadotrophs (L) and lactotrophs (t). AF-PAS-OG procedure, x 800.

3Fig. (13): A section of pars distalis of four-month-old treated male rabbit with tyrosine showing a marked increase in the amount and size of the somatotrophs (S), lactotrophs (t) and ICSH gonadotrophs (I). AF-PAS-OG procedure, x 800.

Fig. (14): A section of pars distalis of four-month-old treated male rabbit with tyrosine showing an obvious increase in the amount and size of the thyrotrophs (T), and FSH gonadotrophs (F).
Ath-PAS-OG procedure, x 800.

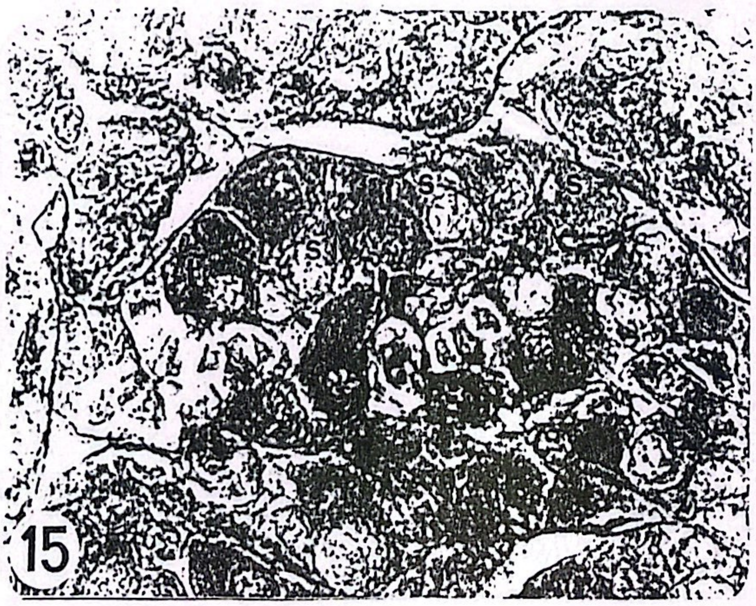

Fig. (15): A section of pars distalis of four-month-old treated female rabbit with tyrosine showing somatotrophs (S), Lactotrophs (t) and few LH gonadotrophs (L).
AF-PAS-OG technique, x 800.

Fig. (16): A section of pars distalis of four-month-old treated female rabbit during the follicular phase showing numerous FSH gonadotrophs (F), thyrotrophs (T) and few LH gonadotrophs (L).
Ath-PAS-OG procedure, x 800.

Fig. (17): A section of pars distalis of four-month-old treated female rabbit during the follicular phase showing numerous adrenocorticotrophs (A).
Ath-PAS-OG procedure, x 800.

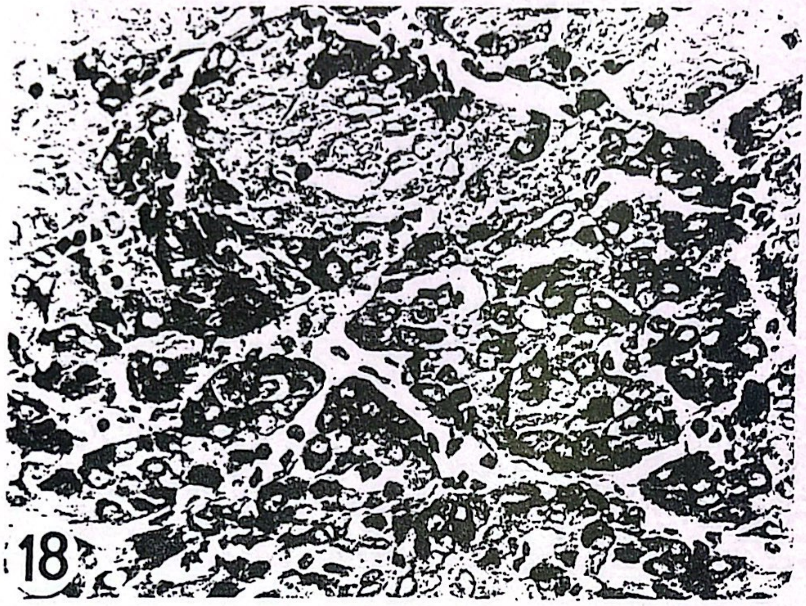

Fig. (18): A section of pars distalis of four-month-old treated female rabbit during the luteal phase showing numerous red lactotrophs and less orange somatotrophs. Modified Heidenhain azan stain, x 410.

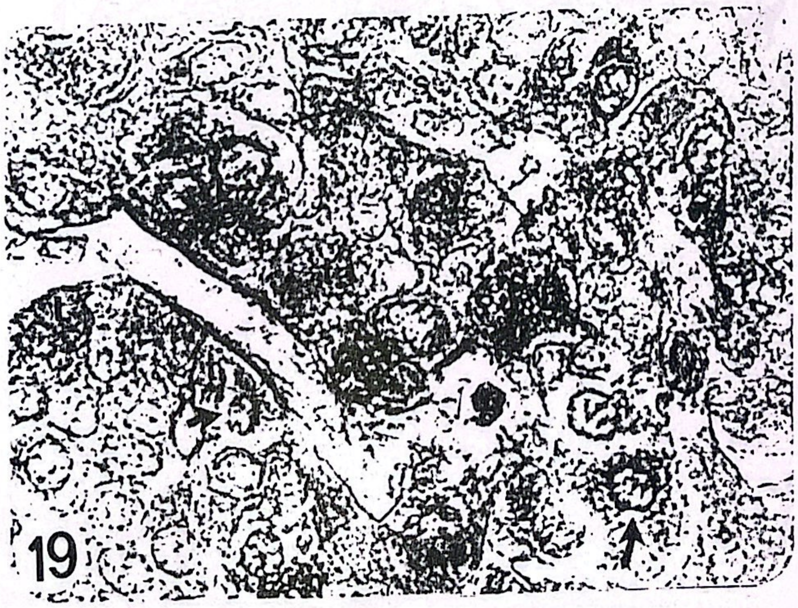

Fig. (19): A section of pars distalis of four-month-old treated female rabbit showing numerous LH gonadotrophs (L), Lactotrophs (t) and less somatotrophs (S). Notice, negative image of Golgi apparatus (arrows).
AF-PAS-OG procedure, x 800.

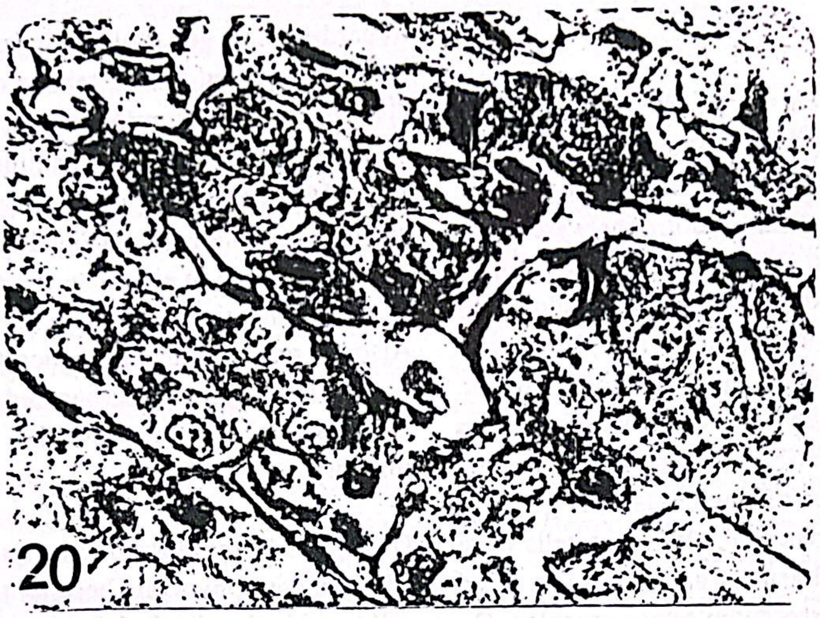

Fig. (20): A section of pars distalis of four-month-old treated female rabbit during the luteal phase showing numerous thyrotrophs (T) and few FSH gonadotrophs (F).
Ath-PAS-OG procedure, xs 800.

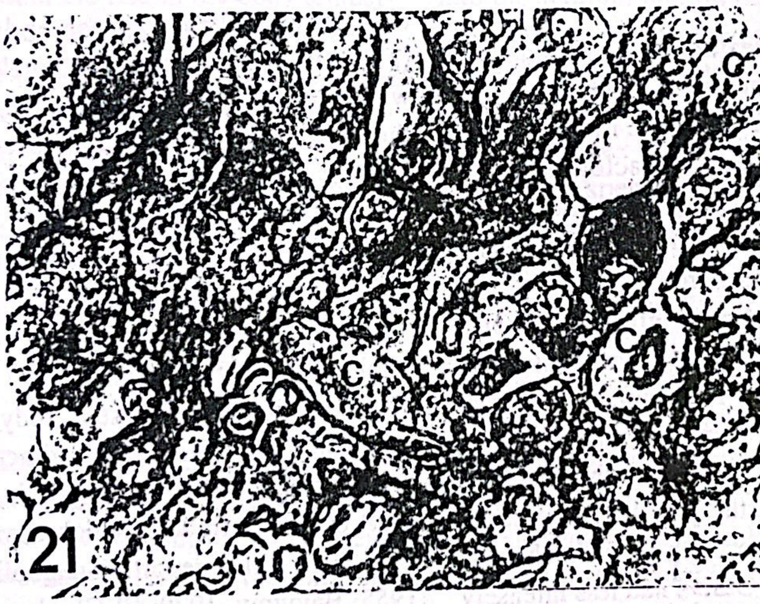

Fig. (21): A section of pars distalis of four-month-old treated male rabbit showing increase in the number of the chromophobes (C).
Ath-PAS-OG procedure, x 800.

Four months old:

With the advancement of age, the pars distalis of four month old male rabbits showed a relative increase in size and mount of somatotrophs, and ICSH gonadotrophs. Also lactotrophs were abundant in the examined sections (Fig.8). In addition, the adrenocorticotrophs and FSH gonadotrophs were also increased in amount (Fig.9). The cytoplasm of these cells were predominantly granular. As the female reached four month of age, the pars distalis during the follicular phase was characterized by the presence of numerous FSH gonadotrophs and thyrotrophs (Fig.10). These cells were enlarged in size and usually appeared to be filled with numerous coarse cytoplasmic granules. On the other hand, the pars distalis of the female rabbits during the luteal phase was marked by an increase in the amount of the lactotrophic cells more than the somatotrophic cells (Fig.11). Howevere, the LH gonadotrophic cells increased in size and number and were arranged in association with blood vessels (Fig.12). The secretory granules of some cells seemed to obscure the nucleus.

The most characteristic feature of the pars distalis of the treated male rabbits with tyrosine at four month old was the marked increase in the amount and size of the somatotrophs, lactotrophs and ICSH gonadotrophs (Fig. 13) than in the control ones. These cells showed various stages of secretory activities, which varied from sparsely granulated cells to even completely granulated cells. The thyrotrophs and FSH gonadotrophs were greatly enlarged (Fig. 14). Their nuclei were usually obscured by the coarse cytoplasmic granules. The latter were dispersed allover the cell and more often condensed at the periphery and under the cell membrane. Some of these cells showed less granular cytoplasm. Others had less intensely stained cytoplasm. Degranulated cells were also observed.

Regarding the gonadotrophic cells in the four month old treated female rabbits during the follicular phase it had been found that, the LH gonadotrophs became few in the examined sections (Fig. 15 & 16). The FSH gonadotrophs on the other hand, became numerous (Fig. 16). They appeared greatly enlarged in size than the control ones, severe degranulation of these cells was recognized. Also thyrotrophs and adrenocorticotrophs were noticed to be more numerous and larger in size in the treated rabbits (Fig. 16 & 17) than in the control ones.

During the luteal phase, the lactotrophic cells and LH gonadotrophic cells became the predominant cell types in the gland of the treated female rabbits (Fig. 18 & 19). Some of these two types of cells appeared degranulated or sparsely granulated. The latter appeared smaller in size, lighter in stain, with indistinct cell membrane. Their nuclei were surrounded by less granular cytoplasm. Moreover, thyrotrophic cells were also numerous in the examined sections. The FSH gonadotrophs, on the other hand, appeared relatively smaller in size than in the follicular phase and less in amount (Fig. 20). In both male and female treated rabbits with tyrosine at four month of age the amount of the chromophobic cells increased by additional number of degranulated chromophilic cells (Fig. 21).

DISCUSSION

Looking through the histological findings of the pituitary gland in the present study there are an increase in the amount, size and activity of the somatotrophs, STH-producing cells, with advancement of age, a finding which came in consistent with some earlier reports (Spagnoli and Charipper 1955; Baioumy, 1979; El-Gharbawy, 1990). Such an increase appeared more prominant in tyrosine-treated rabbits compared to that in control. This finding came to explain the highly significant increase in the body weight and sizes of gonads in the tyrosine treated rabbits when compared to that of the control (Abo-Elross, 1992). On these findings, it could be anticipated that tyrosine acts as a growth promoting factor. This anticipation came in accordance with that reported earlierly where increasing the circulating tyrosine activates the hypothalamic catecholamine, dopamine, which in turn activate the release of growth hormone (Muller, 1973), in addition to its importance in formation of thyroid stimulating hormone and protein synthesis (Harper et al., 1980).

The present study revealed that while the thyrotrophs, TSH-producing cells, in the pars distalis of the control rabbits were predominantly granular, they increased in amount and size with granulated, sparsely granulated and/or degranulated forms in the pars distalis of tyrosine-treated rabbits, a finding indicating that tyrosine might induce hyperactivity in the thyrotrophic cells resulting in the secretion of TSH in excess amount. This, consequently, will stimulate the thyroid gland to produce thyroxine which is essential for promoting the basal metabolic rate and energy intake. This finding might explain the rise in the body temperature in tyrosine-treated rabbits when compared to that of the control (Abo Elroos, 1992). This might be attributed to the assumption that brain catecholamine, norepinephrine and dopamine are synthesized by the physiologic precursor L-tyrosine (Gibson and Wurtman, 1977; Badawy and Williams, 1982), and that norepinephrine rather than dopa is the hypothalamic catecholamine of importance in activating the release of TSH (Grimm and Reichlin, 1973).

Comparing the effect of tyrosine on the development of the gonadotrophic cells (FSH & ICSH-producing cells) to that of control, the present study showed a marked increase in the number, size and the secretory activity of both types of cells when tyrosine was given even at the second month of age. Concerning the effect of tyrosine on the rabbit testes, Abo-Elroos (1992) noticed earlier appearance of spermatozoa in the seminiferous tubules at two month old and the interstitial leydig cells appeared larger in size in form of large clusters indicating their activity when compared to that in control. From the clinical observations of the same author, he had been noticed an increase in the testes size, the testicular descent into the scrotum tooke place much earlier during the second month of age, as well as, the tyrosine treated bucks were able to do successful mounting with the spermatozoa in their ejaculate at the beginning of the third month of age earlier than that occurred with the control. This could be recognised as a sign of steroid activity of the testis in the male before reaching the expected age of puberty in rabbits. It has been reported that the testicular descent was completed under the influence of androgen secreted by the testis (Hafez, 1986). In the sametime Klaws (1985) and Lebas et. al., (1986) indicated that the testicular descent in the scrotum took place shortly before puberty at age of 3-4 months.

Bearing in mind that ensuing the testicular descent into the scrotum and on completing the testicular development, the testes began to be functioning (Hafez, 1986). As the testis has a dual function of producing viable sperm in the ejaculate and secretion of male sex hormones, androgens, so the appearance of spermatozoa in the ejaculate for the first time and exhibition of sexual interest might be considered as an indication of onset of puberty (Asdell, 1946; Sand, 1979).

These findings added further support to the suggestion that tyrosine might induce early puberty in male rabbits as a growth promoting factor (Muller, 1973) and a stimulant to the gonadotrophin releasing factor (Kamberi et al., 1971) which potentiate the testicular function.

Not only males, but also the tyrosine treated females showed hyperactivity of the gonadotrophs (FSH and LH-producing cells). Abo-Elroos

(1992) observed marked changes in the ovarian structures in the tyrosine treated rabbits starting from the age of two month. The ovaries showed numerous Graafian follicles with thickened zona pellucida, highly vascular stroma and an increase in size of the ovaries and the interstitial gland cells. The same author added that the tyrosine treated females of two months old showed a prepubertal sexual activation exhibited by their acceptance to be mated by males much earlier than control. The sexual behaviour of females was synchronized by the ovarian activity (Hafez, 1986) as the presence of developing follicles in the ovaries was followed by secretion of estrogen resulting in the female standing position to be mated by the male. It has been found that tyrosine by its function in synthesis of the cerebral catecholamine was shown to activate the hypothalamus to release GnRH (Hammerl and Russe, 1987; Arthur, 1989) which stimulate the pituitary gland to secrete gonadotrophins (FSH & LH) activating the ovaries. Kamberi et al., (1971) reported that dompamine created from the amino acid precursor L-tyrosine, might function as a synaptic transmitter to potentiate FSH releasing factor (FRF) or LH-Releasing factor (LRF) or both. From these findings on male and females, it could be emphasized that tyrosine plays an important role on the regulating functions of the pituitary gland and gonads possibly as a hormonal inducing factor. Importance of FSH & LH (ICSH) in regulating the gonadal functions has been recognized as shown from some earlier studies (Robertson and Rakha, 1966; Hansel and Snocke, 1970; Hafez, 1986).

There was a marked increase in the amount and size of lactotrophs in the pituitary gland of tyrosine treated rabbits starting from the second month of age, with various stages of secretory activity from sparse granulation to complete degranulation. Such actvity of lactotrophs particularly at the third month of age came to support the concept that tyrosine induces an early puberty. The lactotrophic cell secretion, prolactin, was found to regulate spermatogensis, sperm production a leydig cells maturation in the male of differe species (Bartke, 1966; Swanson, et al., 197 Al-Guedawy, 1980). In the female, there was hyperactivity in the lactotrophic cells especiall during the luteal phase, a finding which came t support the role played by prolactin in controlli the corpus luteum for normal progesterone synthesis in different species (McNatty, et al., 1974; Wolinska and Domanski, 1976).

The present study showed an increse in the amount, size and the secretory activity of adrenocorticotrophs, ACTH-producing cells, in the pars distalis of the tyrosine treated rabbits, a finding which came to eliminate the promotive action of tyrosine on the adrenocorticotrophs to release ACTH which stimulates the adrenal cortex to secrete an excess of the steroid hormones. The latter might have a synergestic effect with the gonadotrophins from the pituitary gland to evoke the ovarian activity particulary before reaching puberty.This concept came in agreement with Hifny et al., (1982) where a positive relationship has been existing between the pituitary and adrenal gland in their effect on the ovarian activity.

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