trolled by the drug relapsed when a placebo was substituted, but immediately regained their normal health after Dramamine was again administered. Twelve patients (27.8%) of the 43 obtained no relief from the drug.

In summary, although the number of patients treated with Dramamine is small, the results are so encouraging that the Allergy Clinic and the Obstetrical Clinic of the Johns Hopkins Hospital and University are making an extensive comparative study. These data will be published in a subsequent report.

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Plasma and Liver Protein Levels in Rats Fed the Carcinogen 2-Acetylaminofluorene[1]

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Cook, Griffin, and Luck (*1*) have recently reported that azo dyes decrease plasma albumin and increase gamma globulin in rats. In addition, the carcinogenic activity of the drug can be correlated with the degree of change induced in these plasma components. The non-azo dye, though its carcinogenic action is well known. Whether or not the drug would alter plasma protein levels when fed at different concentrations and for a longer time was considered of interest in elucidating this drug's actions.

The azo dyes induce liver tumors and have a definite effect on nucleic acid content of this organ (*2, 3, 6, 7*). The non-azo dye 2AAF also causes formation of liver tumors and increases liver weight (*8*). We have extended these data to include estimations of liver water and protein in an effort to correlate the liver and plasma proteins, since the liver is a source of plasma albumin.

Forty-day-old female rats were maintained on Purina fox chow to which 0.03% or 0.15% of 2-acetylaminofluorene was added. The diets were fed ad lib. for 100 days, after which time the rats were bled by cardiac puncture under light ether anesthesia and the plasma was analyzed for nonprotein nitrogen, total plasma protein, and albumin and globulin concentrations by salt fractionation methods previously reported (*5*). The liver was dried to constant weight, ground to uniform consistency, and analyzed for total nitrogen. The nitrogen values were converted to protein by use of the factor 6.25.

Body weight increase was recorded at weekly intervals and the control rats increased from 100 to 237 g in 100 days. Body weight increase of rats fed 0.03% of 2AAF followed the controls for 11 weeks, starting at 102 g and increasing to 202 g, and then leveled off. The incorporation of 0.15% 2AAF in the diet resulted in an average body weight change from 90 to 164 g. These rats' weight at 6 weeks was constant for a 2-week period, then it increased slowly for 4 weeks but leveled off again. The results simulate those reported by Wilson *et al.* (*9*).

TABLE 1

PLASMA PROTEIN CONCENTRATIONS OF FEMALE RATS FED 2-ACETYLAMINOFLUORENE FOR 100 DAYS

Diet	No. of rats	Hematocrit %	NPN in mg%	Plasma proteins in g%*		
				total	albumin	globulin
Fox chow	6	40.4 ± 1.2	50 ± 3.0	4.99 ± 0.11	2.42 ± 0.06	2.57 ± 0.11
Fox chow + 0.03% drug	6	42.4 ± 1.2	51 ± 2.4	5.06 ± 0.14	2.52 ± 0.07	2.54 ± 0.18
Fox chow + 0.15% drug	5	40.4 ± 1.1	47 ± 2.0	4.64 ± 0.09	1.99 ± 0.13	2.65 ± 0.13

* $\varepsilon = \sqrt{\frac{\Sigma d^2}{N(N-1)}}$

TABLE 2

LIVER PROTEIN OF FEMALE RATS FED 2-ACETYLAMINOFLUORENE FOR 100 DAYS

Diet	No. of rats	Wt in g	H_2O %	Liver protein*		
				Dry wt %	Total g	Total g/100g BW
Fox chow	6	7.77 ± 0.4	70.1 ± 1.2	65.4 ± 0.8	1.43 ± 0.2	0.629 ± 0.015 (0.589 – 0.696)
Fox chow + 0.03% drug	7	8.08 ± 0.3	70.3 ± 0.3	60.8 ± 1.0	1.44 ± 0.04	0.710 ± 0.015 (0.665 – 0.791)
Fox chow + 0.15% drug	7	7.39 ± 0.4	70.3 ± 0.2	61.1 ± 1.9	1.36 ± 0.05	0.852 ± 0.024 (0.755 – 0.939)

* $\varepsilon = \sqrt{\frac{\Sigma d^2}{N(N-1)}}$

Table 1 shows the hematocrit, plasma nonprotein nitrogen, and plasma protein concentrations. Plasma albumin concentration was significantly subnormal in rats fed 0.015% of 2AAF, but other analyses were unchanged.

To determine whether liver size or protein content was

2-acetylaminofluorene (2AAF), however, failed to alter plasma protein levels after a 6-week feeding period, al-

[1] Supported in part under a grant-in-aid from the American Cancer Society upon recommendation of the Committee on Growth of the National Research Council.

altered in rats exhibiting subnormal plasma albumin levels, these organs were analyzed for total protein, and the data are presented in Table 2. It is apparent that liver size and water content were unchanged by the drug, and despite a slight decrease in percentage of protein the total protein content of the liver was normal. Since the animals fed the drug lagged in growth rate the liver protein in relation to body weight was significantly increased and in proportion to the amount of drug fed. This is interesting, in that the slower growth rate with reduced food intake would seem more likely to be associated with a smaller liver. Reduction of food intake will rapidly decrease liver size and protein level (*4*). 2-Acetylaminofluorene can therefore significantly increase liver protein to body weight ratios without altering plasma protein concentrations, but a decrease in plasma albumin can be induced if drug concentration is high.

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Correlation of Browning, Fluorescence, and Amino Nitrogen Change with Destruction of Methionine by Autoclaving with Glucose[1]

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The destruction of lysine by autoclaving in the presence of glucose was demonstrated by Stevens and McGinnis (*8*). These workers observed that the autoclaved mixture of glucose and lysine was dark brown in color. Patton and Hill (*6*) reported that tryptophane, in a bacteriological culture medium containing glucose, was destroyed to a certain extent by autoclaving. This destruction was not observed when sucrose was substituted as a source of carbohydrate. Hsu, McGinnis, and Graham (*4*) found that methionine was destroyed or rendered unavailable to chicks by autoclaving in the presence of either glucose or lactose, and to a certain extent in the presence of sucrose. In contrast, methionine was unaffected by heating in the presence of starch or dextrin. Acid hydrolysis of the autoclaved mixture of glucose and methionine failed to liberate the amino acid for support of chick growth. They also found that autoclaving a soybean protein with glucose damaged the protein to the extent that supplementary methionine, lysine, and tryptophane failed to restore its nutritive value for chicks. These observations indicate that other amino acids, in addition to the three named, were destroyed or rendered unavailable. Evans and McGinnis (*2*) showed that cystine in soybean oil meal was destroyed during autoclaving. In contrast, the same autoclaving treatment failed to alter the methionine content. Patton, Hill, and Foreman (*7*) reported that lysine, arginine, tryptophane, and histidine were destroyed when an intact soybean protein was refluxed in a 5% glucose solution for 24 hr. In view of the results reported by Hsu, Graham, and McGinnis (*5*) showing that the concentration of amino acids or crude protein in an aqueous solution of glucose markedly influenced the amount of browning and destruction of amino acids, it should be pointed out that the concentration of protein used by Patton, Hill, and Foreman (*7*) was only 1%.

Chen, Medler, and Harte (*1*) found that highly fluorescent substances were formed from certain amino acids when they were heated with Denigès reagent (paraformaldehyde and sulfuric acid). A similar observation

TABLE 1

Correlation of Browning, Fluorescence, and Amino Nitrogen Change with Destruction of Methionine by Autoclaving with Glucose

Methionine mg/culture	Dry wt of mold in mg			Brown color: optical density at 380 mμ (×100)	Fluorescence equivalents: mg quinine sulfate/g methionine	α-Amino nitrogen: % of theoretical value
0.1*	11.1	11.1	11.1§	0	0	102.2
0.2	18.5	18.5	18.5			
0.4	32.0	34.4	33.2			
0.6	55.2	53.2	54.2			
0.8	64.9	61.9	63.4			
1.0	69.7	68.9	69.3			
0.1†	11.4	11.2	11.3	5.6	.965	93.7
0.2	18.3	18.3	18.3			
0.4	31.8	34.9	33.4			
0.6	50.2	52.4	51.3			
0.8	58.9	62.9	60.9			
1.0	67.0	63.1	65.1			
0.1‡	..	3.5	3.5	180	14.25	15.1
0.2	3.8	3.8	3.8			
0.4	5.8	5.8	5.8			
0.6	6.7	6.2	6.5			
0.8	8.2	8.2	8.2			
1.0	9.5	9.6	9.6			

* Methionine autoclaved alone for 2 hr at 120° C.

† Methionine (2 g) dissolved in 100 ml of 8% glucose solution and autoclaved 2 hr at 120° C.

‡ Methionine (2 g) mixed with glucose (8 g) and autoclaved 2 hr at 120° C.

§ Average of duplicates.

[1] Published as Scientific Paper No. 829, Washington Agricultural Experiment Station, Institute of Agricultural Sciences, State College of Washington, Pullman.

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