

in the production of tumours, compared with a full diet. However, sixteen similar rats have been fed on this modified diet, supplemented with *p*-aminoazobenzene (at first 300 mgm. per 100 gm. diet, and, later, 200 mgm. per 100 gm. diet), for more than eighteen months, so far. Of eight rats now dead, one (dying at thirteen months) had a few whitish spots visible to the naked eye, in the liver, and these proved on microscopic examination by Dr. P. R. Peacock to be small hepatomas. Two other rats died at seventeen months, both having very large tumours in one lobe and smaller tumours in the other lobes of the liver; in one case, the liver weight (including tumours) was 47.8 gm. These tumours were liver-cell carcinomas which were metastasizing via blood-vessels to the mesentery. It is hoped to publish, in conjunction with Dr. P. R. Peacock, a full account of the pathology of these lesions elsewhere; but it may now be said that *p*-aminoazobenzene is carcinogenic for rats fed the dye in a somewhat restricted diet for a long time.

This finding is in accordance with the results obtained by Kensler *et al.*<sup>5,6</sup> and Potter<sup>8</sup>, who found various enzyme systems to be inhibited by the *p*-diamines which are liberated from butter-yellow and related azo-dyes when the azo-link is reduced. Thus *N,N*-dimethyl-*p*-phenylenediamine caused 64 per cent inhibition of urease at a molarity of  $1 \times 10^{-3}$ . *p*-Phenylenediamine at the same concentration caused 45 per cent inhibition<sup>9</sup>. Similarly, in the cases of succinoxidase, yeast carboxylase and coenzyme-I, *p*-phenylenediamine caused a significant degree of inhibition. If this effect on enzymes plays a part in the process of liver carcinogenesis, then it would be reasonable to expect that aminoazobenzene would be carcinogenic, though less so than the fully methylated compound. This is what we have found to be the case. It is, moreover, clear that the butter-yellow split-product must have its effect prior to the demethylation process, that is, reduction of the azo-link must precede demethylation; otherwise the two dyes would eventually yield the same split-product, *p*-phenylenediamine, and have the same degree of carcinogenic power.

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<sup>1</sup> Kinoshita, *Trans. Jap. Path. Soc.*, **27**, 665 (1937).

<sup>2</sup> Stevenson, Dobriner and Rhoads, *Cancer Res.*, **2**, 160 (1942).

<sup>3</sup> Hashimoto, *Gann.*, **29**, 306 (1935).

<sup>4</sup> Jacobi and Baumann, *Cancer Res.*, **2**, 175 (1942).

<sup>5</sup> Kensler, Dexter and Rhoads, *Cancer Res.*, **2**, 1 (1942).

<sup>6</sup> Law, *Cancer Res.*, **1**, 397 (1941).

<sup>7</sup> Miller, Miner, Rusch and Baumann, *Cancer Res.*, **1**, 699 (1941).

<sup>8</sup> Kensler, Young and Rhoads, *J. Biol. Chem.*, **143**, 465 (1942).

<sup>9</sup> Potter, *Cancer Res.*, **2**, 688 (1942).

### Taste of Thiouracil and Phenylthiocarbamide

TWELVE years ago, Fox<sup>1</sup> discovered a curious property of phenylthiocarbamide. He was putting some of the substance into a bottle when a colleague complained of the extremely bitter taste, which Fox himself was unable to confirm. The question was investigated by Blakeslee<sup>2</sup>, who found that a sample of the American population contained 40 per cent of individuals who were non-tasters. Furthermore, it was found that if two non-tasters married, their

children were also non-tasters. The ability to taste (*T*) is dominant to non-tasting (*t*), so that parents having the constitution *Tt* may have non-tasting children; but if one of them is homozygous, *TT*, then all the children will be tasters of phenylthiocarbamide. The test has been used as a genetic marker in the investigation of human pedigrees<sup>3,4,5</sup>.

As the chemical constitution of thiouracil and phenylthiocarbamide indicate a common origin, it was considered desirable to investigate the taste of the former. Sixty volunteers submitted to the tests. Approximately one half of a 0.2 gm. tablet of thiouracil was chewed, and the subject was asked to state what taste it had. The responses varied from intensely bitter to a chalky taste, but there was no difficulty in identifying the tasters from the non-tasters. A solution of phenylthiocarbamide was prepared containing 0.005 per cent, and the subjects were given a teaspoonful each. This solution divided the group into two, tasters and non-tasters, in the same manner as the thiouracil, with one exception. This was a male who considered that thiouracil was intensely bitter, but was unable to taste 0.005 per cent phenylthiocarbamide although a 0.01 per cent solution was tasted. He was considered to be a taster.

	Tasters	Non-tasters	Total
Males	23	10	33
Females	20	7	27
Total	43	17	60

The proportion of tasters to non-tasters is shown in the accompanying table. The numbers were too small to establish the excess of non-tasting males which is known to occur. The material included a female taster who had a non-tasting husband. They have two children, a non-tasting boy and a tasting girl. It follows that the woman is probably heterozygous (*Tt*) for the factor concerned in controlling the taste of both thiouracil and phenylthiocarbamide. Two identical twins were both tasters.

It would appear that the ability to taste thiouracil is inherited in the same manner as that of phenylthiocarbamide. A few subjects taking thiouracil therapeutically showed nothing to suggest that their response differed in any way from the majority. So far as our knowledge goes, this peculiar property has only genetic significance.

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<sup>1</sup> Fox, A. L., *Proc. U.S. Nat. Acad. Sci.*, **18**, 115 (1932).

<sup>2</sup> Blakeslee, A. F., *Proc. U.S. Nat. Acad. Sci.*, **18**, 120 (1932).

<sup>3</sup> Boyd, W. C., and Boyd, L. G., *Ann. Eugenics*, **8**, 46 (1937).

<sup>4</sup> Riddell, W. J. B., *Trans. Ophth. Soc.*, **69**, 275 (1939).

<sup>5</sup> Riddell, W. J. B., *Ann. Eugenics*, **10**, 1 (1940).

### Apparent Vitamin C as a Possible Precursor of True Vitamin C in Walnuts

UNRIPE walnuts have previously been reported<sup>1,2</sup> to contain considerable amounts of apparent vitamin C, the provisional term suggested<sup>3</sup> for substances which so closely resemble true vitamin C in chemical and physical properties that they may be confused with the latter when it is being estimated by the usual dye titration method, though they may be distinguished from it by modifications<sup>4,5</sup> of Lugg's