THE EFFECTS OF CONTINUOUS LIGHT OR DARKNESS ON THYROID AND GONAD FUNCTION IN RATS AND MICE

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THE EFFECTS OF CONTINUOUS LIGHT OR DARKNESS ON THYROID AND GONAD FUNCTION IN RATS AND MICE

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INTRODUCTION

It has long been established that there are numerous variations in cyclic sexual activity among different species associated with environmental changes in temperature, light, food, humidity, altitude, rainfall, etc. The cyclic initiation of sexual activity in some species seems to depend primarily on lengthening or shortening of days, while others are indifferent to the amount of light and respond to such factors as changes in temperature. Presumably these environmental factors stimulate sexual function through nervous pathways to the anterior pituitary, which is induced to increase its secretion of gonadotropic hormones and thereby initiate gonadal function.

Sufficient data are available to indicate that the thyroid gland, as well as the gonads, exerts important influences on reproductive function. This gland, as well as the gonads, is controlled by the anterior pituitary, and has also been shown to be influenced by environmental factors, particularly changes in temperature. Inasmuch as only fragmentary and inconclusive data are available on the effects of light on thyroid function, it was the principal objective of this research to determine whether or not any conclusive relationship could be demonstrated. This was done by placing mice under continuous light or darkness for a period of twenty-eight days, and testing their level of thyroid activity by administering a constant amount of thiouracil or a tracer dose of radioactive iodine.

In addition to the above, the effects of a continuous twenty-eight-day period of light or darkness on the response of the gonads to administration of a constant dose of gonadotropic hormone (pregnant mares' serum) were also studied. Although numerous studies have already been made on the influence of light increments on normal gonadal function in birds and mammals, only one report has been found dealing with the effects of light on gonadal reaction to administered gonadotropic hormones. Inasmuch as the gonadotropic hormone of pregnant mares' serum has received wide use in animal practice, it was considered especially pertinent to determine whether light or darkness affected its action.

The data obtained in these studies indicate that changes in light increment definitely influence the thyroid secretion rate of mice, and also alter the gonadal response of rats to pregnant mares' serum. Inasmuch as alterations in thyroid activity have previously been shown to influence the reaction of the gonads of rats and mice to pregnant mares' serum (Meites and Chandrashaker, 1949; Johnson, 1949), the data reported here suggest that the gonadal reaction to pregnant mares' serum may be similarly affected via light-induced changes in thyroid function.

These data raise two interesting questions, namely: (1) can the reports of alterations in thyroid function which have been attributed in the past solely to temperature changes also be due, in part at least, to changes in light increment? (2) to what extent may light-induced changes in thyroid function have accounted for results previously attributed only to temperature or light-induced changes in pituitary gonadotropic function?

REVIEW OF THE LITERATURE

Effects of Light on Thyroid Function. The possible effects of light on the thyroid gland may be important in explaining reproductive behaviour because of the intimate relation of this gland to gonadal function. However, only meager information is available in the literature on this subject.

Dempsey (1943) described the histological changes of the thyroid glands of six female rats with severed pituitary stalks and six intact female rats which were kept under continuous light for one month. The thyroids showed a reduction in cell height, from which he assumed a reduction in secretion of thyrotropic hormone by the anterior pituitary. He found the same histological characteristics in the thyroids of six female rats which were exposed to heat for one month. Exposure to cold resulted in increased thyroid cell height.

Kleinpeter and Mixner (1947) determined the effects of the quantity and quality (wave length) of light on the thyroid activity of baby chicks during fourteen-day periods of illumination. They showed that increased quantities of light slightly increased thyroid function when compared to controls kept under normal light conditions. No relationship between the quality of light and thyroid function could be demonstrated.

Reineke and Turner (1945) worked on the seasonal rhythm in the thyroid hormone secretion rate of the chick, and reported that in both female and male chicks thyroid secretion reached a maximum level in the fall (October and November) and declined thereafter during February and early March. During the latter part of March, thyroid secretion declined further in females and males, and remained at a low level until August; during October the thyroid secretion rose again towards the normal winter levels observed during the previous year. It seems possible that the thyroid secretion level may also have been influenced by seasonal variations in day-light. If so, it would be logical to assume that increasing quantities of light decrease thyroid secretion in chicks.

Turner (1948) reported that the thyroid secretion rate of White Leghorn hens when two years old was decreased when compared with either the same breed or White Plymouth Rocks at six months of age. He also found that there was no seasonal decline in thyroid secretion rate between January and March. By May the secretion of thyroxine had declined as did also egg production. This decline in thyroid secretion rate during warmer weather may again be correlated with increasing day-light as well as increasing temperature.

Stein and Carpenter (1943) reported that the adult green Triturus viridescens (salamander) exposed to normal daylight for forty days during September and October showed an increase in thyroid activity. The glands had more colloid droplets and vacuoles, higher and more vacuolated cells, and more oval basal nuclei than those of animals kept in darkness. Measurement of cell heights corroborated the histological data and differences were significant whether based on the number of cells measured or on the number of animals observed. Exposure of Triturus viridescens to artificial illumination for 150 days resulted in a greater degree of stimulation. Controls kept in darkness had less active thyroids. Low temperature also had a stimulating effect as great or greater than that of light. It was concluded that light probably plays a role in the annual thyroid cycle in Triturus viridescens as well as temperature. It will be seen in the experiments reported here that the thyroids of mice react just opposite to those of the salamanders when exposed to continuous light or darkness.

Berliner and Warbritton (1937) observed poor fertility in rams during the summer months and suggested that it was due to a decrease in thyroid secretion rate as a result of high summer temperatures. Bogart and Mayer (1946) also reported that high temperatures (85° - 90° F.) in the summer reduced activity of the reproductive organs of rams by inducing hypothyroidism. They found that when thyroprotein or thyroxine were given to rams during the period of high temperatures the reproductive organs and sexual activities were restored to a level near that of the breeding season (fall and winter). It seems possible that the hypothyroidism found in the above rams during summer may also have been induced in part by the greater quantities of light present at that time. This would seem to be substantiated by the findings of Yeates (1949) that breeding activity in sheep can be controlled at will by artificially altering light duration. This worker induced anestrus in sheep during the breeding season (winter) by putting them under increasing periods of artificial light, and induced estrus and breeding activity during the non-breeding season (summer) by artificially decreasing the daily light periods. The effects of light duration on breeding activities in this species may be more important than temperature changes.

Effects of Light on the Sexual Activity of Birds. Since the times of Pliny and Aristotle the cyclic changes in the size of the avian gonads have been recognized to be correlated with the seasons of the year. In studies of migratory species many workers have advanced the theory that the migratory urge may be related to gonadal changes.

Some of the most widely quoted investigatory efforts in this connection have been those of William Rowan (1929) whose original experiments dealt chiefly with the junco. This worker observed that the interstitial tissue of the testis and ovary commences its spring recrudescence prior to the initiation of migratory movement, and reaches a maximum approximately at the time of the northward migration to the breeding ground. At this time the interstitial tissue and germinal elements increase and reproductive activity takes place. Towards the end of the period of northern residence the gonads exhibit a second burst of interstitial activity, and this flurry of function within the secretory portion of the gonads occurs just before and during southward migration.

Rowan (1931) utilized the above observations to formulate a definite theory, holding that the secretions of the sex glands are primarily responsible for migratory behaviour. By artificially altering the duration of illumination in each twenty-four-hour period, he was able to control the stage of gonadal development in various migratory species. Thus birds could be brought into either the migratory or full breeding condition during the dead of winter. Since the interstitial tissue in the testis was most prominent during the periods of gonadal recrudescence and regression, Rowan (1931) concluded that in the case of the junco at least, the hormones elaborated by this cellular type constituted the physiologic stimulus to migration.

In a discussion of factors contributing to the migratory urge in birds, Wolfson (1940) regarded increasing daylight and consequent pituitary stimulation as important events in the chain of physiological processes which are essential to the seasonal flights. Bissonette's studies (1932) of light-induced changes in the testis of the starling led him to believe that wave length as well as amount of illumination may also be an important factor in this respect.

A study of the greenfinch by van Oordt and Damste (1939) has generally confirmed the original observations of Rowan (1931) and Bissonette (1932). Birds placed in the dark at the beginning of May, when they were in full song, were killed at varying intervals. It was found that while in the dark both the testes and the ovaries decreased considerably in size and spermatogenesis came to an end. When birds were brought into the light in August, after being in the dark, their gonads increased, spermatogenesis was re-initiated and the birds began to sing. It was also found that putting finches in the dark caused them to moult in June instead of at their usual time in August.

Cole (1933), working on captive mourning doves, found that reproductive activity could be induced by increasing the duration of the daily light period. Egg laying and gonadal activity can be stimulated in ring-necked pheasants by constant illumination, according to Clark, Leonard and Bump (1939). These workers found that an increase in total illumination produces an increase in the number eggs laid in this species. Riley and Witschi (1938) reported that ovarian development may be stimulated in female sparrows during the fall and winter by increasing the light ration.

Benoit (1936, 1937) made the significant observation in ducks that removal of the eyeballs and severance of the optic nerves did not inhibit capacity to breed when artificial light was directed through a fine glass tube into the eye socket or on the pituitary. Ringoen and Kirschbaum (1939) reported that there was no gonadal response to light in sparrows if the eyes were covered.

Lamoreux (1943) found that White Leghorn males exposed to twelve hours or more of light daily made significantly greater gain in semen yield than males exposed to light less than one hour.

Effects of Light on the Sexual Activity of Mammals. The first corroboration in mammals of Rowan's (1929) work in birds was made by Bissonette (1932) and Baker and Ranson (1932) in voles and ferrets. Since then a large amount of work on the effect of light has been done on many species of vertebrates, and this has been summarized in papers by Bissonette (1936), Marshall (1936) and Rowan (1938).

Marshall (1940) reported that in female ferrets subjected to different degrees of light intensity, as measured by putting them at different distances from a 1000 watt bulb, the acceleration of the estrous cycle was roughly correlated with the degree of light intensity. Morgan (1949), working on the female opossum during the non-breeding season, also reported that increases in the size and weight of the reproductive tract of the opossum appeared to be directly proportional to the amount of radiant energy received through lamps with and without filters.

On the assumption that light exerts its seasonal effect by way of the pituitary, several investigators have attempted to determine the path of transmission of the stimulus. Le Gros Clark (1939) studied the path of transmission of the light stimuli in ferrets. He found that when the optic nerves were sectioned, these animals did not come in heat at all, or else came in heat much later than the normal time. He also found that the normal response to visual stimulation can occur even in the absence of the visual centers of the cortex, through impulses passing either to the ventral nucleous of the lateral geniculate body or to the hypothalamus by the way of the accessory optic tracts.

Whitaker (1940) reported that when white-footed mice were blinded by removal of the eyes, they were not rendered sterile but exhibited no cyclic sexual activity. Those kept in continuous darkness exhibited a reduced and entirely non-cyclical reproductive activity. Furthermore, with light of the low intensity of one foot-candle power, breeding took place throughout the short portion of the year and the animals failed to go into a state of anestrus. Even at lower temperatures, when the litter could seldom be successfully reared, the mice did not go into anestrus if provided with sufficient additional light.

Hemmingsen and Krarup (1937) have shown that there is a correlation between the estrous cycle and the ordinary daylight diurnal rhythm in the rat. Sexual heat and muscular activity (as recorded by activity cages) were at their maximum in the dark. All the phenomena, (mating instincts, cyclical changes in the vagina and the correlated increases in activity) were shifted 12 hours when an artificial day-night rhythm was established by exposing the animals to light at night and to darkness in the day. An eight-hour alternating rhythm of light and darkness, however, was not followed by any change in sexual rhythm. Constant light was found to stimulate vaginal cornification and induce heat.

Gresson (1940) reported the effect of increased daily illumination and reversed day and night conditions on the estrous cycle of the mouse. Females were kept in darkness for seven to eight hours during the day and under bright electric illumination for the remainder of the twenty-four-hour period. Controls were kept under normal conditions. It was found that "long day" conditions accelerated estrus and induced copulation in mid-winter. Reversed day and night conditions brought about daytime mating.

Meyer and Meyer (1944) stated that cotton rats which were raised in constant darkness displayed retarded development of the reproductive tract and delayed attainment of sexual maturity, but that constant lighting had no perceptible effect on normal development.

In apparent contradiction to the findings of most of the foregoing workers is a report by Chase (1941), who studied reproductive activity in a strain of mice displaying congenital anopthalmia. It was found that females from this eyeless strain showed vaginal introitus somewhat earlier than normal mice, and exhibited the first vaginal cornification considerably earlier. The length of the cycle was said to have been unaffected. Anopthalmic males matured and showed spermatogenesis at the same age as males from a normal strain. It is impossible to compare these results directly with those of the other workers who studied only normal animals, since it is obvious that the genetic factors responsible for congenital eyelessness may well be accompanied by other hereditary abnormalities affecting the reproductive cycle.

Levinson, Welsh and Abramowitz (1941) observed that hypophysectomized female rats displayed a marked decrease in total activity and a complete loss of activity rhythm normally associated with the sex cycle. However, females from which the pituitary had been removed continued to display a diurnal rhythm of activity in which running increased at night and decreased during the daylight hours. This rhythm was reversed when the light-dark periods were inverted by the use of artificial lighting. Since hypophysectomy results in regression of the gonads, adrenals and thyroid, it becomes apparent that diurnal activity (exercise) is independent of secretion from any of these glands as well as from those of the anterior pituitary itself. Apparently the normal pattern of running activity in the female rat consists of a diurnal cycle, the phasic nature of which is independent of any hormonal action. However, any quantitative increase in general activity probably depends upon secretions from the endocrine glands.

Fiske (1939) observed that female rats kept on constant light showed long periods of estrus and diestrus, whereas in rats kept in constant darkness the metaestrous phase was the most protracted portion of the sex cycle. Bioassay revealed that pituitaries of constant-light animals contained high amounts of follicle-stimulating hormone, and those in constant-darkness were characterized by high quantities of luteinizing hormone. Adult males kept in constant darkness had larger pituitaries and more highly developed testes and seminal vesicles than did males in constant light. Female rats raised under constant lighting reached sexual maturity earlier than did females in normal lighting conditions, whereas animals maintained in constant darkness were the last to attain maturity.

In a later paper, Fiske (1941) showed that injections of the gonadotropic hormone of pregnancy urine into male and female rats kept under continuous light for fifteen to twenty days gave better ovarian and seminal vesicle development than in animals living in darkness. Injections of pituitary follicle stimulating hormone (FSH) into immature females kept under continuous light for fifteen to twenty days gave less ovarian growth than in females kept in darkness. Male rats similarly injected with FSH had heavier seminal vesicle when kept in the light than in the dark. These are the only data which the writer has found dealing with the effects of light on the reaction of the gonads to administered gonadotropins. They are difficult to interpret, however, because of the apparent contradiction in the results.

Truscott (1944) reported that the attainment of sexual maturity in rats is accelerated by constant lighting. Furthermore, he found that when the optic nerve was severed, maturation was delayed beyond the normal period despite constant lighting conditions.

Pomerat (1942) claimed that the pituitaries of rats kept in continuous darkness for one and one-half months resembled those of young castrated females. The acidophils were increased, the basophils were doubled in number, and degranulated basophils and castrate cells were present. Many of these changes persisted after three, six and twelve months of darkness but were not as pronounced. He also found that the ovaries of rats kept under continuous light for one and one-half, three or twelve months were consistently smaller than those in control rats of corresponding age, and contained fewer corpora lutea. The ovaries of rats kept in **continuous** darkness showed an even greater reduction in size and in the number of corpora lutea, especially after one and one-half months.

Rice (1942) and Hammond (1938) have summarized the observations pertaining to the stimulating effects of light upon gonadal function in domestic animals. The breeding season in the mare occurs during the spring and summer when the amount of light per twenty-four hours is increasing. Transfer of mares from the northern to the southern hemisphere results in a change of the breeding period to fit the new seasons. Domestic mammals such as sheep, deer and goats breed during short or shortening days. Bissonette (1941) has observed that although goats usually show their last heat period not later than middle of March, fertile mating may be induced in July if the day length is artificially shortened during the preceding two months. Comparable out-of-season sexual behaviour and reproduction has been produced in sheep by Sykes and Cole (1944), and Yeates (1949) as a result of experimental modification of the amount of light per twenty-four hours. Yeates (1949), working with grade sheep and Suffolk ewes, found that the natural sexual season (which embraces the autumn and winter months) may be modified or even reversed by suitable alteration of the daily-light ration. In grade Suffolk ewes he noted that the onset of the sexual season was a response to a decreasing daily amount of light which occurred thirteen to sixteen weeks after the change from increasing to decreasing length of day. These responses occurred irrespective of the level at which the changeover in trend of daily lighting occurred and were unrelated to specific "threshold" amounts of light.

In the latitude of Cambridge, Massachussets, domestic cats usually breed from the middle of January until the middle of July. Dawson (1941) has elicited estrus in this species during November and December by increasing the amount of illumination for each twenty-four hours.

Evidences That Not All Birds and Mammals Are Influenced by Light Changes. In the preceding review, examples have been cited of birds and mammals which respond to changes in light. However, there are exceptions among both. Thus sex activity in the guinea pig is little affected by changes in the amount of light (Dempsey, 1934) and the same appears to be true of the spermophile (Johnson and Gann, 1933). Guinea pigs are tropical animals and live under comparatively uniform daily conditions as regard light and temperature. They probably do not possess the capacity to respond to those seasonal conditions which are the main factors in fixing the periods of breeding among animals living away from the equator. Among birds too, some species do not respond to increase in light, such as the guinea fowl (Scott and Payne, 1937) which likewise inhabits the tropics.

It has been shown that some animals inhabiting tropical lands are as unvarying in their reproductive cycles as others living in temperate climates. The bats described by Baker and Bird (1936) are examples from among mammals. Among birds, the garden whistler inhabiting the northern New Hebrides is as seasonal in its reproduction as are the birds of a temperate climate (Baker, 1940). There is said to be no seasonal change in diet and no other environmental changes are known to control the breeding season.

The outstanding fact remains, however, that in nearly all animals showing sexual periodicity, breeding phenomena occur in response to seasonal changes and in the majority of these animals, as shown by observations under both natural and experimental conditions, the principal stimuli are changes in light duration or changes in temperature. The anterior pituitary is recognized as the organ activated by the light stimulus. Light impulses are received by the eye from which they are probably passed to the hypothalamus and to the pituitary along neural pathways.

<u>Functional Inter-relationships between Thyroid, Gonads and Pituitary Gland</u>. Since this thesis is concerned with the effects of light on the function of the gonads and thyroid gland, it is pertinent to review some of the functional inter-relationships between the thyroid, gonads and pituitary gland. There is ample proof that alterations in thyroid activity may alter gonadal function. Thus Meites and Chandrashaker (1949) reported that in young male rats thyroprotein partially or completely inhibited the response of the seminal vesicles and coagulating glands to a constant dose of pregnant mares' serum, while in young male mice thyroprotein increased the gonadotropic response. These investigators also found that thiouracil increased the gonadal response to pregnant mares' serum in male rats and reduced the response in male mice. Similar findings were reported by Johnson (1949) in immature female rats and mice. The response of the

ovaries of immature female rats to pregnant mares' serum when given thryroxine or thyroprotein was reduced, but was increased when given thiouracil. The response of the ovaries of immature female mice to pregnant mares' serum given thyroprotein was increased, but there was no significant change when given thiouracil.

Reineke, Bergman and Turner (1941) reported that thyroidectomy of male goat kids resulted in a reduction in the gonadotropic content of the pituitary. P'an (1940) likewise found that the gonadotropic potency of the anterior pituitary was decreased following thyroidectomy of normal and castrate rats and normal rabbits. Evans and Simpson (1929) reported that the gonad-stimulating properties of the anterior pituitary from hyperthroid rats were increased, while the glands from hypothyroid rats were less effective than normal.

Chu (1944) noted that in thyroidectomized rabbits the ovaries contained many more large follicles than normal controls, but ovulation did not take place after coitus. The animals that were operated on readily ovulated after the injection of pregnancy urine extract, and the ruptured follicles were more numerous than in normal estrous animals. He also prepared fresh saline extracts from the pituitaries of normal and thyroidectomized rabbits and assayed their relative amounts of ovulating hormone. The pituitaries from the normal animals induced sixty per cent ovulation in estrous rabbits, whereas the pituitary extracts from the thyroidectomized rabbits caused no ovulation and only induced growth of follicles. These results indicate that alterations in thyroid activity may not only affect the gonads directly, but may also change gonadotropic secretion in the anterior pituitary.

PROCEDURE

Effects of Continuous Light or Darkness on Thyroid Function in Mice. These experiments were performed on male and female albino mice (Rockland strain). The animals were fed a balanced stock diet and drinking water was available at all times. In each experiment uniform groups (by weight) of ten animals each were placed in ample-sized screen cages. For those groups which were to be maintained under continuous light, a fifteen watt electric light bulb was placed about four inches in front of each cage. The cages of the animals kept under continuous darkness were completely covered, except that the covers were not tight enough to exclude air circulation. Control groups of animals were kept under the normal day-night conditions prevailing in the animal room, or on about nine hours of light and fifteen hours of darkness daily. All experiments were conducted for twenty-eight days and the animals were sacrificed on the last day.

These experiments (as well as those dealing with gonad function) were all conducted in an air conditioned animal room at a constant temperature of 75°F. Several temperature checks made with a chemical thermometer in both the continuous-light and continuous-dark cages showed that there was not more than one-half degree variation from room temperature. It is believed, therefore, that temperature changes can be excluded as a factor in these experiments.

The procedure used in the thiouracil-treated animals is given in Table 1. A constant dose of ten mg. of thiouracil suspended in 0.1 normal sodium hydroxide was injected subcutaneously

TABLE 1

PROCEDURE IN STUDYING EFFECTS OF LIGHT OR DARKNESS ON THE REACTION OF THE THYROIDS TO THIOURACIL

Group	No. per group	Treatment
I	10	Controls Normal day and night for 28 days
II	10	Controls Normal day and night for 28 days Thiouracil injected during last 10 days
III	10	Continuous light for 28 days Thiouracil injected during last 10 days
IV	10	Continuous darkness for 28 days Thiouracil injected during last 10 days

daily in 0.2 cc. volume to each animal for ten days. On the day of sacrifice, body weights were recorded and the thyroids were carefully removed and weighed on a Roller-Smith balance.

The procedure used in the radioactive-iodine treated animals is given in Table 2. On the day prior to sacrifice each animal was injected intraperitoneally with a tracer dose of I^{131} containing approximately 0.1 microcurie of activity. On the day of sacrifice, the thyroids were removed, weighed, air dried and then placed in small copper discs for counting under a Geiger-Muller tube.

All important data were treated statistically. The standard error of the mean was determined by the following formula:

$$S.E. = \sqrt{\frac{\sum d^2}{n(n-1)}}$$

Significant differences between means were determined by the following formula:

$$S.D. = \frac{m_1 - m_2}{\sqrt{E_1^2 + E_2^2}}$$

Effects of Continuous Light or Darkness on Gonadal Reaction to Pregnant Mares' Serum. These experiments were conducted only in rats (Rockland and Carworth strains) according to the procedure given in Table 3. These animals were kept under continuous light or darkness as in the previous experiments, except that

TABLE 2

PROCEDURE IN STUDYING EFFECTS OF LIGHT OR DARKNESS ON THE UPTAKE OF RADIOACTIVE IODINE BY THE THYROID

Group	No. per Group	Treatment
I	10	Controls Normal day and night for 28 days Radioactive iodine injected 16 hours before sacrifice
II	10	Continuous light for 28 days Radioactive iodine injected 16 hours before sacrifice
III	10	Continuous darkness for 28 days Radioactive iodine injected 16 hours before sacrifice

TABLE 3

PROCEDURE IN STUDYING EFFECTS OF LIGHT OR DARKNESS ON GONADAL REACTION TO PREGNANT MARES' SERUM

Group	No. per group	Treatment
I	10	Controls Normal day and night for 28 days
II	10	Controls Normal day and night for 28 days P.M.S. injected during last 4 days
III	10	Continuous light for 28 days P.M.S. injected during last 4 days
IV	10	Continuous darkness for 28 days P.M.S. injected during last 4 days

a constant dose of pregnant mares' serum (one Cartland-Nelson unit) was injected subcutaneously into each animal during the last four days of the twenty-eight day period. On the day of sacrifice, the ovaries and uterus were dissected out and weighed.

RESULTS

Effects of Continuous Light or Darkness on Thyroid Function

Female Mice - Thiouracil Action. The results of two preliminary experiments in female mice are given in Table 4 and Fig. 1. It can be seen that the thyroids of the animals which were under continuous light plus thiouracil weighed significantly less than the thyroids of the animals kept under normal day-night lighting plus thiouracil. The next experiment (Table 5) also shows that continuous light (group IV) reduced the effectiveness of thiouracil when compared to the controls (group II). In this experiment, continuous darkness did not significantly alter the action of thiouracil (group II). A similar experiment (Table 6, Fig. 2) showed again that continuous light decreased thiouracil action (group IV) while continuous darkness significantly increased thiouracil action (group III) when compared to the controls (group II).

Female Mice - Uptake of Radioactive Iodine. The results of this experiment (Table 7, Fig. 3) corroborate the data obtained in the thiouracil-treated mice. It can be seen that the thyroids of the animals under continuous light (group III) weighed less, while the thyroids of the mice under continuous darkness (group II) weighed more than the controls (group I). The uptake of radioactive iodine by the thyroids of the continuous-light group was significantly less than by the thyroids of the control group, whether calculated on a thyroid or body weight basis. On the other hand, the thyroids of the mice which had been in continuous darkness took up a significantly greater amount of

TABLE 4

EFFECTS OF CONTINUOUS LIGHT OR DARKNESS ON THIOURACIL ACTION IN FEMALE MICE

Group	No. per group	Treatment	Av. original body wt. gm.	Av. final body wt. gm.	Av. thyroid wt. mg.	Av. thyroid wt. / 100 gm. body wt. mg.
I	9	Controls plus thiouracil	28.00	31.33	6.99 ± 0.52 [@]	22.31 ± 1.27 [@]
II	10	Continuous light plus thiouracil	28.70	32.75	4.94 ± 0.33 [@]	15.10 ± 1.00 [@]
						Significant difference = 4.45
I	10	Controls plus thiouracil	25.00	26.00	6.20 ± 0.60 [@]	24.06 ± 1.82 [@]
II	9	Continuous light plus thiouracil	23.80	23.38	3.79 ± 0.69 [@]	16.10 ± 2.27 [@]
						Significant difference = 2.74

@ Standard error of mean

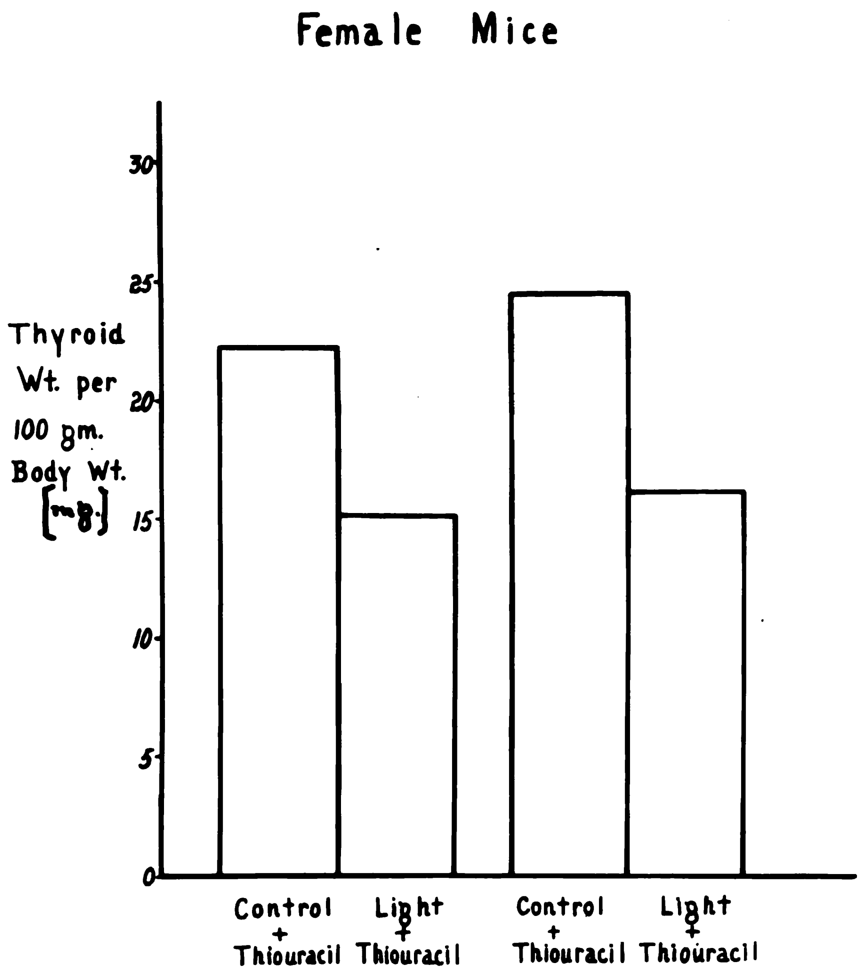

Fig. 1

Effect of Continuous Light on Thiouracil Action in Female Mice

TABLE 5

EFFECT OF CONTINUOUS LIGHT OR DARKNESS ON THIOURACIL ACTION IN FEMALE MICE

Group	No. per group	Treatment	Av. original body wt. gm.	Av. final body wt. gm.	Av. thyroid wt. mg.	Av. thyroid wt. / 100 gm. body wt. mg.
I	10	Controls	23.20	26.28	$1.99 \pm 0.68^{@}$	$7.65 \pm 0.88^{@}$
II	10	Controls plus thiouracil	23.10	25.55	$7.70 \pm 0.83^{@}$	$30.08 \pm 3.16^{@}$
III	9	Continuous darkness plus thiouracil	23.40	28.27	$7.91 \pm 0.46^{@}$	$27.27 \pm 1.29^{@}$
IV	9	Continuous light plus thiouracil	23.40	25.07	$5.53 \pm 0.47^{@}$	$21.92 \pm 1.46^{@}$
						Significant differences: Groups II and III = 0.82; Groups II and IV = 2.34

@ Standard error of mean

TABLE 6

EFFECT OF CONTINUOUS LIGHT OR DARKNESS ON THIOURACIL ACTION IN FEMALE MICE

Group	No. per group	Treatment	Av. original body wt. gm.	Av. final body wt. gm.	Av. thyroid wt. mg.	Av. thyroid wt. / 100 gm. body wt. mg.
I	9	Controls	22.70	27.12	2.70 $\pm$ 0.11@	10.09 $\pm$ 0.60@
II	10	Controls plus thiouracil	22.70	26.31	6.35 $\pm$ 0.59@	24.49 $\pm$ 2.64@
III	9	Continuous darkness plus thiouracil	22.90	25.46	8.01 $\pm$ 0.69@	31.18 $\pm$ 2.01@
IV	9	Continuous light plus thiouracil	22.90	25.56	3.87 $\pm$ 0.58@	15.11 $\pm$ 2.37@

Significant differences:

Groups II and III = 2.02
Groups II and IV = 2.64

@ Standard error of mean

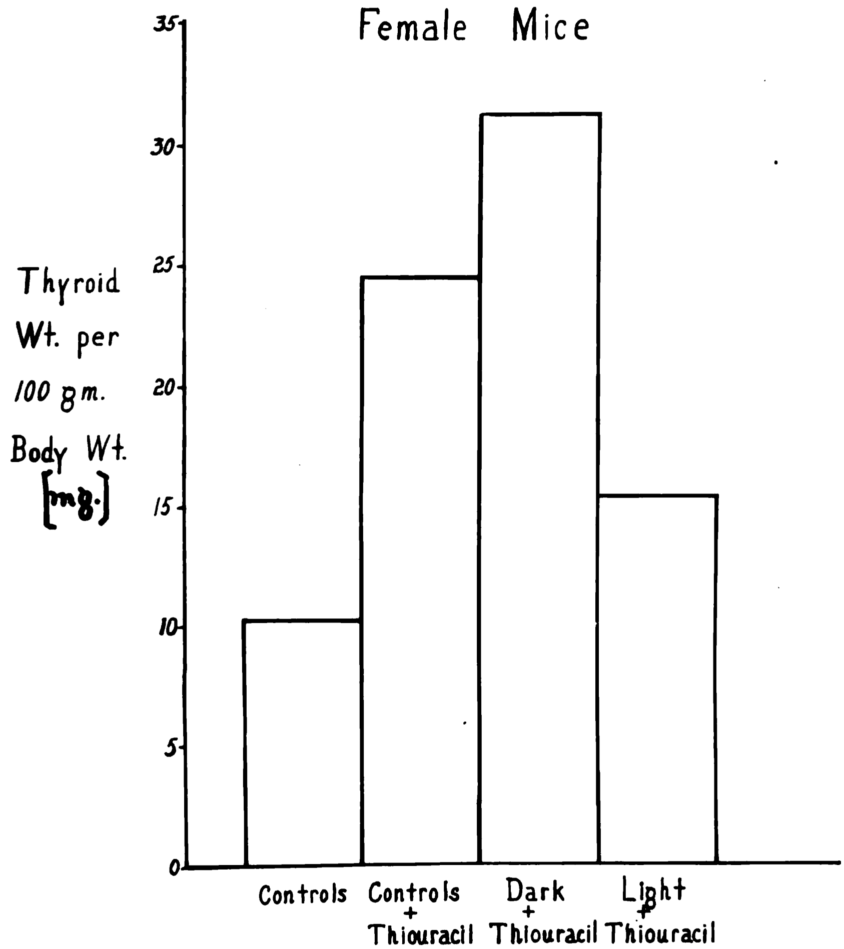

Fig. 2

Effect of Continuous Light or Darkness on Thiouracil Action in Female Mice

TABLE 7

EFFECT OF CONTINUOUS LIGHT OR DARKNESS ON THE UPTAKE OF RADIOACTIVE IODINE IN FEMALE MICE

Group	No. per group	Treatment	Av. orig. body wt. gm.	Av. final body wt. gm.	Av. thyroid wt. mg.	Av. thyroid wt. / 100 gm. body wt. mg.
I	10	Controls	23.70	28.88	2.53 ± 0.11@	8.76 ± 0.36@
II	10	Continuous darkness	24.00	27.94	2.87 ± 0.11@	10.27 ± 0.69@
III	10	Continuous light	24.00	27.53	2.14 ± 0.14@	7.77 ± 0.25@

Group	Radioactivity in counts per second: Av. no. counts per thyroid	Av. no. counts per mg. thyroid	Av. no. counts per thyroid / 100 gm. body wt.
I	21.57 ± 1.72@	8.74 ± 0.38@	75.44 ± 6.59@
II	28.23 ± 2.52@	9.89 ± 0.42@	99.76 ± 6.95@
III	12.39 ± 1.45@	6.01 ± 0.30@	44.21 ± 4.15@
	Significant differences:	Significant differences:	Significant differences:
	Groups	Groups	Groups
	I and II = 2.18	I and II = 2.04	I and II = 2.54
	1 and III = 4.08	I and III = 5.65	I and III = 4.01

@ Standard error of mean

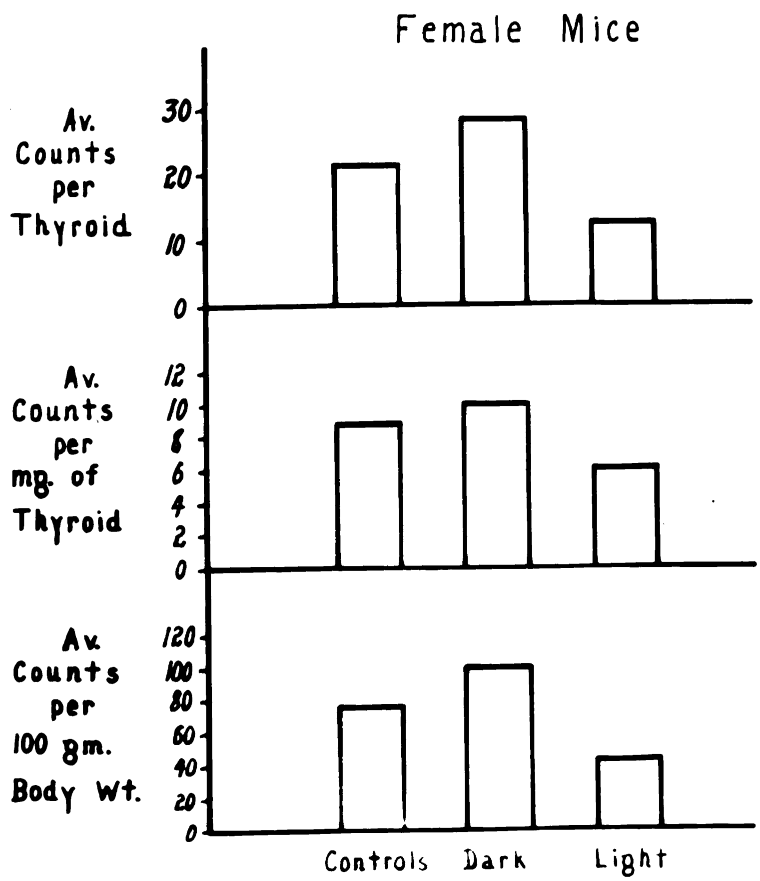

Fig. 3

Effect of Continuous Light or Darkness on the Uptake of Radioactive Iodine by the Thyroids of Female Mice

radioactive iodine than the controls.

Male Mice - Thiouracil Action. Continuous light or darkness in male mice elicited the same reaction to thiouracil as in female mice. The first experiment (Table 8) was performed on an initially mature group of male mice. A younger group of male mice were used in the second experiment (Table 9, Fig. 4). In both, the effect of continuous light (group IV in each experiment) was to significantly reduce the action of thiouracil, while continuous darkness (group III in each experiment) significantly increased the action of thiouracil when compared to the controls (group II in each experiment).

Male Mice - Uptake of Radioactive Iodine. The data obtained in this experiment (Table 10, Fig. 5) corroborate the results obtained with thiouracil. Continuous light produced a significant decrease in thyroid weight (group III) and continuous darkness a significant increase in thyroid weight when compared to the controls (group I). The uptake of radioactive iodine was significantly decreased in the thyroids of the mice under continuous light (group III) and significantly increased in the thyroids of the mice under continuous darkness (group II), when compared to the controls (group I).

In summary, the preceding experiments in female and male mice conclusively demonstrate that continuous light decreases thyroid function, as evidenced by (1) a reduced thyroid reaction to a constant dose of thiouracil (2) a decrease in thyroid weight and (3) a reduced uptake by the thyroids of a tracer dose of radioactive iodine. Continuous darkness, on the other hand, definitely increases thyroid activity, as indicated by (1) an increase in thyroid reaction to a

TABLE 8

EFFECT OF CONTINUOUS LIGHT OR DARKNESS ON THIOURACIL ACTION IN MALE MICE

Group	No. per group	Treatment	Av. original body wt. gm.	Av. final body wt. gm.	Av. thyroid wt. mg.	Av. thyroid wt. / 100 gm. body wt. mg.
I	10	Controls	32.00	35.10	2.55 $\pm$ 0.15 @	7.23 $\pm$ 0.29 @
II	8	Controls plus thiouracil	33.90	38.69	8.36 $\pm$ 0.59 @	21.71 $\pm$ 1.04 @
III	6	Continuous darkness plus thiouracil	33.6	37.17	10.33 $\pm$ 0.99 @	28.10 $\pm$ 2.36 @
IV	10	Continuous light plus thiouracil	32.00	33.01	4.60 $\pm$ 0.50 @	14.64 $\pm$ 1.17 @

Significant differences:

Groups II and III = 2.29

Groups II and IV = 3.74

@ Standard error of mean

TABLE 9

EFFECT OF CONTINUOUS LIGHT OR DARKNESS ON THIOURACIL ACTION IN MALE MICE

Group	No. per group	Treatment	Av. original body wt. gm.	Av. final body wt. gm.	Av. thyroid wt. mg.	Av. thyroid wt. / 100 gm. body wt. mg.
I	10	Controls	21.40	32.06	2.91 $\pm$ 0.34 @	8.92 $\pm$ 0.81 @
II	8	Controls plus thiouracil	21.50	31.06	6.29 $\pm$ 0.61 @	20.74 $\pm$ 2.35 @
III	9	Continuous darkness plus thiouracil	21.40	29.27	7.91 $\pm$ 0.47 @	27.28 $\pm$ 1.30 @
IV	10	Continuous light plus thiouracil	21.50	31.01	4.61 $\pm$ 0.49 @	14.65 $\pm$ 1.18 @
						Significant differences: Groups II and III = 2.43; Groups II and IV = 2.32

@ Standard error of mean

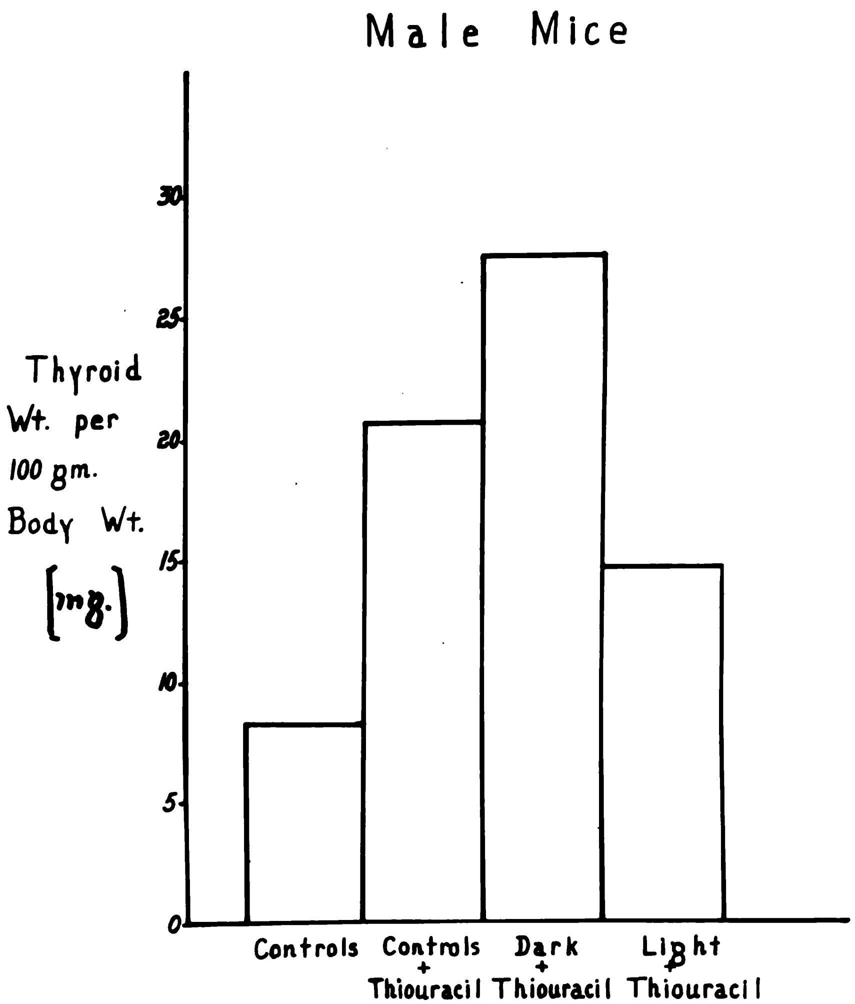

Fig. 4

Effect of Continuous Light or Darkness on Thiouracil Action in Male Mice

TABLE 10

EFFECT OF CONTINUOUS LIGHT OR DARKNESS ON THE UPTAKE OF RADIOACTIVE IODINE IN MALE MICE

Group	No. per group	Treatment	Av. orig. body wt. gm.	Av. final body wt. gm.	Av. thyroid wt. mg.	Av. thyroid wt. / 100 gm. body wt. mg.
I	9	Controls	21.80	31.49	2.19 $\pm$ 0.05@	6.95 $\pm$ 0.43@
II	10	Continuous darkness	21.40	31.76	2.62 $\pm$ 0.21@	8.25 $\pm$ 0.61@
III	9	Continuous light	21.80	31.67	1.93 $\pm$ 0.12@	6.09 $\pm$ 0.36@

Group	Radioactivity in counts per second: Av. no. counts per thyroid	Av. no. counts per mg. thyroid	Av. no. counts per thyroid / 100 gm. body wt.
I	22.60 $\pm$ 2.97@	10.19 $\pm$ 0.46@	74.59 $\pm$ 10.48@
II	31.03 $\pm$ 3.00@	11.51 $\pm$ 0.47@	117.43 $\pm$ 12.35@
III	13.70 $\pm$ 2.26@	6.90 $\pm$ 0.78@	41.77 $\pm$ 6.06@
	Significant differences: Groups I and II = 2.00; I and III = 2.30	Significant differences: Groups I and II = 2.00; I and III = 3.64	Significant differences: Groups I and II = 2.65; I and III = 2.71

@ Standard error of mean

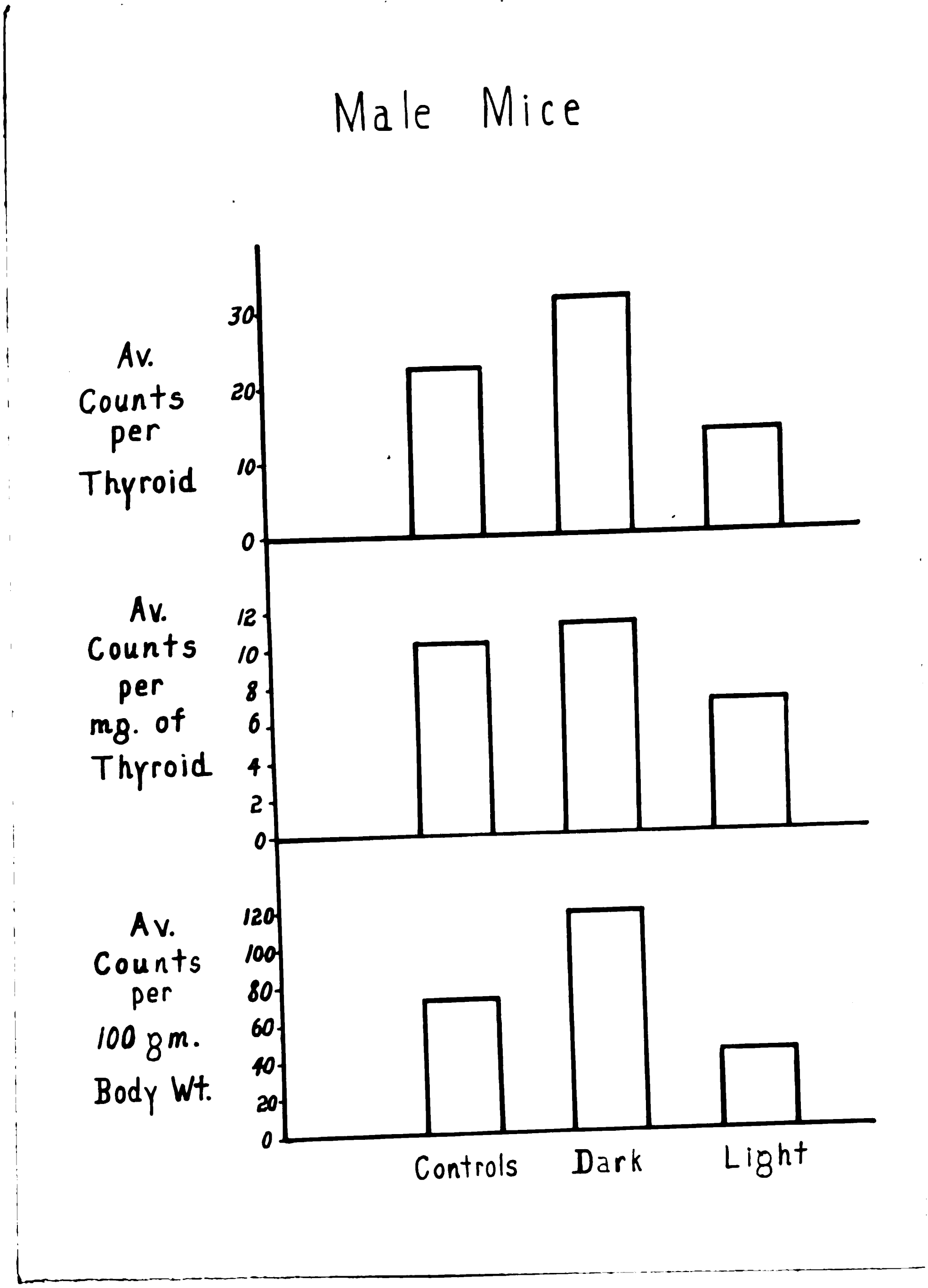

Fig. 5

Effect of Continuous Light or Darkness on the Uptake of Radioactive Iodine by the Thyroids of Male Mice constant dose of thiouracil (2) an increase in thyroid weight and (3) an increase in thyroid uptake of radioactive iodine.

Effects of Continuous Light or Darkness on Gonadogen Action.

Female Rockland Rats. The data given in Table 11, Fig. 6 show that continuous light for twenty-eight days (group III) augmented the action of pregnant mares' serum on the ovaries and uterus of Rockland female rats when compared to the controls which received pregnant mares' serum (group II). Continuous darkness for twenty-eight days (group IV) did not change the activity of the equine gonadotropin.

The results were essentially similar in a repeat experiment (Table 12, Fig. 7). Continuous light again augmented the effects of the gonadotropin on ovarian and uterine weights, while continuous darkness produced no change in ovarian weight. The latter condition, however, did appear to increase the weight of the uterus.

A third repeat experiment (Table 13, Fig. 8) corroborated the results obtained in the previous two experiments. It can be concluded, therefore, that continuous light for twenty-eight days enhances the effects of a constant dose of gonadogen on the ovaries and uterus of Rockland female rats, whereas continuous darkness for twenty-eight days appears to exert no effect on the action of gonadogen.

Female Carworth Rats. The results of two repeat experiments in Carworth rats (Tables 14 and 15) indicate that neither continuous light nor continuous darkness for twenty-eight days influenced the action of a constant dose of equine gonadotropin in

TABLE 11

EFFECT OF CONTINUOUS LIGHT OR DARKNESS ON GONADOGEN ACTION IN FEMALE ROCKLAND RATS

Group	No. per group	Treatment	Av. original body wt. gm.	Av. final body wt. gm.	Av. ovary wt. mg.	Av. uterus wt. mg.	Av. ovary wt./100 gm. body wt. mg.	Av. uterus wt./100 gm. body wt. mg.
I	9	Controls	45.90	120.37	34.27	192.09	28.18 $\pm$ 1.57@	157.12 $\pm$ 23.92@
II	10	Controls plus gonadogen	45.80	125.50	53.14	165.72	42.31 $\pm$ 2.68@	131.90 $\pm$ 7.65@
III	9	Continuous light plus gonadogen	45.70	122.89	60.52	235.48	49.41 $\pm$ 1.58@	191.04 $\pm$ 20.86@
IV	9	Continuous darkness plus gonadogen	45.90	119.39	50.54	173.70	42.52 $\pm$ 2.99@	142.87 $\pm$ 22.77@
							Significant differences: groups II and III = 2.36	Significant differences: groups II and III = 2.66

@ Standard error of mean

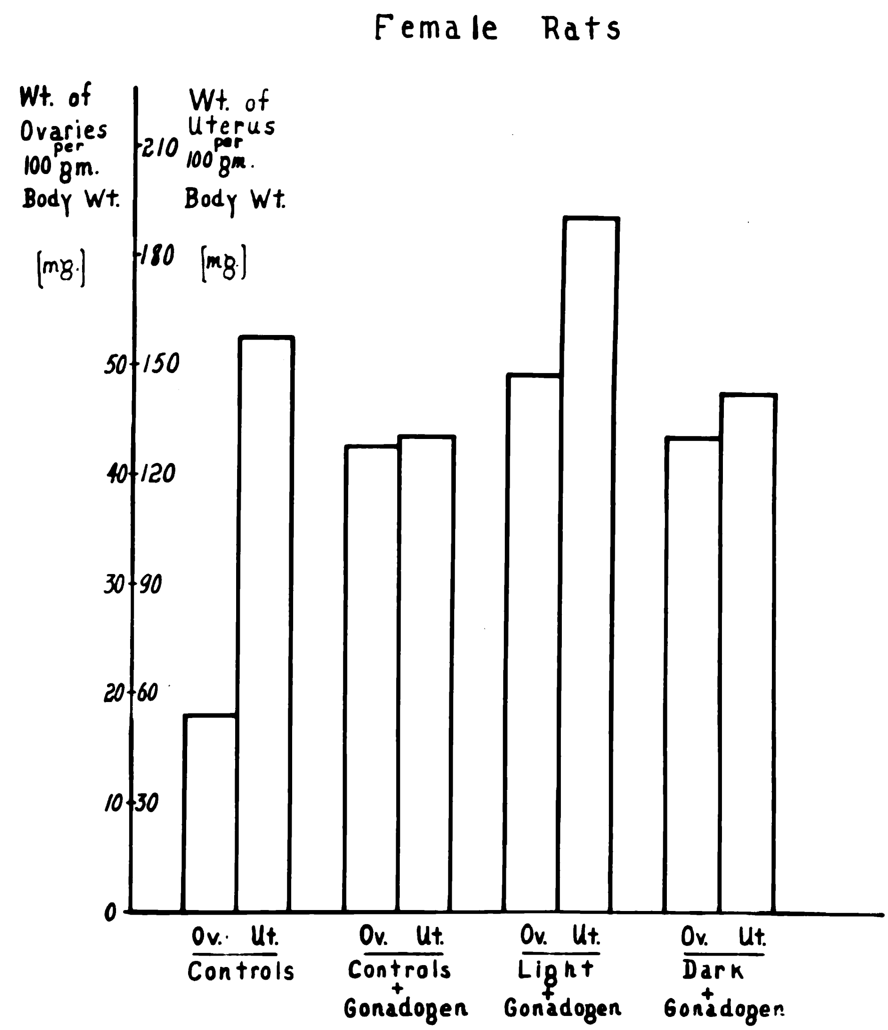

Fig. 6

Effect of Continuous Light or Darkness on Gonadogen Action in Female Rockland Rats

TABLE 12

EFFECT OF CONTINUOUS LIGHT OR DARKNESS ON GONADOGEN ACTION IN FEMALE ROCKLAND RATS

Group	No. per group	Treatment	Av. original body wt. gm.	Av. final body wt. gm.	Av. ovary wt. mg.	Av. uterus wt. mg.	Av. ovary wt. / 100 gm. body wt. mg.	Av. uterus wt. / 100 gm. body wt. mg.
I	10	Controls	36.90	109.50	28.00	118.30	25.53 $\pm$ 1.99[@]	105.01 $\pm$ 17.79[@]
II	10	Controls plus gonadogen	36.90	113.60	49.60	113.40	43.01 $\pm$ 3.02[@]	117.46 $\pm$ 6.62[@]
III	10	Continuous light plus gonadogen	36.70	110.40	59.80	203.50	56.71 $\pm$ 2.68[@]	184.15 $\pm$ 17.94[@]
IV	10	Continuous darkness plus gonadogen	36.80	117.20	51.90	180.70	45.04 $\pm$ 3.51[@]	153.90 $\pm$ 12.81[@]
							Significant differences: groups II and III = 3.43	Significant differences: groups II and III = 3.49

@ Standard error of mean

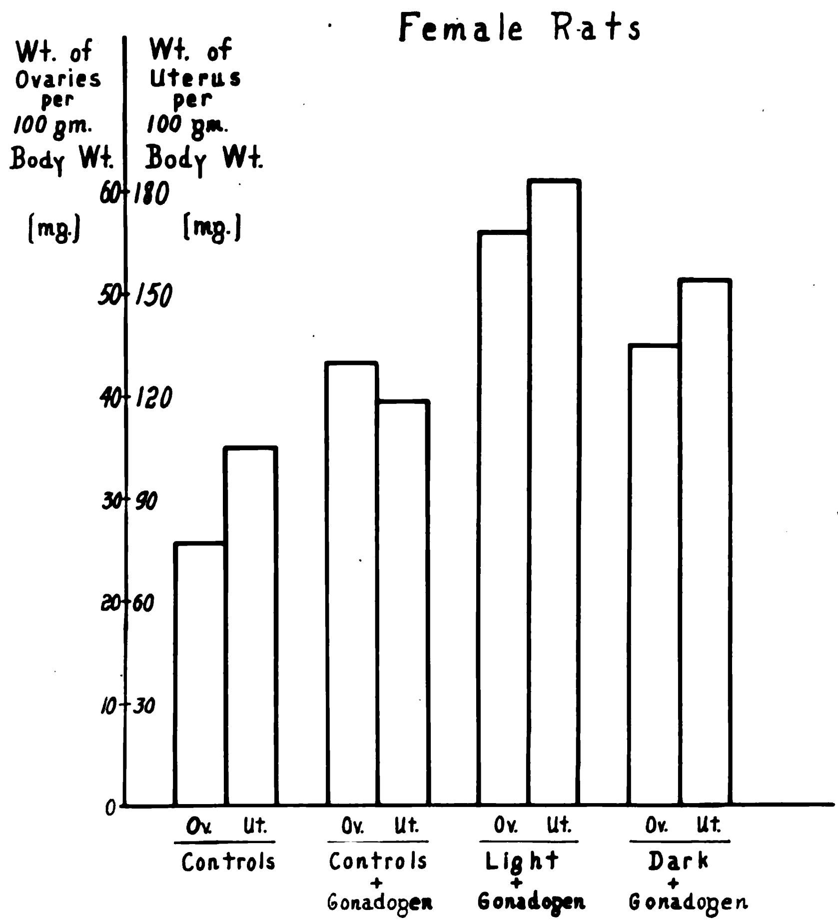

Fig. 7

Effect of Continuous Light or Darkness on Gonadogen Action in Female Rockland Rats

TABLE 13

EFFECT OF CONTINUOUS LIGHT OR DARKNESS ON GONADOGEN ACTION IN FEMALE ROCKLAND RATS

Group	No. per group	Treatment	Av. original body wt. gm.	Av. final body wt. gm.	Av. ovary wt. mg.	Av. uterus wt. mg.	Av. ovary wt. / 100 gm. body wt. mg.	Av. uterus wt. / 100 gm. body wt. mg.
I	10	Controls	44.60	132.93	29.71	156.06	23.71 $\pm$ 1.78 @	117.06 $\pm$ 4.85 @
II	8	Controls plus gonadogen	44.70	136.91	61.65	191.15	45.49 $\pm$ 3.23 @	137.16 $\pm$ 9.24 @
III	9	Continuous light plus gonadogen	44.70	128.24	71.76	209.49	55.71 $\pm$ 3.37 @	163.49 $\pm$ 8.16 @
IV	10	Continuous darkness plus gonadogen	44.70	132.92	64.74	185.25	48.88 $\pm$ 3.23 @	137.90 $\pm$ 12.4 @
							Significant differences: groups II and III = 2.19	Significant differences: groups II and III = 2.14

@ Standard error of mean

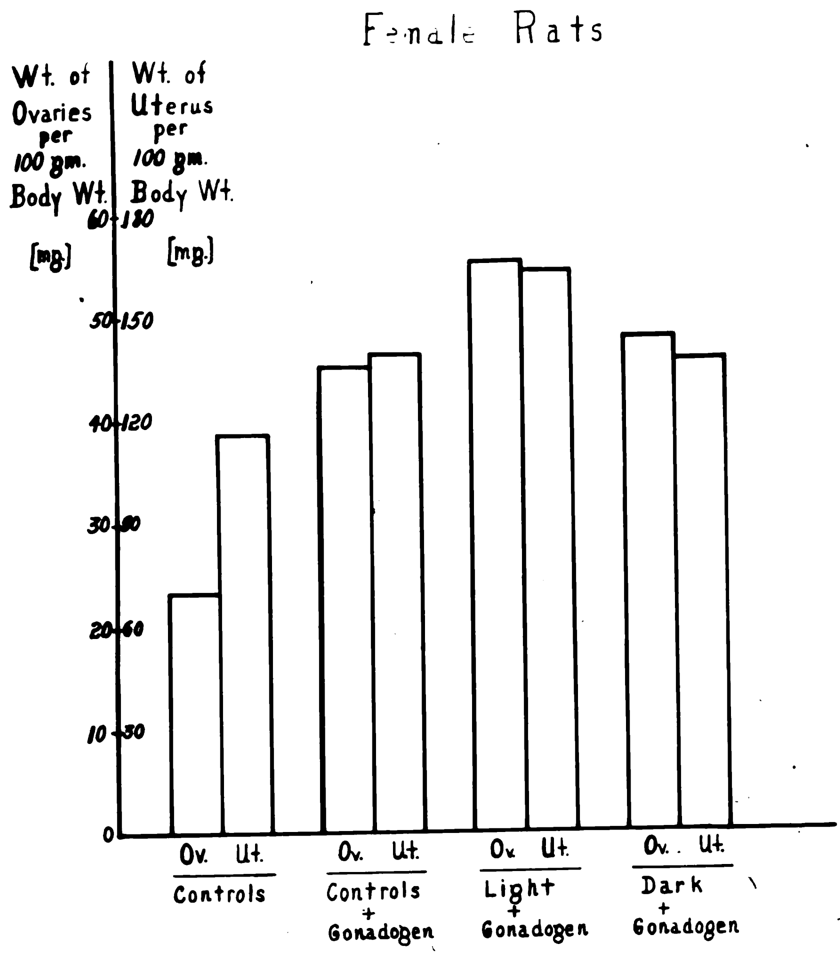

Fig. 8

Effect of Continuous Light or Darkness on Gonadogen Action in Female Rockland Rats

TABLE 14

EFFECT OF CONTINUOUS LIGHT OR DARKNESS ON GONADOGEN IN FEMALE CARWORTH RATS

Group	No. per group	Treatment	Av. original body wt. gm.	Av. final body wt. gm.	Av. ovary wt. mg.	Av. uterus wt. mg.	Av. ovary wt. / 100 gm. body wt. mg.	Av. uterus wt. / 100 gm. body wt. mg.
I	8	Controls	47.40	136.55	38.83	360.80	$27.79 \pm 4.24^{@}$	$262.90 \pm 57.24^{@}$
II	10	Controls plus gonadogen	47.60	130.29	52.58	268.08	$39.69 \pm 2.95^{@}$	$208.49 \pm 47.40^{@}$
III	10	Continuous light plus gonadogen	47.70	134.09	53.21	281.48	$39.86 \pm 2.52^{@}$	$212.13 \pm 63.41^{@}$
IV	9	Continuous darkness plus gonadogen	47.50	133.68	48.69	251.18	$36.94 \pm 1.99^{@}$	$189.13 \pm 31.03^{@}$

@ Standard error of mean

TABLE 15

EFFECT OF CONTINUOUS LIGHT OR DARKNESS ON GONADOGEN IN FEMALE CARWORTH RATS

Group	No. per group	Treatment	Av. original body wt. gm.	Av. final body wt. gm.	Av. ovary wt. mg.	Av. uterus wt. mg.	Av. ovary wt. / 100 gm. body wt. mg.	Av. uterus wt. / 100 gm. body wt. mg.
I	8	Controls	53.60	141.41	37.81	211.21	26.39 ± 1.82@	149.51 ± 5.77@
II	10	Controls plus gonadogen	53.60	135.64	74.51	308.95	54.91 ± 2.61@	227.72 ± 15.66@
III	9	Continuous light plus gonadogen	53.70	127.93	61.81	346.69	48.85 ± 2.76@	272.12 ± 55.43@
IV	8	Continuous darkness plus gonadogen	53.80	141.26	73.18	288.18	53.50 ± 2.55@	203.51 ± 16.55@

@ Standard error of mean

this strain. A preliminary experiment on Carworth female rats indicated that more than one Cartland-Nelson unit of Gonadogen would be required to give an increase in the weight of the ovaries and uterus. Thus, the rats shown in Table 14 were given 1.5 units while the rats shown in Table 15 were given 2.0 units of Gonadogen. Although the rats of this strain were comparable in age and weight to the Rockland female rats previously used, it would appear that they were insensitive to continuous light, and perhaps this was a reflection of their lower gonadal sensitivity to Gonadogen.

DISCUSSION

Three kinds of evidence substantiate the conclusion that continuous light reduces thyroid function and that continuous darkness increases thyroid function in Rockland mice of both sexes.

Thiouracil was used in most of the measurements of thyroid function in these experiments. It was assumed at the outset that if each animal were injected with the same dose of thiouracil, there should have been the same average increase in thyroid weight of each animal. Thyrotropic activity by the anterior pituitary would presumably be stimulated to the same degree in all animals. However, if continuous light induced an initially lower level of thyrotropic and thyroid function, then the administration of thiouracil might be expected to produce a smaller increase in thyroid weight. Under continuous darkness, an initially higher level of thyrotropic and thyroid activity would be expected, with a subsequently greater increase in thyroid weight through thiouracil action. In other words, thiouracil would be equally effective in all the mice, and the only variable factors would be the changes in thyrotropic and thyroid function induced by either continuous light or darkness. On the whole this hypothesis seems reasonable, although alternative explanations may be possible.

In the male and female mice which were injected with a tracer dose of radioactive I^{131} the day before sacrifice, continuous light resulted in a decrease and continuous darkness in an increase in thyroid weight. It is not believed that the single injection of such a minute quantity of I^{131} influenced thyroid weight in these animals. Although changes in thyroid weight do not always represent changes in function, it appears logical to make this conclusion insofar as these experiments are concerned, since they are in agreement with the other measures of thyroid function.

Insofar as the "uptake" of radioactive iodine is concerned, it is believed that a more active thyroid would take up more and a less active thyroid less of the iodine. It is recognized that not all the I^{131} found in the thyroid necessarily represents "uptake" exclusively, since some of the iodine present may only indicate retention and slow excretion from the gland. However, it seems doubtful that the latter would be major factors in the time interval (sixteen hours) which elapsed between the injection of the I^{131} and sacrifice of the mice. Furthermore, these tests of thyroid activity with radioactive iodine are entirely in agreement with the other two measures of thyroid function used in these experiments.

It remains to be explained how light or darkness influenced thyroid activity in the mice. Several interpretations seem possible. Light, through direct stimulation of the eyes, may send nervous impulses to the anterior pituitary which would induce a decrease in thyrotropic secretion. The absence of light, or darkness, would presumably remove the light-induced inhibition of thyrotropic function.

An alternative hypothesis would give primacy to the effects of light on FSH (follicle stimulating hormone) function by the anterior pituitary. It has been quite well established that FSH and thyrotropic hormone are both elaborated by the same cell type in the anterior pituitary, namely the basophils (Severinghaus, 1939). Thus, if the primary effect of light is to increase FSH production by the anterior pituitary, and sufficient evidence (see review of literature) has already been presented to indicate that light can increase FSH production in birds and mammals, then the subsequent or secondary effect would be to decrease thyrotropic hormone synthesis. Contrawise, under continuous darkness, FSH synthesis by the basophils would be reduced, thereby permitting more thyrotropic hormone to be secreted.

Another factor which may be important in explaining the results obtained in the mice is the possible influence of continuous light or darkness on general body activity. Mice, like rats, may be more active during the night than during the day. These daily cycles of activity, while shown to be a fact in rats during normal twenty-four hour periods of light and darkness, may not apply to prolonged periods of light or darkness, such as were used in the present experiments. Indirect evidence that changes in body activity may not be a factor in these experiments are the data showing that the body weights of the mice under continuous light or darkness did not differ from those maintained under normal day-night conditions.

The results obtained with pregnant mares' serum in the rats seem logical in view of the numerous reports of the stimulating effects of light on gonad function in birds and mammals. Continuous light, by increasing FSH production in the anterior pituitary, may have sensitized the ovaries of the Rockland rats to further stimulation by injection of pregnant mares' serum. It is difficult to understand why the Carworth strain of rats failed to respond similarly to continuous light. The fact that this strain of rats required larger quantities of pregnant mares' serum to stimulate the ovaries and uterus than were required by the Rockland rats provides a possible clue. This may indicate that the ovaries of these rats are less sensitive to stimulation by gonadotropic hormones coming from their own pituitaries as well as to injected gonadotropins. In other words, it is quite possible that the pituitaries of these animals were stimulated by continuous light to secrete more FSH, but that their ovaries did not respond. This seems not unlikely in view of the fact that the increases in ovarian and uterine weight obtained even in the Rockland rats under continuous light plus Gonadogen were significant but by no means extraordinarily large.

The greater increase in the weights of the ovaries and uterus of the Rockland rats kept under continuous light plus Gonadogen may be due, in part at least, to a reduction in thyroid function. Although thyroid function was not measured in these rats, the report by Dempsey (1943) of reduced thyroid function in twelve rats kept under continuous light would appear to support this view. It has been amply demonstrated that experimentally induced hypothyroidism in rats increases their gonadal response to a constant dose of administered Gonadogen (Meites and Chandrashaker, 1949; Johnson, 1949).

The two questions asked in the introduction have been only partially answered by the present experiments. The finding that light and darkness influence thyroid activity in Rockland mice is believed to be conclusive. Further work will need to be done to determine whether light and darkness similarly influence thyroid function in other species, and whether these changes in thyroid function can account to any extent for alterations in gonadotropic function. It would be particularly valuable to determine the effects of light and darkness on thyroid function in sheep, since light and darkness have already been shown to play a major role in initiating gonadal function in this species.

SUMMARY

1. The effects of continuous artificial light or darkness for a twenty-eight day period on thyroid activity were determined in 242 Rockland mice of both sexes. Four experiments were done with females and three with males. Thyroid activity was measured by determining (a) the weight increase of the thyroids following injections for ten days of a constant dose of thiouracil (b) the normal weight changes of the thyroids of the mice kept under light or darkness, and (c) the uptake by the thyroid of a singly-injected tracer dose of radioactive iodine administered sixteen hours prior to sacrifice.

2. Continuous light induced the following average changes in the thyroids of female and male mice, respectively, on a 100 gram body weight basis as compared to controls: (a) decreases in thyroid weight of 11.30 and 12.37 percent; (b) reductions in thyroid responses of 32.89 and 31.04 percent to thiouracil, and (c) reductions of 44.00 and 44.00 percent in thyroid uptake of radioactive iodine.

3. Continuous darkness induced the following average changes in the thyroids of female and male mice, respectively, on a 100 gram body weight basis as compared to controls: (a) increases in thyroid weight of 17.24 and 18.71 percent; (b) increases in thyroid weight of 22.70 and 30.43 percent above the controls in response to thiouracil, and (c) increases of 41.40 and 57.43 percent in thyroid uptake of radioactive iodine.

4. In a second group of experiments the effects of continuous light or darkness for twenty-eight days on gonadal func-

tion were determined in 186 young Rockland and Carworth female rats. Three experiments were carried out on Rockland and two on Carworth rats. During the last four of the twenty-eight days each rat of each experiment was injected with a constant dose of pregnant mares' serum.

5. Under continuous light the Rockland rats showed average weight increases of ovaries and uterus in response to injections of pregnant mares' serum of 23.72 and 39.37 percent above the controls. Continuous darkness produced no significant change in the response of the ovaries and uterus to the gonadotropin when compared with the controls.

6. In the Carworth rats, neither continuous light nor continuous darkness appeared to influence the response of the ovaries and uterus to pregnant mares' serum. Since more pregnant mares' serum was required to elicit an increase in gonadal response in this strain comparable to that obtained in the Rockland rats, it seems possible that any light-induced changes were equally less effective in this strain.

7. The following hypotheses have been presented to explain the inhibiting effects of continuous light and the stimulating effects of continuous darkness on thyroid function in Rockland mice: (a) Light, acting through the eyes and through nervous pathways to the anterior pituitary, may induce a decrease in thyrotropic hormone secretion; darkness would remove this inhibition to thyrotropic hormone secretion; (b) The primary effect of light may be to stimulate FSH secretion by the anterior pituitary. Since both

FSH and thyrotropin are produced by the basophils of the anterior pituitary, stimulation of synthesis of the former may induce a corresponding decrease in synthesis of the latter. Darkness would decrease FSH secretion and elicit a corresponding increase in thyrotropin secretaion, (c) A third explanation is that continuous light may decrease general body activity and continuous darkness increase activity in the mice. This seems unlikely, however, since the body weights of the mice under altered light conditions did not differ from those of the controls.

8. The following hypotheses have been presented to explain the stimulating effects of continuous light on gonadal reaction to pregnant mares' serum in young Rockland rats: (a) Continuous light, by increasing FSH production by the anterior pituitary, may sensitize the ovaries to pregnant mares' serum, and (b) Continuous light, by inducing a decrease in thyrotropic and thyroid activity, would increase the response of the ovaries to equine gonadotropin.

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