Influence of Melatonin, Constant Light, or Blinding on Reproductive System of Gerbils (*Meriones unguiculatus*)[1]

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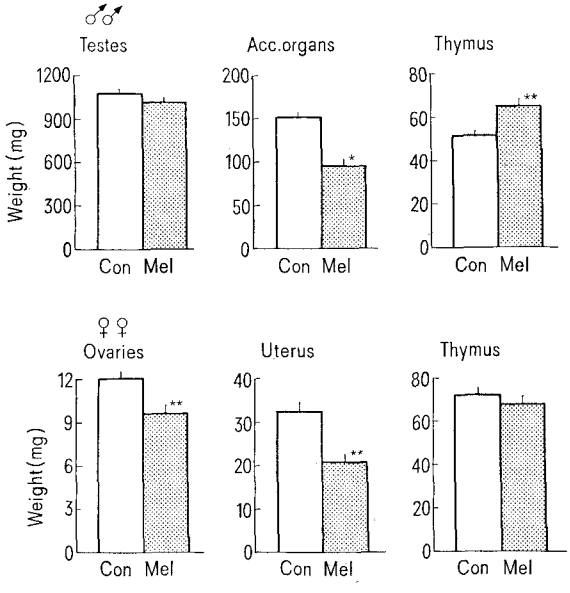
Summary. Male and female gerbils were implanted s.c. with a pellet containing 2 mg melatonin/23 mg beeswax every 2 weeks for a total of 3 implants. A significant depression of ovarian and uterine weight was noted in female gerbils receiving melatonin implants. In the melatonin-treated male gerbils, growth of the accessory organs was significantly inhibited although testis size was not depressed.

Light deprivation due to either blinding or photic restriction results in some species, such as the hamster, in a dramatic involution of the gonads; this response is completely prevented by pinealectomy[2]. The causative factor(s) responsible for gonadal collapse is still unknown, although both pineal indoles and polypeptides have been investigated as possible pineal antigonadotrophic substances[2]. Melatonin, a methoxyindole synthesized by the pineal gland of mammals, reportedly exerts an inhibitory influence on some aspects of reproductive physiology in the rat[3,4] and mouse[5,6] while having a counter-antigonadotrophic effect in golden[7] and dwarf[8] hamsters. Since no information is available on the response of the reproductive organs of gerbils to melatonin treatment, the principal purpose of this study was to examine the effects of administering this indole chronically. In a subsequent preliminary experiment the effects of constant light, blinding and pinealectomy on reproductive organ weights were examined.

Gerbils used in these experiments were from an inbred colony maintained in a room providing 14 h of light per day. In the 1st experiment, observations were made on 20 male and 23 female gerbils implanted with melatonin-beeswax pellets every 2 weeks beginning at 5 weeks of age. The animals were anesthesized with sodium pentobarbital (Pentosol) and the pellet containing 2 mg melatonin (Sigma)/23 mg beeswax or beeswax only was implanted s.c. on the dorsum of the back. A total of 3 implants were made in each gerbil and the animals were killed at 13 weeks of age. Testes, accessory organs (seminal vesicles + coagulating glands), thymuses, ovaries, uteri and the left adrenal glands were weighed. In the 2nd experiment, approximately 1-month-old male gerbils were anesthesized with sodium pentobarbital and groups were either blinded, castrated or pinealectomized and returned to an animal room providing 14 h of light per day. Another group of similarly aged male gerbils was placed in a room providing constant illumination. After 4 months, the gerbils were killed by decapitation and the testes and accessory organs were removed. Organs from both experiments were weighed to the nearest 0.1 mg on a Cahn DTL electrobalance. Results were analyzed by a Student's *t*-test or a oneway analysis of variance on a Programma 101 computer.

In a 3rd experiment, breeding pairs of gerbils were either maintained under constant light or in 14 h of light per day for their entire reproductive life span. The birth of litters, including the number of pups at birth and at weaning, were recorded.

Growth of the accessory organs of melatonin-treated male gerbils was significantly inhibited although testes size was not depressed (Figure, top). Both ovaries and uteri of melatonin-treated gerbils were significantly depressed compared to those of control (beeswax-treated) animals (Figure, bottom). No significant differences were observed in either sex in body weight or adrenal weight. The thymuses of melatonin-treated male but not female gerbils were significantly heavier than control thymus glands (Figure). In experiment 2, pinealectomy alone produced within 8 h grand mal type seizures in most gerbils, resulting in death in over 50% of operated animals. This phenomenon curtailed observations on the effects of pinealectomy on organ weights; the seizures after pinealectomy will be examined in another communication. In the surviving 5 pinealectomized males, no



Effect of melatonin pellets on gonadal and accessory organ and thymus weights in male (top) and female (bottom) gerbils. A total of 3 pellets containing 2 mg of melatonin in 23 mg beeswax were implanted subcutaneously. Open bars indicate control animals while cross-hatched bars indicate melatonin-treated animals. Standard errors are indicated. $*p < 0.001$; $**p < 0.01$ vs. controls.

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Effect of constant light, blinding, castration or pinealectomy on gonadal and accessory organ weights (Mean + SE) in male gerbils

Treatment	N	BW (g)	Testes (mg)	Accessory organs (mg)
Controls	11	76.3 ± 2.5	1249 ± 37	247.5 ± 19.4
Constant light	4	72.8 ± 1.6	1073 ± 34[b]	159.0 ± 11.0[b]
Blind	5	72.3 ± 3.7	1098 ± 27[b]	179.4 ± 10.1[b]
Castrate	2	102.5 ± 16.5	—	3.9 ± 0.3[c]
Pinealectomy	5	74.4 ± 5.3	1146 ± 45	173.6 ± 19.7[a]

[a] $P < 0.02$ vs. controls. [b] $P < 0.01$ vs. controls. [c] $P < 0.001$ vs. controls.

significant differences in body or testicular weights were noted, although accessory organ weights were slightly depressed (Table). Either blinding or maintenance under constant light caused a significant reduction in testes and accessory organ weights when these organs were compared to those of control animals. However, in experiment 3, breeding pairs of gerbils maintained under constant light for their entire reproductive life span showed no impairment of breeding capability as measured by total number of litters produced, number of young per litter, ability to raise young to weaning, or occurrence of postpartum estrus.

The data relating to body weight and ovarian and uterine weights of female gerbils from the first experiment agree with previously published normal growth data for similarly-aged female gerbils[9]. The literature concerning chronic administration of melatonin to normal male or female rats is controversial with references supporting a progonadotrophic, antigonadotrophic or no effect on the gonads and accessory organs[2]. In some species, such as the ferret[10], melatonin delayed estrus despite exposure to long photoperiods, while in the weasel[11], melatonin decreased testis size as measured by palpation. The present data indicate that melatonin is antigonadotrophic in male and female gerbils. Whether other pineal indoles or polypeptides would also inhibit reproductive organ growth is unknown. The observation that the thymuses or melatonin-treated males were significantly elevated while accessory organs were depressed is consistent with the hypothesis that there were less circulating androgen levels.

Blinding in some species such as the hamster leads to dramatic involution of the testes as well as the accessory organs. In the rat, however, blinding alone has little or no effect of testicular weight unless it is combined with other potentiating procedures such as anosmia, androgen sterilization or underfeeding[2]. Gonadal weights of blinded gerbils were significantly reduced but total involution, as previously seen in the hamster[2], was not observed. Although constant light also apparently depressed reproductive organ growth, supporting data from the breeding colony indicate that pairs maintained under constant illumination are fully capable of producing as many litters as pairs in alternating light-dark conditions, in our colony and as previously described in the literature[12]. Whether blinded gerbils are capable of reproducing has not yet been investigated.

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Proestrous Gonadotropin Levels in Thyroparathyroidectomized Female Rats

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Summary. Intact and TPTx animals showed the expected afternoon increase in serum LH, FSH and prolactin levels. But the afternoon increase in serum LH levels in TPTx rats was less than that observed for intact animals ($p < 0.01$). Neither serum prolactin nor FSH levels were altered by TPTx.

Increasing evidence implicates thyroxine as a phasing agent for several rhythmic endocrine functions[4-6]. We previously reported that thyroidectomy in the female was followed by a reduction in the number of eggs ovulated[7] and recently we observed a marked phase shift in the LH and prolactin rhythms in male rats after thyroidectomy[6].

The present study was undertaken to evaluate the effect of thyroidectomy on the serum proestrous pattern of circulating gonadotropins in the female rat.

Materials and methods. Only adult female Sprague-Dawley (Charles River, CD) rats housed under conditions of controlled lighting (fluorescent illumination from 04.00 to 18.00 h) and temperature (24 ± 2 °C) were used in the present study. Thyroparathyroidectomy (TPTx) was performed surgically at approximately 40 days of age. 30 days later blood collection procedures for obtaining serum LH, FSH and prolactin were initiated. After surgery TPTx rats were indiscriminately housed 2/cage with intact or TPTx animals. Vaginal smears were taken 6 days a week. This served not only to assess the ovarian cycle but also to familiarize the animals with activity in the animal quarters, opening of their cage, and removal from