

## Lack of Refractoriness to Prolonged Thyrotropin Administration in Birds.

DOROTHEA STARBUCK MILLER. (Introduced by Emil Witschi.)\*

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It has been reported by many investigators that prolonged injection of thyrotropic hormone induces refractoriness in the response of the mammalian thyroid. The initial stimulation of the glands is followed by a regression in all the indications of hyperthyroidism. Within 2 to 3 weeks the hyperplastic thyroids and the elevated metabolic rate return to normal.

In a preliminary series of thyrotropin injections in the English sparrow, the symptoms of hyperthyroidism apparently persisted over a period of 6 weeks. Therefore 2 additional groups of sparrows were injected continuously for longer periods to test whether the thyroids would become refractory. The thyrotropic fraction used was a benzoic acid precipitate of a pyridine extract of dry anterior pituitary of sheep, prepared according to the method of Greep.<sup>1</sup>

The first group of 3 female and 2 male sparrows were injected daily or every other day from January 10 to March 23, a 10-weeks period. The second group of 3 females and 3 males received injections from October 18 to March 10, a period of 20 weeks. As criteria of thyrotropic activity, the condition of the thyroids and elevation in the metabolic rate were considered.

*Size of the Thyroids.* The thyroids of all the birds killed after continuous thyrotropin administration were considerably enlarged. In Fig. 1 are shown camera lucida drawings of the thyroids of a control female, a female after 4 injections, and a female injected over a 10-weeks period.

*Histological Findings.* The enlarged thyroids show a high degree of hyperplasia characteristic of the stimulated gland. The photograph in Fig. 2 shows a thyroid section from a female sparrow killed after 10 weeks' injection, which may be compared with the control gland in Fig. 3.

*Metabolic Rate.* The basal metabolic rate, measured on a Bene-

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<sup>1</sup> Greep, R. O., *Am. J. Physiol.*, 1935, **110**, 692.

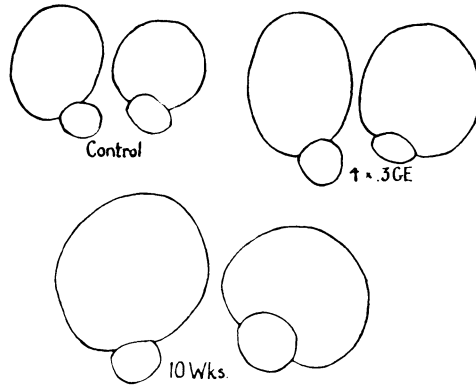


FIG. 1.

Camera lucida drawings of thyroids of female sparrows. Upper left, control; upper right, after 4 injections of thyrotropin; below, after thyrotropin injection for 10 weeks.  $\times 10$ .

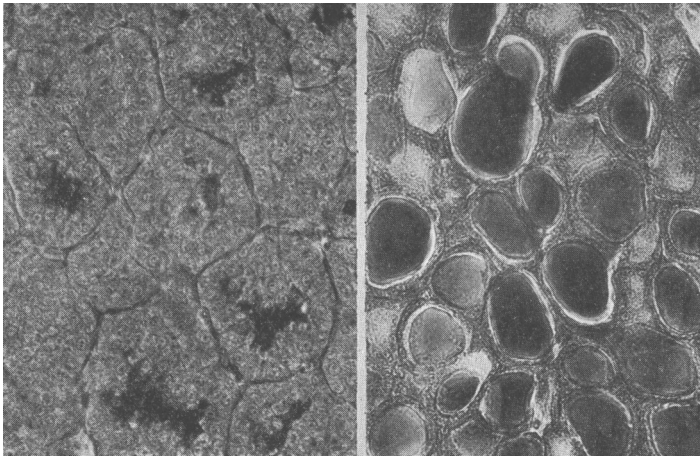


FIG. 2.

Section of sparrow thyroid, preserved after 10 weeks' injection with thyrotropin.  $\times 360$ .

FIG. 3.

Section of thyroid from control sparrow.  $\times 360$ .

dict closed-circuit apparatus,† remained elevated throughout the experimental period. The results of these determinations are presented in Table I. Each value is based upon 2 experimental birds and 2 or more controls. The percentage elevation in metabolic rate is the increase over that of the controls used in that particular run. Since the average deviation for all controls is  $\pm 3\%$ , the elevated metabolic rate observed in the experimental birds is significant.

† The apparatus was kindly placed at our disposal by the Physiology Department of the University of Iowa, College of Medicine.

TABLE I.  
Elevation in Metabolic Rate in English Sparrows Receiving Continuous Injections of Thyrotropin.

|                               | Date     | Injection period, wks | % elev. in MR |
|-------------------------------|----------|-----------------------|---------------|
| 1st Group<br>(begun 1-10-37)  | 3-3-37   | 7½                    | +20.30        |
|                               | 3-15-37  | 9                     | +17.09        |
| 2nd Group<br>(begun 10-18-37) | 11-2-37  | 2                     | +16.14        |
|                               | 11-23-37 | 5                     | +15.75        |
|                               | 3-10-38  | 20½                   | +12.86        |

These results indicate that the sparrow thyroid does not become refractory to continued pituitary administration. Greep, using the same thyrotropic preparation, reported that during continuous injections, the guinea pig thyroid returns to normal within 4 weeks. Evidently the bird is peculiar in failing to show this type of immunity reaction.

*Summary.* In the English sparrow, prolonged injection of sheep thyrotropic hormone does not lead to the development of refractoriness. The thyroids remain enlarged and hyperplastic, and the elevation in metabolic rate is maintained over periods up to 5 months.

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### Testes and Hypophyses in Gassed Male Rats.

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A degree of chronic carbon monoxide asphyxia in man is frequent since daily inhalation of small amounts of illuminating gas is common experience. Williams and Smith<sup>1</sup> have shown typical asphyxial blood changes, decrease in body weight, and sterility to occur in male rats treated daily with illuminating gas. The present study concerns testicular and hypophyseal changes.

Eighty-eight male albino rats, Ames-Wistar strain, were arranged in 2 groups of 44 each, litter mates being equally distributed. A closed circuit respiratory apparatus into which illuminating gas could be measured directly from the city main was used; one group

\* Aided by a grant from the Committee on Scientific Research of the American Medical Association.

<sup>1</sup> Williams, I. R., and Smith, Erma, *Am. J. Physiol.*, 1935, **110**, 611.