

Despite the difference in formazan patterns the total amount of reduced TTC per mg of kidney tissue is approximately the same in normal and hypertensive kidneys, as is the oxygen consumption determined by the conventional micro-respiration technic. Concurrent studies of VEM metabolism show the uniform restriction of VEM production to anaerobiosis in normal kidneys, and the formation of VEM under both anaerobic and aerobic conditions by the hypertensive kidneys of animal and human subjects. When the VEM metabolism of a kidney from a normotensive rat, dog or human is transformed to the hypertensive type by a period of prior anaerobiosis *in vitro*, there is a parallel development of the characteristic hypertensive formazan pattern in the proximal convoluted tubules.

The reduction of TTC to the insoluble formazan results from an interaction between

TTC and enzyme systems within the cell. The observations reported would indicate some alteration in the metabolic characteristics of the proximal convoluted tubules in experimental renal and essential hypertension. The association of these histochemical changes in the proximal convoluted tubules with alterations of the VEM mechanisms in experimental and human hypertension suggests, 1) that the proximal tubules may be the site of VEM formation, and 2) that the failure of the hypertensive kidney to limit VEM formation to anaerobiosis may be related to the enzymatic disorganization revealed by TTC.

Finally, the data presented provide specific evidence for a similarity between experimental renal hypertension and essential hypertension in man.

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Procarcinogenic Effect of Vitamin B₁₂ on p-Dimethylaminoazobenzene-Fed Rats.* (18067)

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Diet is known to influence the carcinogenicity of p-dimethylaminoazobenzene (DAB). Riboflavin has been shown to exert a protective effect(1) while it has been reported that biotin is procarcinogenic(2). The experiments to be reported in this paper indicate that vitamin B₁₂ exerts a marked procarcinogenic effect on DAB-fed rats.

Experimental. Weanling female Sprague-Dawley rats were fed a purified diet consist-

ing of the following: isolated soybean protein,[†] 18 g; sucrose, 67.4 g; hydrogenated vegetable oil, 8 g; cod liver oil, 2 g; salt mixture(3), 4 g; choline chloride, 0.1 g; inositol, 10 mg; thiamine chloride, 1.5 mg; riboflavin, 0.5 mg; nicotinamide, 2 mg; calcium pantothenate, 1.0 mg; pyridoxine hydrochloride, 0.5 mg; vitamin K, 0.025 mg; biotin, 0.005 mg; folic acid, 0.5 mg; and p-dimethylaminoazobenzene, 70 mg. This diet contains approximately 0.27% methionine. One group of rats received this diet unsupplemented, one group received this diet plus 5 micrograms of vitamin B₁₂ (Rubramin) per 100 g, a third group received this diet plus 0.6% DL-methionine, and a fourth group received the

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[†] "Alpha Protein," obtained from the Glidden Company, Chicago.

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TABLE I.
Influence of Vitamin B₁₂ and Methionine on Incidence of Hepatomas in p-Dimethylaminoazobenzene-Fed Rats.

Supplement to diet	Avg daily food intake, g	Avg daily wt gain, g	Incidence of hepatomas, %	Liver wt*—% of body wt
None	6.4	0.1	17	9.3
Vitamin B ₁₂	7.0	0.2	78	15.7
Methionine	8.1	1.2	11	7.0
Methionine + vit. B ₁₂	10.5	1.2	33	11.0

* Liver weights include tumors, where present.

diet supplemented with both vitamin B₁₂ and methionine. The rats were fed these diets for 170 days and were then killed and autopsied. The incidence of gross hepatomas was recorded. There were 9 rats in each group. Three rats in the unsupplemented group died without hepatomas during the experimental period. Two rats receiving vitamin B₁₂, one rat receiving methionine, and one rat receiving vitamin B₁₂ plus methionine died with hepatomas during the experimental period. The incidence of hepatomas is based on those rats either surviving the 170-day period or dying with hepatomas.

Results and discussion. The pertinent data are presented in Table I. The addition of vitamin B₁₂ to the DAB-containing, methionine-deficient diet increased the incidence of hepatomas from 17% to 78%. The addition of vitamin B₁₂ to the methionine-containing diet increased the incidence of hepatomas only from 11% to 33%; thus methionine appeared to afford some protection.

The procarcinogenic effect of vitamin B₁₂ may indicate that this vitamin is required for

tumor growth or it may be a reflection of an influence of vitamin B₁₂ on metabolic transformations of the carcinogen p-dimethylaminoazobenzene. In the former event these results might have general application to the entire field of cancer. Experiments are in progress to elucidate the mechanism of the procarcinogenic effect of vitamin B₁₂.

It would be unfortunate if the conclusion were drawn from these experiments that vitamin B₁₂ itself is carcinogenic. There is no evidence that such is the case. On the contrary, a control group of rats receiving the soybean protein diet with vitamin B₁₂, but without p-dimethylaminoazobenzene, showed no hepatic tumors.

Summary. Vitamin B₁₂ has been found to enhance markedly the carcinogenic effect of p-dimethylaminoazobenzene in rats receiving a methionine-deficient diet. However, a control group of rats receiving this diet without p-dimethylaminoazobenzene showed no hepatic tumors.

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Life Maintaining Activity of Δ^1 Desoxycorticosterone Acetate.* (18068)

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Life maintaining activity in adrenalectomized rats has been obtained with Δ^1 allo-pregnen-21-ol-3, 20-dione 21 acetate for which

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the trivial name Δ^1 desoxycorticosterone acetate was suggested(1). This steroid has been compared with desoxycorticosterone acetate (Percorten, Ciba) for life maintaining

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