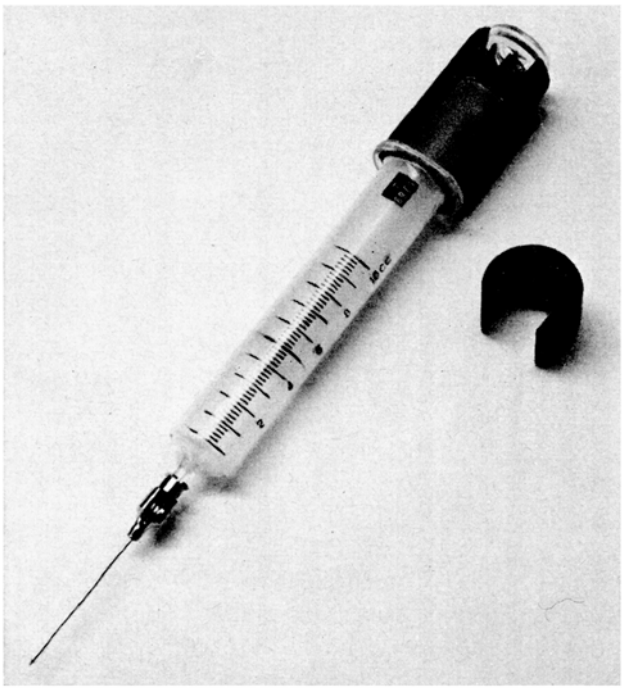

Calibration of volumetric syringes

Volume (ml)	Range (ml)	Average Deviation (ml)
9.0117	0.0013	± 0.0006
3.2957	0.0014	± 0.0007
0.6116	0,001	± 0.0005

T. G. TRAYLOR[2] and R. A. CRANE

The Dow Chemical Company, Pittsburg (Calif.), April 20, 1960.

STUDIORUM PROGESSUS

Quinine Dimorphism among 'Non-Tasters' of 6-n-Propylthiouracil

Introduction. It appears that the history of the thyroid gland has been one in which a feeding structure has been transformed into a gland of internal secretion. The thyroid hormone can be administered orally, whereas other hormones in an unaltered state are destroyed by gastric and intestinal fluids.

It is therefore of great interest from both the phylogenetical as well as the clinical point of view that thresholds for certain taste qualities are under control of thyroid hormones[1].

We started by investigating the role of saliva in the mechanism of 'taste-blindness' to phenylthiourea and similar antithyroid compounds[2]. The differential reactivity of the saliva of 'tasters' as opposed to that of 'non-tasters' led us to attempt to lower chemically the taste-threshold of 'tasters' towards the two bitter compounds 6-*n*-propylthiouracil and quinine[3].

Specifically subthreshold concentrations of l-tyrosine and or its mono- and diiodo-derivatives, in fact do lower 4–32 fold the taste-threshold of a 'taster' towards 6-*n*-propylthiouracil or quinine if administered simultaneously. Since high or low taste-thresholds towards these bitter compounds largely determine whether or not an individual belongs to a low or high food dislike category[4], we wondered about the mechanism by which quinine and 6-*n*-propylthiouracil thresholds affect an individual's likes and dislikes for food.

The existence of a quinine dimorphism has been postulated and though the genetic mechanism of this dimorphism has not yet been established, its existence is beyond doubt.

We can differentiate namely subjects with high or low taste thresholds for quinine through a simple saliva-color test (to be published) and this is irrespective of whether a subject belongs to the 'taster' or 'non-taster' mode of 6-*n*-propylthiouracil.

Materials and Method. D-Sucrose (USP, C-grade of the California Corporation for Biochemical Research), sodium chloride 'Baker Analyzed' Reagent of the J. T. Baker Chemical Company), hydrochloric acid (Certified Reagent of the Fisher Scientific Company), and quinine sulfate (U.S.P. Crystals of the Mallinckrodt Chemical Works), were used to test taste sensitivity. 6-*n*-propylthiouracil (from Nutritional Biochemicals Corporation) was chosen as a differentiator between 'tasters' and 'non-tasters'[1,2]. The compounds were dissolved in double distilled copper-free water. Serial dilutions were made, each numbered step representing a doubling concentration of the same molarity for any one compound. Taste-thresholds of 42 subjects were determined for all of the 5 taste qualities mentioned. Six additional subjects were tested only for their quinine and 6-*n*-propylthiouracil thresholds. All the 48 subjects were healthy men ($N = 37$) and women ($N = 11$), 77% of whom belonged to the 18–26 year age group.

Determination of taste-thresholds was carried out according to the HARRIS and KALMUS[5] procedure involving the final sorting out technique. In the first 2 h session the subjects were taught the taste-testing procedure by use of an instruction sheet and active participation after practical demonstration. Three ounce 'Lily' paper cups (No. 44 of the Lily Tulip Cup Corporation, New York 17, New York) were used for both the compounds and the placebo. A few days later the subjects' taste-thresholds were determined at a morning session in the following order: D-sucrose, sodium chloride, hydrochloric acid, quinine, and 6-*n*-propylthiouracil.

After the lapse of approximately a two-week interval the taste-thresholds were redetermined to check the reliability of the results. In approximately 50% of cases the thresholds were found to be identical with the value initially obtained. When variations occurred, they were in the + 0/− 1 threshold range. Stressful situations, seasonal change, the third trimester of pregnancy and thyroid administration caused greater variations in taste-threshold and subjects displaying these variations were excluded from this study[3].

Results. Figure 1 (A) depicts the distribution of taste-thresholds for 6-*n*-propylthiouracil of 48 subjects into 27

[1] F. GRIFFIN and R. FISCHER Nature *187*, 417 (1960).
[2] R. FISCHER and F. GRIFFIN, Exper. *15*, 447 (1959).
[3] R. FISCHER and F. GRIFFIN. Read at the Ann. Meeting of the Soc. Biol. Psychiatry, June 12–14, 1960, Miami, Fla.
[4] R. FISCHER, F. GRIFFIN, and ST. M. GARN, Science (submitted to).
[5] H. HARRIS and H. KALMUS, Ann. Eugen. (London) *15*, 24 (1949).

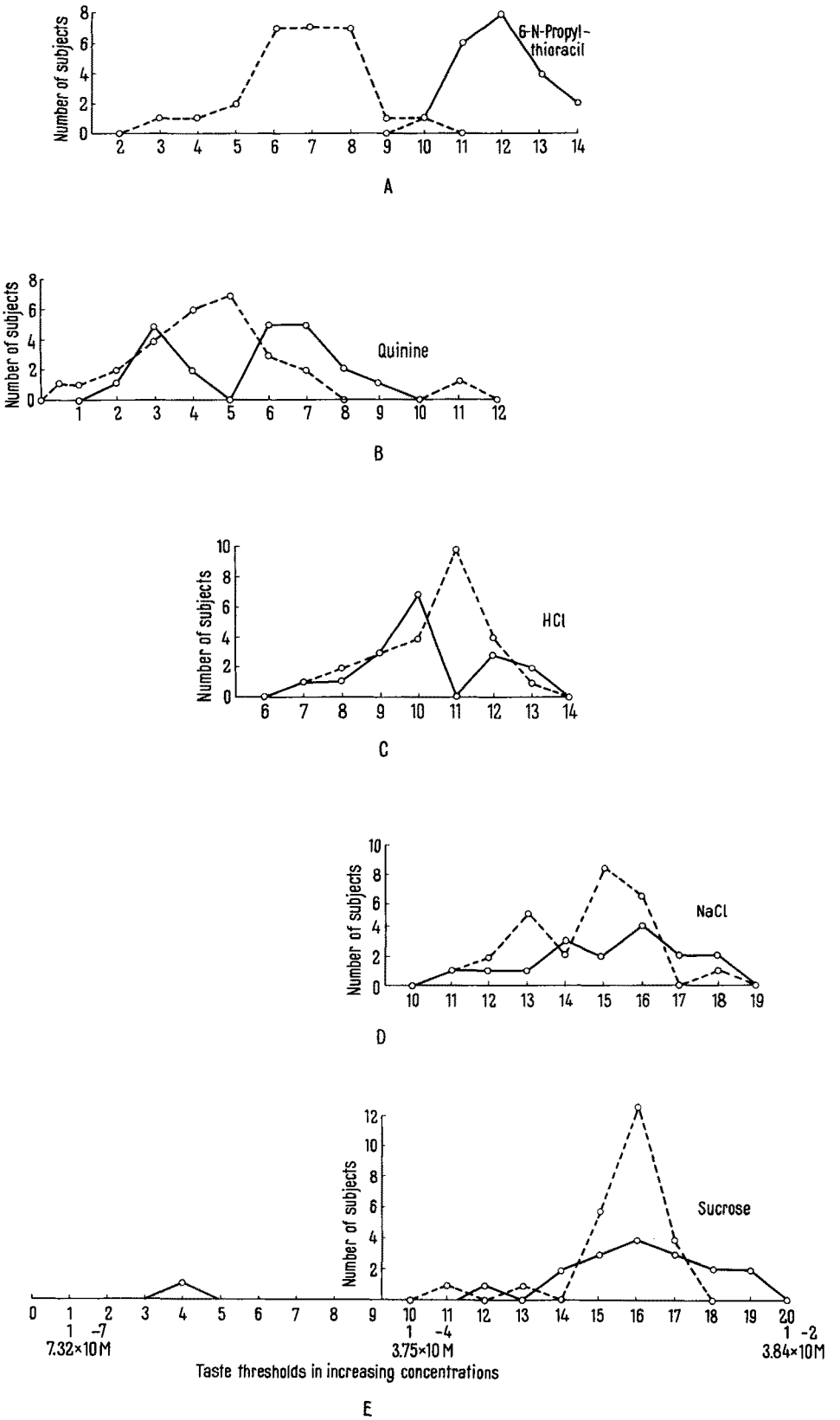

Fig. 1. Quinine dimorphism of 'tasters' and 'non-tasters' of 6-*n*-propylthiouracil (A): low and high quinine threshold tasters (B): low and high HCl threshold tasters (C): low and high NaCl tasters (D) and low and high D-sucrose tasters. Taste-threshold numbers 1–20 denote serial dilutions expressed in molarity, each succeeding step representing a twofold concentration of the previous for any one compound.

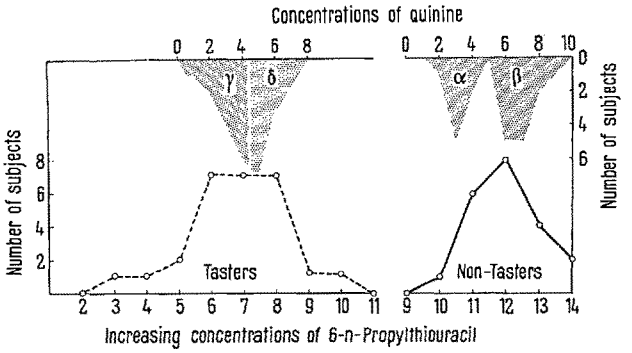

Fig. 2. Classification of 6-*n*-propylthiouracil 'non-tasters' into a low quinine threshold (α) and high quinine threshold (*β*)-*taste group;* the *γ*- and *δ-taste group* embraces 6-*n*-propylthiouracil tasters of the low and high quinine threshold category respectively.

'tasters' ($N = 21♂ + 6♀$) and 21 'non tasters' ($N = 16♂ + 5♀$). Figure 1 (B) shows a division at threshold 5 of our *6-n-propylthiouracil 'non-tasters'* into (α) a *low quinine* threshold category ($N = 8♂$) and (*β*) a *high quinine* threshold category ($N = 8♂ + 5♀$).

An analogous dichotomy results for hydrochloric acid if two categories are set apart through partition at concentration 11. The low *hydrochlorid acid category* ($N = 10♂ + 2♀$) contains 10 healthy males only, 8 of whom are identical with those of the α – low quinine threshold category.

The phenomenon repeats itself when dividing the sodium chloride thresholds of our 6-*n*-propylthiouracil 'non-tasters' at number 15.5 (see Fig. 1D). The low sodium chloride threshold category ($N = 8♂$) contains again the very same eight males of the α low-quinine and low hydrochloric acid categories. These 8 males re-appear once more among the total of 10 males of the low D-sucrose category which results (Fig. 1D) through partition at number 16.5 of D-sucrose thresholds. These data – and data obtained through determination of taste thresholds of 6-*n*-propylthiouracil and quinine on additional 21 subjects – suggest that in 'non-tasters' of 6-*n*-propylthiouracil *low* thresholds for the four classical taste qualities are likely to be the result of a common genetic mechanism.

It is also of interest to record another observation (to be published in detail with WM. HUNT et al.) according to which subjects (of another separate study) with paroxysmal vascular headache (migraine) with a strong family trend and with no visible electroencephalographic anomaly apparently *exclusively* belong to the *high* quinine threshold category of 6-*n*-propylthiouracil 'non-tasters' (Fig. 1B). More specifically such patients are clustered between quinine thresholds 7 to 10, i. e., they can only taste *very high* quinine concentrations.

The re-occurrence of our (α) low quinine threshold subjects in the low threshold category for the other taste qualities probably justifies our defining this category as the *α-Taste Group*. The phenomenon of clustering of migraine patients exclusively among the very high quinine tasters, on the other hand, probably justifies the use of the term *β-Taste Group* for the category of these 'non-tasters' of 6-*n*-propylthiouracil as well as quinine. We, therefore, tentatively introduce the terms α- and *β-Taste Group* in analogy to the blood group concept (see Fig. 2) and also assume at least hypothetically (and hope to publish later on supporting experimental evidence) the existence of *γ*- and *δ-Taste Groups*[6].

Another interesting corollary: 78% of our healthy subjects of the *γ-Taste Group* are people showing high selectivity and culinary sensitivity in food preferences, whereas 75% of our *β-Taste Group* subjects have very few or no food dislikes[4].

It is our contention that the elucidation of the genetic mechanism underlying the described quinine dimorphism of 6-*n*-propylthiouracil will eventually justify the introduction of our *Taste Groups*.

Zusammenfassung. Geschmacksblinde gegenüber 6-*n*-Propylthiouracil zerfallen in zwei Gruppen (Dimorphismus): eine mit niedrigen und eine mit hohen Geschmacksschwellenwerten gegenüber Chinin. Jene der ersten Gruppe haben niedrige Schwellenwerte auch gegenüber den andere Geschmacksqualitäten – sauer, salzig und süss – und gehören zur α-Geschmacksgruppe. Vertreter der zweiten Gruppe, das heisst 6-*n*-Propylthiouracil-Geschmacksblinde mit hohen Geschmacksschwellenwerten gegenüber Chinin gehören zu der *β*-Geschmacksgruppe. Patienten mit paroxysmal vaskulärem Kopfschmerz (Migräne mit familiärer Komponente), jedoch ohne elektronencephalographische Anomalie, gehören ausschliesslich zu der *β*-Geschmacksgruppe. Die Eltern von mongoloiden Kindern weisen hohe Geschmacksschwellenwerte gegenüber Chinin auf, wobei die Väter zur *β*-Geschmacksgruppe gehören.

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[6] A preliminary pilot trial with 20 parents of mongoloids revealed that *all* fathers and 40% of the mothers belong to the *β-taste group*, whereas 60% of the mothers belong to the *δ-taste group*. It is of extreme interest that *all* parents belong to *taste groups* characterized by high quinine thresholds ('quinine-non-tasters').

[7] Meiner *Alma Mater*, der Universität Basel, zu ihrem 500jährigen Jubiläum in Dankbarkeit gewidmet.

[8] *Acknowledgements.* This work has been supported by the State of Ohio, Department of Mental Hygiene and the U.S. Public Health Service, National Institutes of Health, Division of Mental Health, Grant No. M-2731. The active interest and helpful suggestions of Dr. B. PASAMANICK is thankfully acknowledged. Our very special and sincere thanks go to Mr. S. ENGLAND for his most valuable assistance, advice, and skillful help during many phases of this study.

Reserpin und γ-Aminobuttersäuregehalt des Gehirns

1. Die Annahme kausaler Beziehungen zwischen den zentralen Wirkungen des Reserpins und dem *Aminstoffwechsel* des Gehirns kann sich auf folgende Tatsachen stützen: a) nach Reserpin, das zu Sedation, Verlängerung der Evipannarkose[1] und Erniedrigung der Krampfschwelle für Elektroschock und Cardiazol führt[2], nimmt der Amingehalt des Gehirns ab[3]: Serotonin, Noradrenalin, Dopamin. b) Iproniazid (Isonicotinyl-isopropylhydrazin), das die pharmakologischen Wirkungen des Reserpins

[1] A. GOLDIN, D. DENNIS, J. VENDITTI und S. HUMPHREYS, Science *121*, 364 (1955). – J. R. FOUTS und B. B. BRODIE, J. Pharmacol. exp.Therap. *116*, 480 (1956). – F. M. STURTEVANT, Naturwissensch. *43*, 67 (1956).

[2] G. CHEN, C. R. ENSOR und B. BOHNER, Proc. Soc. exp. Biol. Med., N. Y. *86*, 507 (1954).

[3] B. B. BRODIE, J. S. OLIN, R. G. KUNTZMAN und P. H. SHORE, Science *125*, 1293 (1957).