

Therefore, one may conclude that runting is not identical with homologous disease and that the latter is not caused by an infectious agent.

*Summary.* Studies of homologous disease in newborn mice using axenic and conventional animals (a) provide evidence that for the same dosage of cells, populations of spleen cells have different effects according to their origin. They are more efficient if donors are conventional or immunized axenic, and less efficient if the donors are only axenic. The basis for these differences has not been determined. (b) Provide no evidence that superinfection plays a role in the G.V.H. reaction in this short time system; (c) definitely separate homologous disease of newborn from similar syndromes induced by other investigators with experimental infectious agents.

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1. Nisbet, N. W., Heslop, B. F., *Brit. Med. J.*, 1962, no. 5272, 5273, 129, 206.
2. Billingham, R. E., Brent, L., *Transplant. Bull.*, 1957, v4, 67.
3. Billingham, R. E., Brown, J. B., Defendi, V., Silvers, W. K., Sternmuller, D., *Ann. N. Y. Acad. Sci.*, 1960, v87, 457.
4. Simonsen, M., in *Progress in Allergy*, Karger Bale, New York, 1962, v6, 349.

5. Cooper, G. N., Howard, J. G., *Brit. J. Exp. Path.*, 1961, v42, 558.
6. Stewart, J. S., Eddy, B. E., Stanton, M. F., *Acta Unio Internat. Contr. Canc.*, 1959, v15, 842.
7. Kraemer, P. M., *J. Nat. Cancer Inst.*, 1962, v28, 437.
8. Vandeputte, M., De Somer, P., *ibid.*, 1965, v35, 237.
9. Hotchin, J., in *Cold Spring Harbor Symposium of Quantitative Biology*, 1962, v27, 479.
10. Walters, M. N. I., Joske, R. A., Leak, P. Y., Stanley, N. F., *Brit. J. Exp. Path.*, 1963, v44, 427.
11. Rowe, W. P., Capps, W. I., *J. Exp. Med.*, 1961, v113, 831.
12. Schlesinger, M., Mark, R., *Science*, 1964, v143, 965.
13. Salomen, J. C., unpublished.
14. Miller, J. F. A. P., *Proc. Roy. Soc.*, 1962, vB, 157, 415.
15. Wilson, R., Sjodin, K., Bealmear, M., *Proc. Soc. Exp. Biol. and Med.*, 1964, v117, 237.
16. Mac Intire, K. R., Sell, B., Miller, J.F.A.P., *Nature*, 1964, v204, 151.
17. Salomon, J. C., *C. R. Acad. Sci.*, 1965, v260, 4862.
18. Pollard, M., *Progr. Med. Virol.*, 1965, v7, 362.
19. de Harven, E., *J. Exp. Med.*, 1964, v120, 857.
20. Pollard, M., *Science*, 1964, v145, 247.
21. Thorbecke, G. J., *Ann. N. Y. Acad. Sci.*, 1959, v78, 237.
22. Siskind, G. W., Thomas L., in *Biological Problems of Grafting*, Albert and Medawar, eds., Blackwell, 1959, p176.

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## Effect of Pinealectomy and Melatonin on Feed Consumption and Thyroid Hormone Secretion Rate.\*† (31215)

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Evidence that the pineal is an endocrine gland and secretes the hormone, melatonin, has been suggested by recent research(1). When rats were pinealectomized, it was shown that the ovaries hypertrophied similarly to

the effect produced by constant light(2). It was then shown that constant light tended to depress the secretion of melatonin and darkness stimulated its production(3). It would thus appear that melatonin depressed the precocious development of the ovary, and light, by depressing melatonin secretion, stimulates the gonadotropic hormones and ovarian development.

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The possible relation of the pineal gland and melatonin to other endocrine gland functions requires study. Evidence indicating a relation to the adrenal gland has been presented(4). Kitay and Altschule(5) summarized the literature on the relation of pinealectomy to the thyroid gland, citing references indicating hypertrophy or no change. Malm *et al*(8) reported that pinealectomy stimulated the growth of rats up to the 14th week.

In a continuation of our studies on the effect of the removal of endocrine glands and their replacement on feed consumption, the effect of pinealectomy and melatonin is reported as well as the effect upon thyroid hormone secretion rate (TSR).

*Materials and methods.* Pinealectomy was performed in Sprague-Dawley-Rolfsmeyer female rats as follows: Nembutal at a level of 4.0 mg/100 g BW was administered to induce anesthesia. The rats were tied to an operating board with the dorsal side up. The hair was shaved from the top of the head and washed with alcohol. An incision in the skin about 15 mm long was then made in the midline at the top of the head. A small hole was then drilled through the skull at the top of the head above the pineal gland. The pineal gland was then removed with a pair of fine forceps from under the blood vessel. The incision was then sealed with a skin clip [see illustrations and further details in Kitay and Altschule(5)].

To determine feed consumption, the rats were placed in metabolism cages so constructed as to prevent coprophagy and feed wastage. Mean daily feed consumption was determined for 7 days—both before and after the operations. The control group was sham-operated in the same manner as the experimental animals. The operated rats were allowed a 6-day recovery period prior to determination of feed consumption. Room temperature was maintained at  $78 \pm 1^\circ\text{F}$  and room was artificially illuminated during daylight hours.

The thyroid hormone secretion rate (TSR) was determined by the method described previously(6) comparing the TSR of sham-operated rats with pinealectomized rats.

In the study of the effect of melatonin on

feed consumption, a group of 16 rats were used with feed consumption determined for 7 days. Then melatonin dissolved in saline was administered subcutaneously at the rate of 40  $\mu\text{g}/\text{day}$  for 10 days. Feed consumption was again determined during this period. For the TSR study, a group of 16 immature rats were used as controls and 17 immature rats were injected with 20  $\mu\text{g}$  melatonin/day for 10 days. All the control animals were injected with 0.1 ml of saline/100 g BW/day.

*Results.* The mean daily feed intake of the 15 sham-operated rats weighing 222 g was 13.87 g/day and 6.24 g/100 g BW (Table I). In comparison, 15 pinealectomized rats weighing a mean of 227 g consumed a mean of 14.89 g/day and 6.60 g/100 g BW, an increase of 7.4% and 5.8%, respectively. When feed intake before and after the operation was compared, the sham-operated rats showed a decrease of 1.8% in feed/day and a 7.1% ( $P < 0.05$ ) decrease/100 g BW, whereas the pinealectomized rats showed an increase of 4.1% ( $P < 0.05$ ) in feed intake/day and 1.2% ( $P < 0.20$ ) increase/100 g BW.

The mean TSR of the sham-operated rats was 1.26  $\mu\text{g}$  L- $\text{T}_4$ /100 g BW, whereas in the pinealectomized rats, the mean TSR was 1.43  $\mu\text{g}/100$  g BW, an increase of 11.8% ( $P < 0.05$ ). Since the TSR of rats tends to decline slightly with age(7), the increase observed is of significance.

The mean daily feed consumption of the 16 rats weighing 218 g prior to melatonin administration was 14.21 g/day or 6.52 g/100 g BW (Table II). During the period that 40  $\mu\text{g}/\text{day}$  of melatonin was administered, the same rats weighing 229 g consumed 13.16 g/day and 5.74 g/100 g BW, a decrease of 12.0% ( $P < 0.001$ ).

The mean TSR of 16 immature control rats was 1.53  $\mu\text{g}$  L- $\text{T}_4$ /100 g BW (Table III), whereas during the administration of 20  $\mu\text{g}$  melatonin/day the mean TSR of 17 experimental rats was 1.28  $\mu\text{g}/100$  g BW, a decrease of 16% ( $P < 0.025$ ).

*Discussion.* The recent discovery that the pineal is an endocrine gland and secretes the hormone, melatonin, is of great significance in relation to the role of light in seasonal breeding animals.

TABLE I. Effect of Pinealectomy on Feed Consumption and Thyroxine Secretion Rate (TSR) in Rats.

| Treatment             | No. of animals | Before operation |                        | After operation |             | TSR                         |                                                  |
|-----------------------|----------------|------------------|------------------------|-----------------|-------------|-----------------------------|--------------------------------------------------|
|                       |                | Body wt (g)      | Feed consumption g/day | g/100 g BW      | Body wt (g) | Feed consumption g/100 g BW | Change (%)                                       |
| Sham-operated control | 15             | 210.4 ± 2.4      | 14.12 ± .24            | 6.72 ± .06      | 222.3 ± 2.5 | 13.87 ± .18                 | -1.77 <sup>1</sup> 6.24 ± .05 -7.14 <sup>2</sup> |
| Pinealectomy          | 15             | 219.3 ± 2.3      | 14.30 ± .22            | 6.52 ± .05      | 227.1 ± 1.6 | 14.89 ± .21                 | +4.13 <sup>2</sup> 6.60 ± .05 +1.23 <sup>1</sup> |
|                       |                |                  |                        |                 |             |                             | 1.26 ± .06 1.43 ± .07 +11.8 <sup>2</sup>         |

All weights accompanied by standard error of mean.

Student's "t" test <sup>1</sup>P < .20<sup>2</sup>P < .05

TABLE II. Effect of Melatonin on Feed Consumption in Rats.

| Treatment                             | No. of animals | Before treatment |             |            | After treatment |             |                    |            |                    |
|---------------------------------------|----------------|------------------|-------------|------------|-----------------|-------------|--------------------|------------|--------------------|
|                                       |                | Body wt (g)      | g/day       | g/100 g BW | Body wt (g)     | g/day       | Change (%)         | g/100 g BW | Change (%)         |
| Control (.1 ml saline)                | 16             | 215.9 ± 2.1      | 14.04 ± .17 | 6.50 ± .05 | 226.1 ± 1.8     | 14.60 ± .21 | +3.99 <sup>1</sup> | 6.46 ± .05 | — .62 <sup>2</sup> |
| Melatonin (40 µg/day in .1 ml saline) | 16             | 218.0 ± 1.8      | 14.21 ± .12 | 6.52 ± .04 | 229.4 ± 1.6     | 13.16 ± .18 | —7.39 <sup>3</sup> | 5.74 ± .05 | —12.0 <sup>3</sup> |

All weights accompanied by standard error of mean.

Student's "t" test <sup>1</sup>P < .05<sup>2</sup>P < .70<sup>3</sup>P < .001

TABLE III. Effect of Melatonin on Thyroxine Secretion Rate (TSR) in Immature Rats.

| Treatment                                        | No. of animals | Body wt (g)     | TSR                                  |                    |
|--------------------------------------------------|----------------|-----------------|--------------------------------------|--------------------|
|                                                  |                |                 | $\mu\text{g L-T}_4/100 \text{ g BW}$ | Change (%)         |
| Control (.1 mg saline)                           | 16             | 127.9 $\pm$ 2.3 | 1.53 $\pm$ .07                       |                    |
| Melatonin (20 $\mu\text{g/day}$ in .1 ml saline) | 17             | 128.7 $\pm$ 2.7 | 1.28 $\pm$ .09                       | -16.3 <sup>1</sup> |

All weights accompanied by standard error of mean.

<sup>1</sup> Student's "t" test,  $P < .025$ .

While melatonin appears to be concerned primarily with the secretion of the gonadotropic hormones and ovarian development, it may influence other endocrine systems. These effects may be direct or indirect in relation to alterations in feed consumption.

The present study indicates that pinealectomy stimulates feed consumption slightly but not significantly. It was shown also to stimulate an 11.8% increase in TSR.

The slight increase in feed consumption and TSR may explain the favorable effect of pinealectomy upon body growth of rats up to the 14th week reported by Malm *et al*(8).

The administration of 40  $\mu\text{g}$  and 20  $\mu\text{g/day}$  of melatonin had an opposite effect on feed consumption and TSR in comparison with pinealectomy, decreasing feed consumption 12% and TSR 16%.

These data indicate that the absence of melatonin (pinealectomy) tends to increase feed consumption and TSR, whereas melatonin has an opposite effect.

**Summary.** The effect of pinealectomy upon feed consumption and thyroid hormone secre-

tion rate was studied in Sprague-Dawley-Rolfsmeyer female rats. Feed consumption was increased 5.77% in association with an increase of 11.8% in TSR. In a second group of 16 rats, daily injection of 40  $\mu\text{g/day}$  of melatonin depressed feed consumption 12.0%, whereas injection of 20  $\mu\text{g/day}$  of melatonin into young rats depressed TSR 16%.

1. Wurtman, R. J., Axelrod, J., Chu, E. W., Science, 1963, v141, 277.
2. Wurtman, R. J., Roth, W., Altschule, M. D., Wurtman, J. J., Acta Endocrinol., 1961, v36, 617.
3. Wurtman, R. J., Axelrod, J., Chu, E. W., Ann. N. Y. Acad. Sci., 1964, v117, 229.
4. Fiske, V. M., Lambert, H. H., Endocrinology, 1962, v71, 667.
5. Kitay, J. I., Altschule, M. D., The Pineal Gland, Harvard Univ. Press, Cambridge, Mass., 1954.
6. Grosvenor, C. E., Turner, C. W., Proc. Soc. Exp. Biol. and Med., 1958, v99, 517.
7. Narang, G. D., Turner C. W., *ibid.*, 1966, v121, 203.
8. Malm, O. J., Skang, O. E., Jaerde, P. L., Acta Endocrinol., 1959, v30, 22.

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## Tolerance to Sucrose in Adapted and Nonadapted Rats. (31216)

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While hypertonic solutions of sucrose given intravenously or intraperitoneally are known to produce vacuolizations of the convoluted tubules of the kidney, it is not altogether clear to what extent these morphological changes are involved in the general function of the kidney. From the results of studies on rabbits(1), dogs(2), rats(3) and man(4,5) it appears generally agreed that unless very

large doses of sucrose are given at frequent intervals (3-4 days), the development of the tubular vacuolizations does not compromise renal function as it is commonly measured. The time course for the development and regression of renal vacuolization in the rat has been examined histologically(3). In animals injected intraperitoneally with hypertonic sucrose, vacuolizations developed within 3