

PTC Taste Sensitivity and Endemic Goiter in Brazil

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HARRIS, Kalmus, and Trotter (1949) and Kitchin et al. (1959) showed that homozygotes for the recessive gene governing inability to taste phenylthio-carbamide (PTC) are more susceptible than tasters to nonendemic nodular goiter. The results for toxic diffuse goiter were contradictory, the first study showing no association while the second gave a significant excess of tasters. Memoria (1959) found no relation between juvenile endemic diffuse goiter and PTC sensitivity in Brazil, while Brand (1963) encountered in Israel a strong association of endemic nodular goiter with nontasters. Failure to observe an association of nontaster status with nodular goiter was reported from Japan by Hollingsworth (1963), who used paper strips impregnated with PTC. This investigator obtained a frequency of nontasters twice as high as other studies of the Japanese (Beiguelman, 1962), which is consistent with the general experience that PTC impregnated paper will give false negative results.

MATERIAL AND METHODS

We have recently completed observations at the Hospedaria de Imigrantes in São Paulo on more than 1,000 families migrating from northeastern Brazil, mostly from the interior of the states of Bahia and Minas Gerais (Morton, 1964). Both diffuse and nodular goiter are endemic in this region. In the course of the study, 4,177 persons age nine years or more submitted to a medical examination in which a nurse determined PTC sensitivity and a physician (E. A.) then inspected and palpated the thyroid and looked for physical signs of thyrotoxicosis. The PTC test was a modification by Dr. Walter E. Nance of the sorting technique of Harris and Kalmus (1949) in which solutions 8 to 2 were administered as jets from polyethylene wash bottles. (Dr. Donald Merritt has recently suggested a further modification which eliminates the taste of polyethylene by enclosing the test solution in a cellophane bag within the wash bottle.) To be scored as tasters of a particular dilution, subjects were required to discriminate eight samples, four with the given concentration and four with water. Boiled tap water was used as the diluent and the control and to rinse the mouth before each sample was tasted. Subjects were classified as nontasters if they could not discriminate the supra-

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antimodal solution 5, which contains 81.25 mg PTC/liter. Children age eight years or less could not be classified because of multiple sorting errors; among those classified, the frequency of nontasters was significantly higher than among older persons. Accordingly, we have excluded children age eight years or less from consideration. Shepard and Gartler (1960) and Fraser (1961) have reported an excess of nontasters among athyrotic cretins, but our experience suggests that any mentally retarded group would behave as young children in giving a high frequency of nontasters among classifiable subjects.

The frequency of nontasters was 14.4%, indicating a gene frequency of $t = \sqrt{.144} = .379$. This agrees well with Saldanha's (1962) estimate that the population is a nearly equal mixture of Portuguese, with gene frequency $t = .506$, and Negroes and Indians, with $t = .207$. There were 46 cases of nodular goiter (1.1%) and 143 cases of diffuse goiter (3.4%), all but one nontoxic. The data were analysed at the Computing Center of the University of Hawaii by a general multiple regression program (MULREG) for the IBM 7040.

RESULTS

Pooling the diffuse and nodular types, the frequency of goiter rose with age, was higher in females than males, and increased from the northeast coast southwesterly to Minas Gerais. There was no significant association with social level, literacy, inbreeding, race, or taster status. The pooled data of Harris, Kalmus, and Trotter (1949) and Kitchin *et al.* (1959) on nonendemic goiter also show no significant association with taste sensitivity, since there were 30.6% nontasters in 806 controls and 32.7% in 783 cases of goiter ($\chi^2 = .77$).

Nontaster status is significantly associated with nodular goiter ($\chi^2_{[1]} = 4.83$, $P < .04$), and even the interaction of this effect with age, sex, and longitude is significant ($\chi^2_{[8]} = 19.92$, $P < .001$), nodular goiter being more dependent on age, sex, and longitude in nontasters than in tasters. These associations remain significant when the residual variance among families is used as error ($\chi^2_{[4]} = 18.74$, $P < .001$). There is no effect of nodular goiter on taste threshold within the taster group, either in the pooled data (Table 1) or by multiple regression with age, sex, and other factors held constant. Therefore the inability to taste PTC is not an effect of nodular goiter.

Diffuse goiter is not significantly related to taster status. However, the interactions between PTC response and age, sex, and longitude are opposite in sign and significantly different in nodular and diffuse goiter ($\chi^2_{[8]} = 8.74$, $P < .04$), suggesting that the effect of taster status is reversed in the two forms (Table 2).

The mechanism for the susceptibility of nontasters to nodular goiter, both endemic and nonendemic, has not been demonstrated. Since the total frequency of goiter is not significantly greater in nontasters, it seems unlikely that taster status affects directly the efficiency of iodine uptake or binding. Apparently iodine deficiency and other factors, perhaps including goitrogens related to PTC in cruciferous plants (Clements, 1960), tend to produce cyclic

TABLE 1. TASTE TESTING THRESHOLD FOR GOITER AND NORMALS,
EXCLUDING CHILDREN AGE EIGHT YEARS OR LESS

	Nontasters			Tasters			Total	Per cent nontasters
	<3	3	4	5	6	≥7		
Nodular goiter	12	-	-	-	2	32	46	26.1
Diffuse goiter	14	6	1	4	8	110	143	14.7
Normals	406	103	57	75	127	3220	3988	14.2

Nodular goiter vs. others: $\chi^2_{[1]} = 5.22$ $P < .03$

TABLE 2. PARTIAL REGRESSION COEFFICIENTS

Nodular, diffuse: affected = 1, normal = 0

PTC: taster = 1, nontaster = 0

Sex: male = 1, female = -1

	Nodular	Diffuse
PTC	.1822**	-.1487
Age	.0016***	-.0002
Sex	-.0153***	-.0134
Longitude	.0061***	.0052
PTC × Sex	.0095*	-.0035
PTC × Age	-.0011**	.0001
PTC × Longitude	-.0041*	.0037

* $P < .05$; ** $P < .01$; *** $P < .001$.

thyroid hyperplasia leading to nodular goiter in nontasters but a more uniform and persistently diffuse hyperplasia in tasters.

SUMMARY

In the endemic area of Brazil, nodular goiter is significantly elevated in nontasters of phenylthiocarbamide (PTC). The data suggest that the risk for first-stage diffuse goiter is little affected by taster status but that goiter in a nontaster is more likely to evolve into the nodular form.

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