tent was increased to 80%. That the nervous system is not rendered entirely insensitive to convulsive agents by the low O_2, high CO_2 atmospheres is indicated by the fact that we were able to induce typical metrazol convulsions within the usual time under these conditions.

It may be concluded tentatively from the foregoing experiments that marked lowering of the O_2 content or marked increase in the CO_2 content of the respired air tends to inhibit rather than to accelerate insulin convulsions in the normal, fasting dog under the conditions described. While severe hypoglycemia appears to be the most important known causative factor, these experiments indicate that some additional physiological disturbance is involved in the mechanism of insulin convulsions.

10260 P

Inhibition of Growth of Rat by Oral Administration of Methylcholanthrene. Effects of Dietary Cystine and Methionine Supplements.*

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In the present communication it is desired to report preliminary results obtained in studies of the effects of certain carcinogenic substances on sulfur metabolism. The experimental approach employed in the first series of investigations is similar to that which has resulted in the demonstration that bromobenzene,[1] cholic acid,[2] naphthalene,[3] and iodoacetic acid[4] exert an inhibiting effect on the growth of the young white rat when any one of these compounds is incorporated into a basal diet of relatively low protein content. The addition of either l-cystine or dl-methionine to the basal diet containing either bromobenzene, cholic acid, naphthalene, or iodoacetic acid resulted in a prompt stimulation of growth, despite the continued presence of the foreign organic compound in the diet. It was sug-

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1 White, A., and Jackson, R. W., *J. Biol. Chem.*, 1935, **111**, 507.

2 White, A., *J. Biol. Chem.*, 1935, **112**, 503.

3 Stekol, J. A., *J. Biol. Chem.*, 1937, **121**, 87.

4 Simon, E. E., and White, A., *J. Biol. Chem.*, 1938, **123**, cix.

gested that these organic substances are capable of producing a specific deficiency in the sulfur-containing amino acids, probably through the requirements of the organism for organic sulfur, in the form of cystine or methionine, for detoxication mechanisms. This conclusion is supported by the observation that inorganic sulfate, amino acid nitrogen in the form of a casein digest, and organic sulfur in the form of that found in taurine will not stimulate the growth of animals stunted by the administration of either bromobenzene, cholic acid or iodoacetic acid.

In the present studies, male rats at weaning have been placed on a basal diet of the following composition: casein† 6, starch 50, lard 24, sucrose 15, cod liver oil 1, and inorganic salts‡ 4%. In addition, each animal received a daily supplement of 400 mg of yeast.§ When the rats reached a body weight of 75 to 85 g, methylcholanthrene‖ was incorporated into the basal diet. After a number of preliminary

TABLE I.
The Effect of Methylcholanthrene-containing Diets on the Growth of the Rat.

Rat No.	Diet	Avg daily wt change, g	Avg daily food consumption, g
2	Basal	+1.6	4.8
	" + methylcholanthrene*	+0.5	5.5
	" + " + methionine	+1.4	5.8
5	"	+1.4	6.1
	" + methylcholanthrene	+0.6	5.9
	" + " + glycine	+0.5	6.2
7	"	+1.8	6.4
	" + methylcholanthrene	+0.6	6.4
	" + " + sodium sulfate	+0.8	7.3
8	"	+1.8	6.8
	" + methylcholanthrene	+0.3	6.0
	" + " + taurine	+0.5	5.9
11	"	+1.5	5.5
	" + methylcholanthrene	+0.4	6.1
	" + " + cystine	+1.5	5.8

*All of the methylcholanthrene-containing diets in this table had 60 mg of the hydrocarbon added for each 100 g of the basal ration. In experiments now being conducted, it has been observed that increasing the methylcholanthrene concentration to 70 mg per each 100 g of the basal diet results in an average daily growth increment of approximately 0.1 g. The effects of methionine or cystine supplements can thus be made even more striking.

† Casein No. 453, Casein Company of America, Inc.

‡ Osborne and Mendel salt mixture (Osborne, T. B., and Mendel, L. B., *J. Biol. Chem.*, 1919, **37**, 572).

§ Product of the Northwestern Yeast Company.

‖ Purchased from the Eastman Kodak Company.

trials, it was observed that when 60 mg of methylcholanthrene were incorporated into each 100 g of the basal diet, growth is inhibited. Although the rats do continue to grow, the rate of weight increase is markedly less than that observed in control animals ingesting the basal ration alone.

The incorporation of l-cystine (400 mg) or dl-methionine (500 mg) into each 100 g of the basal diet containing the methylcholanthrene results in a prompt stimulation of growth, with a resulting daily weight increment approximating that observed on the basal diet alone. On the other hand, supplements of glycine (500 mg), taurine (500 mg), or anhydrous sodium sulfate (500 mg), each added to 100 g of the basal diet containing methylcholanthrene, produced no increase in growth rate. Some typical data are presented in Table I. It appears, therefore, that cystine and methionine exhibit a specific ability to overcome the growth-inhibitory effect of methylcholanthrene. These results suggest that methylcholanthrene may produce a deficiency in the sulfur-containing amino acids, possibly by virtue of the involvement of these amino acids in the detoxication of the hydrocarbon. The metabolic fate of methylcholanthrene is being studied in order to obtain further evidence bearing on this suggestion, and similar methods are being extended to other carcinogenic substances.

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"Acid" Phosphatase and Functional Activity of the Prostate (Man) and Preputial Glands (Rat).

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While investigating the source of marked outpourings of "acid" phosphatase in the urine of adult men, Kutscher and Wolbergs[1] discovered that normal adult prostate tissue is extremely rich in a phosphatase, apparently specific,[2] with optimal activity at approximately pH 5.0. At about the same time, Moore and Hanzel[3] noted that prostate tissue extracts split off inorganic phosphorus from sodium nucleinate, a "nuclease" effect attributable to nucleotidases, which

1 Kutscher, W., and Wolbergs, H., *Z. f. physiol. Chem.*, 1935, **236**, 237.

2 Kutscher, W., and Wörner, A., *Z. f. physiol. Chem.*, 1936, **239**, 109.

3 Moore, R. A., and Hanzel, R. F., *Arch. Path.*, 1936, **22**, 41.