11202 P

Evidence for the Detoxication of Diphenyl Through a Sulfur Mechanism.

HAROLD D. WEST. (Introduced by E. L. Turner.)

From the Department of Biochemistry, Meharry Medical College, Nashville, Tennessee.

Naphthalene[1, 2] and anthracene[3] as well as monohalogenated benzenes[4, 5] fed to animals are converted in part to mercapturic acids. Increased neutral sulfur excretion following the administration of benzene[6, 7] and phenanthrene[7] seems to indicate that these hydrocarbons are similarly detoxicated. Growth of rats fed a casein-low ration is inhibited by incorporation in the diet of bromobenzene,[5] naphthalene,[8] phenanthrene,[9] certain complex hydrocarbons—both carcinogenic and non-carcinogenic,[10] or other substances.[11, 12] This deficiency may be relieved by simultaneous administration of dl-methionine or of l-cystine and certain of its derivatives. Presumably hydrocarbons produce a deficiency in the sulfur-containing amino acids available to the organism, because of the preferential utilization of these acids for detoxication reactions. Thus added evidence is available for mercapturic acid formation by phenanthrene and certain of the more complex hydrocarbons.

The chemical relationship of diphenyl to bromobenzene, and to naphthalene, anthracene, and other aromatic hydrocarbons previously studied suggests the possibility that this substance may be handled similarly by the animal organism. Preliminary results from growth experiments obtained in a study of the fate of this hydrocarbon are now being reported.

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Albino rats were used in the experiments. The basal diet (Diet 1-A) was similar to that used by White and Jackson[5] except that dextrin and a small amount of agar agar were used in place of the starch. It contained casein, 6%; salt mixture,[13] 4; sucrose, 15; dextrin, 48; agar agar, 2; lard, 22; and cod liver oil, 3. When a diet was supplemented, the dextrin was reduced by the amount of the supplement. Diet 1-D contained 1% of diphenyl. Diets 1-D-C, 1-D-M, 1-D-T, and 1-D-S contained, in addition to 1% of diphenyl, 0.120% of l-cystine, 0.150% of dl-methionine, 0.250% of taurine and 0.750% of sodium sulfate (anhydrous) respectively. Vitamin B factors were furnished in the form of pills given once daily to each rat. Each pill contained 0.4 g of brewers' yeast powder and a small amount of dextrin. Water and food were given *ad libitum*.

Results of the experiments are given in Table I. In each case complete failure of growth invariably ensued immediately when a diet was supplemented either with diphenyl alone or together with

TABLE I.*

Inhibition of growth of young rats† by diphenyl on diets low in casein and the subsequent effects of supplementation with l-cystine, dl-methionine, taurine, or sodium sulfate.

Sex	Rat No.	Days	Diet	Total change in wt	Daily food consumption	Wt at beginning of each period
♂	11	36	1-A	18.2	4.7	67.1
		32	1-D	—11.9	3.9	85.3
♂	8	16	1-A	15.4	5.5	64.5
		24	1-D	—12.0	3.4	79.9
		32	1-D-C	9.2	5.0	67.9
♂	10	16	1-A	7.3	4.1	60.1
		24	1-D	— 7.5	3.5	67.4
		32	1-D-M	6.2	3.8	59.9
♀	14	16	1-A	4.1	4.4	63.5
		44	1-D	— 6.5	3.1	67.6
		8	1-D-T	— 2.3	3.3	61.1
♀	15	16	1-A	6.3	5.8	68.7
		44	1-D	— 8.8	3.7	75.0
		8	1-D-S	— 0.4	4.0	66.2

* The data for rat 11 is typical of results with 3 animals; for rat 8, 4 animals; for rat 10, 5 animals; for rat 14, 3 animals; and for rat 15, 3 animals.

† Histological examination of livers and kidneys of 2 animals which had received Diet 1-D for several weeks was carried out by Dr. J. R. Cuff of the Department of Pathology, who is due our thanks. Beginning fatty change was observed in the livers and mild toxic (tubular) change was seen in the kidney sections.

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taurine or sodium sulfate. When diets containing diphenyl were supplemented with l-cystine or dl-methionine, however, the deficiency imposed by the diphenyl was promptly removed and growth was resumed. The results indicate that diphenyl is handled in the organism of the rat by some mechanism which involves the sulfur of sulfur-containing amino acids ordinarily available for growth.

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Prolonged Maintenance of a Mammary Carcinoma in Vitamin E-Deficient Rats.*

W. LAMAR BRYAN AND KARL E. MASON.

From the Department of Anatomy, Vanderbilt University School of Medicine, Nashville, Tenn.

Observations concerning a possible relationship between vitamin E and the incidence and growth of neoplasms are fragmentary, and are characterized by wide differences in the type of animal, neoplasm, and experimental method used. Adamstone[1] has described the occurrence of a transplantable lymphoblastoma in young chicks fed a mixed diet treated with ferric chloride in ether to destroy vitamin E. It may be noted, however, that the domestic fowl is prone to spontaneous manifestation of leucemic disease. Furthermore, our own experiences in experiments with rats indicate that ferric chloride treatment of mixed diets does not consistently destroy all traces of vitamin E present, especially when the fat content of the diet is low. The experiments of Davidson[2, 3] suggest that an excess of vitamins, especially liberal additions of vitamin E, decreases the incidence of tar carcinoma in mice. However, in repeating these studies Cameron and Meltzer[4, 5] observed only a delay in the appearance of the growth, which they attributed to the larger size and increased resistance of the vitamin-fed animals rather than to a specific vitamin effect. These

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