

Summary. Stilbestrol treatment of mature spayed rats for 10 days caused serous or milk secretion from partially developed lobule-alveolar glands. The lactogenic hormone content of the pituitaries per 100 g body weight was increased as much as 226% through an increase in size of the pituitary and content per milligram.

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Influence of Environmental Temperature on Growth of Mammary Lobule-Alveolar System.*†

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Many studies have been reported indicating that variations in such environmental factors as light, temperature, and diet influence the secretion of the anterior pituitary hormones. In several instances it has been shown these same factors do not adversely influence the ability of the end organs such as the gonads and the thyroid to respond to their growth stimuli. Thus in the case of underfeeding, the testes¹ and the thyroid² are responsive to less gonadotropic and thyrotropic hormone respectively than the glands of animals on a normal ration.

Recently, Trentin and Turner³ showed that the amount of estrogen required to stimulate the growth of the mammary duct system increased as the food intake was decreased. In the light of previous work it was suggested that in this case also the inanition might decrease the responsiveness of the pituitary to estrogen stimulation resulting in the production of a much smaller amount of the pituitary mammogenic duct growth factor. The responsiveness of the pituitary would thus be involved rather than the responsiveness of the end organ, the mammary gland.

During periods of high environmental temperature in the summer of 1941, it was observed that progesterone alone and with estrogens failed to stimulate the same degree of mammary lobule-alveolar de-

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¹ Breneman, W. R., *Endocrinology*, 1940, **25**, 1094.

² Stevens, D. J., *Endocrinology*, 1940, **26**, 490.

³ Trentin, J. J., and Turner, C. W., *Endocrinology*, in press.

velopment as that obtained earlier in the spring. It thus appeared that high environmental temperature as well as inanition might influence mammogen secretion by the anterior pituitary.

It seemed of interest, therefore, to compare the influence of 2 environmental temperature levels upon the responsiveness of the mammary lobule-alveolar system to progesterone[†] (plus estrogen) and an anterior pituitary extract which contained the mammogenic lobule-alveolar growth factor. According to the pituitary-mammogen theory of mammary gland growth^{4, 5} progestin (with estrogen) acts through the pituitary to cause an increased secretion there of the mammogenic lobule-alveolar growth factor, which directly stimulates mammary lobule-alveolar growth.

Procedure. Both progesterone and the pituitary initial extract, each with estrone, were assayed for their mammary lobule-alveolar proliferating properties by a technic recently described.⁶ The percentage of ovariectomized mice showing a minimum amount of lobule-alveolar growth after 10 daily subcutaneous injections was used as the criterion of response. Olive oil was used as the carrier for the progesterone and estrone. The pituitary initial extract was prepared according to a method described by Bergman and Turner.⁷ A uniform grain ration was fed to all mice *ad libitum*. The assay mice were maintained in constant temperature chambers regulated to 25° and 35°C respectively.

Results. At the 35°C temperature approximately 50% of the

TABLE I.
Lobule-Alveolar Responses of Castrate Female Mice Kept at Different Environmental Temperatures to Injections of Progesterone and a Pituitary Extract.

No. of mice	Injection materials	Total dosage	Temperature °C	Results		% Positive
				+	-	
29	Progesterone	1.25 mg	25	15	14	51.7
	Estrone	75 I.U.				
15	Progesterone	1.25 mg	35	1	14	6.7
	Estrone	75 I.U.				
15	Pituitary extract	12.5 mg	25	13	2	86.7
	Estrone	75 I.U.				
8	Pituitary extract	12.5 mg	35	7	1	87.5
	Estrone	75 I.U.				
14	Pituitary extract	17.5 mg	25	13	1	92.9
	Estrone	75 I.U.				
8	Pituitary extract	17.5 mg	35	8	0	100.0
	Estrone	75 I.U.				

† Progesterone was kindly supplied by Dr. E. Schwenk, Schering Corporation.

⁴ Gomez, E. T., and Turner, C. W., *Missouri Agr. Exp. Sta. Res. Bul.* 259, 1937.

⁵ Mixner, J. P., Lewis, A. A., and Turner, C. W., *Endocrinology*, 1940, **27**, 888.

⁶ Mixner, J. P., and Turner, C. W., *Endocrinology*, 1941, **29**, 324.

⁷ Bergman, A. J., and Turner, C. W., *J. Biol. Chem.*, 1938, **123**, 474.

animals on both progesterone and the pituitary initial extract died during the assay period. Only surviving animals are included in the data presented in Table I.

At the more normal temperature of 25°C, 1.25 mg of progesterone and 75 i.u. of estrone stimulated lobule-alveolar growth in 51.7% of the animals. This is considered a unit response. On the same level of hormone injection but at 35°C the response dropped to 6.7%, confirming our earlier observations at a high but variable environmental temperature. Thus the high temperature adversely affected the ability of the anterior pituitary to secrete the mammogenic lobule-alveolar growth factor in response to the stimulation of progesterone and estrone. This is in contrast to the results secured with the pituitary initial extract. In this case at the 12.5 mg and the 17.5 mg dosage levels, the percent of positive responses were about equal in both the 25° and 35°C groups, the higher temperature in no way inhibiting the ability of the mammary glands, as end organs, to respond to their direct growth stimulus. The results secured and the suggested explanations fit very well with the pituitary-mammogen theory of mammary gland growth, and these experiments are interpreted as adding further indirect evidence for the validity of this theory.

Summary. Ovariectomized virgin female mice kept at a high environmental temperature (35°C) had a decreased ability to respond to progesterone and estrone injections with mammary lobule-alveolar growth. This same high temperature did not inhibit this response in animals injected with a pituitary extract containing the mammogenic lobule-alveolar growth factor which directly stimulates mammary gland growth. Thus the anterior pituitaries of animals kept at a high environmental temperature have a decreased ability to respond to the stimulus of progesterone plus estrone with the secretion of the mammogenic lobule-alveolar growth factor.