

Obviously, as with growth factors, the effectiveness of various substances on the respiration of yeast will depend upon the strain of yeast, the medium, and the general technique. The present results are of value in checking against the activity of various fractions from yeast and animal tissues which we are assaying by means of the technique used in this paper. Under different conditions certain of the apparently inactive materials may assume importance when they become limiting substances. Suggestions of this are seen in the case of several amino acids and vitamin B<sub>6</sub>.

*Summary.* A number of amino acids, members of the vitamin B complex, and miscellaneous substances have been examined for their effects on the respiration of Fleischmann's bakers' yeast. Most of the substances are inactive or only slightly active, but thiamin, or a mixture of its pyrimidine and thiazole components, and insulin have marked activity.

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#### Quantitative Studies of Cell Types in Rat Hypophysis Following Administration of Antigonadotropic Serum.\*

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Several reports in the literature have shown that treatment of animals with antigonadotropic serum causes a condition in the pituitary gland analogous to that found in castrated animals. Severinghaus and Thompson<sup>1, 2</sup> have described cytological changes in the hypophyses of dogs injected with antihormones. In these animals there was an increase in the basophile cells and a corresponding decrease in the chromophobes which was associated with an atrophy of the gonads, thyroids, and adrenals. Physiological effects have been demonstrated in rats by Meyer and Kupperman<sup>3</sup> who

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<sup>1</sup> Severinghaus, A. E., and Thompson, K. W., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 627.

<sup>2</sup> Severinghaus, A. E., and Thompson, K. W., *Am. J. Path.*, 1939, **15**, 391.

<sup>3</sup> Meyer, R. K., and Kupperman, H. S., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **42**, 285.

found that hypersecretion of the pituitary gonadotropic hormone followed treatment with antigonadotropic serum. This effect was determined by precocious development of the ovaries after discontinuing the injections and by ovarian hypertrophy in female rats in parabiosis with pretreated male or female littermates. The work to be reported here corroborates these findings and describes the changes in the number of cells of each of the types in the pituitary gland of female rats following a short period of antigonadotropic serum treatment.

*Experimental procedure.* Twenty-one female rats were injected subcutaneously from the 10th to the 20th day of life with 0.5 cc per day, or a total dose of 5 cc of antigonadotropic serum obtained from rabbits which had been injected daily with an aqueous extract of whole dried pituitary gland of sheep for a period of 2 months or longer. The serum was shown to be capable of inhibiting the gonadotropic effects of sheep, rat, and human pituitaries, and of pregnant mare serum and prolactin. Three rats were killed on the 1st, 3rd, 5th, 7th, 9th, 12th, and 15th day after discontinuing the treatment. Littermate control rats were autopsied at the same age. Pituitary and ovarian weights with the qualitative ovarian response were noted for both the experimental and control animals. The pituitary glands were serially sectioned at 6 microns after fixation in Bouin's fluid and stained with a modification of Mallory's trichrome stain (Rasmussen<sup>4</sup>). Three horizontal sections from equidistant levels in the gland were studied in each animal. In each of these sections all the cells in every tenth field were differentially counted. An average of 2800 cells was counted in each gland.

*Results and discussion.* The changes in the percentages of cell

TABLE I.  
Ovarian Weights and Percentage of Pituitary Cell Types After Antigonadotropic Treatment.

Group*	Day killed	Avg ovarian wt (mg)	Avg % of pituitary cell types		
			Basophiles	Acidophiles	Chromophobes
1	20	5.0	31.9	17.3	50.8
2	22	7.5	27.4	17.2	53.9
3	24	20.0	20.8	18.0	61.4
4	26	20.0	18.3	18.9	62.8
5	28	20.7	14.8	18.3	66.9
6	31	30.3	12.4	20.3	67.2
7	34	59.7	9.3	19.4	71.3

\*Each group was comprised of 3 rats which were injected from the 10th to the 20th day of life.

<sup>4</sup>Rasmussen, A. T., *Am. J. Anat.*, 1930, **46**, 461.

types in the pituitary gland and the resulting ovarian weights which follow cessation of the antigonadotropic serum treatment are recorded in Table I.

In rats treated for 10 days with antigonadotropic serum and killed on the day following the last injection, the pituitary glands exhibited a picture of extreme basophilism; 31.9% of all the cells were basophiles, in contrast to 5-10% found in normal animals of the same age. The average percentage of chromophobes in these treated animals was 50, showing a definite decrease from the normal level of 70% found in littermate controls. Since no perceptible variation could be detected in the percentage of acidophiles from the normal level during or after treatment, the increase in the number of basophiles appeared to account for the corresponding decrease in chromophobes. The basophilism produced by the injection of antigonadotropic serum appeared to be the same as that found in castrated rats.

Animals killed at later intervals after cessation of treatment showed a progressive decrease in the percentage of basophiles and a proportionate increase in the percentage of chromophobes until about 15 days after the injections were discontinued. At this time the normal ratio of cell types again prevailed, indicating a change of basophiles to chromophobes. Accompanying the decrease in the basophilic elements of the pituitary gland there was a rapid ovarian growth which approached the normal level between the 3rd and 5th days and continued to increase far beyond normal so that by the 15th day after cessation of treatment an average ovarian weight of 59.7 mg had been attained. The average ovarian weight of littermate controls at this age was 17 mg.

*Summary.* Treatment with antigonadotropic serum resulted in extreme basophilism of the hypophysis of young female rats. When the treatment was discontinued the percentage of basophiles gradually returned to normal with a corresponding increase in the percentage of chromophobes, and marked increase in the size of the ovaries over that of littermate controls.