Table II. Effect of histidine in the medium or preincubation with histidine (his) on the initial uptake of tryptophan by brain slices

	No of slices	Tryptophan uptake (μmole/ml of tissue water)
Without preincubation		
Controls	29	1.39 ± 0.06
In presence of his 1 m*M*	18	1.29 ± 0.05
5 m*M*	10	0.91 ± 0.05
With preincubation		
Controls	12	1.04 ± 0.06
Loaded with his	14	1.35 ± 0.06

Tryptophan uptake was determined after 3 min incubation with tryptophan 1 m*M* in the medium. In the experiments with princubation, brain slices were preincubated for 30 min without amino acids (controls) or in presence of histidine 5 m*M* (loaded); after a three-second washing in cold medium, they were incubated with tryptophan. The concentration of histidine in the slices at the end of preincubation with this amino acid was 22.9 ± 0.8 μmole/ml tissue water. Figures are means ± S.E.M.

Results and discussion. When brain slices are incubated in the presence of an amino acid for 60 min, the accumulation of the latter in the tissue approaches a steady level, which is dependent on its initial concentration on the suspending medium and on the presence of other amino acids. The data of Table I were obtained with these types of experiments. It is shown that the accumulation of tryptophan or histidine is decreased in presence of equimolar amounts of phenylalanine. Similarly, the accumulation of phenylalanine or histidine is decreased in presence of tryptophan. However, the accumulation of tryptophan or phenylalanine is increased in the presence of equimolar amounts of histidine.

The inhibiton of the accumulation of histidine by phenylalanine and by tryptophan is in agreement with the results of NEAME[10].

Accumulation experiments, such as those shown in Table I, while simulating more closely the physiological steady state condition, cannot explain in detail the dynamics of the uni-directional fluxes occurring at the cell membrane. Therefore, we have further studied, in short term incubations, the effect of histidine on the uptake of tryptophan. Table II shows that the initial (3 min) uptake of tryptophan by fresh tissue is decreased by the presence of histidine in the medium, in particular when the concentration of histidine is greater than that of tryptophan. On the other hand, Table II shows, also, that preloading of the slices with histidine enhances the initial uptake of tryptophan; in parallel experiments it was found that the incubation of the histidine preloaded slices with tryptophan (1 m*M*), roughly doubles the initial exit rate of histidine from the tissue. Therefore, from the data of Table II, it seems that both amino acids compete for the membrane carrier when they are on the same side of the cell membrane, but, when they are on opposite sides, intracellular histidine exchanges with extracellular tryptophan. Such a type of exchange diffusion could explain the enhancing effect of histidine on the accumulation of tryptophan in the long term experiments of Table I.

Resumen. La concentración de triptófano en cortes de cerebro incubados con este aminoácido durante 60 min, es disminuida por la presencia de fenilalanina pero aumentada por la histidina. El efecto de la histidina se puede explicar por intercambio a nivel de la membrana entre la histidina intracelular y el triptófano extracelular.

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The Threshold for the Smell of Acetone and its Relationship to the Ability to Taste Phenylthiocarbamate[1]

The odor of acetone in the breath of patients in diabetic coma has long been thought to be of diagnostic significance. Since many experienced clinicians are unable to detect any distinctive odor in such patients[2], while others can, we investigated the smell threshold for the odor of acetone and compared it with the ability to taste phenylthiocarbamate (PTC) of the same subjects. The population studied, mostly students and clerks, included 211 subjects, 86 between 15 and 19 years of age, 65 between 20 and 39 and 60 between 40 and 69.

Nine dilutions of reagent grade acetone in deionized water were prepared in glass-stoppered test tubes 1–2 h before each test session. They ranged in concentration (vol./vol.) from 8.0 to 0.01% (legend, Figure 1). Each tube was mixed by inversion before being presented to the subject to smell. The tubes were offered in order of increasing concentration after familiarizing the subject with the smell of acetone. When the approximate threshold was reached, the corresponding tube was placed together with 3 tubes of deionized water for identification as suggested by the method of HARRIS and KALMUS[3] for determining the threshold for the taste of PTC. The lowest concentration of acetone correctly identified from among the tubes of water was taken to be the threshold.

Ability to taste PTC was determined by having the subject taste a drop of an aqueous solution of 8.125 mg PTC per 100 ml, the antimode in the distribution of PTC thresholds[3]. If the subject noted any taste at all he was considered a taster.

When the distribution of thresholds for the smell of acetone in young subjects (aged 15–39) was plotted separately for males and females, 3 definite peaks were found in each graph (Figure 1). In the graph of the older subjects (aged 40–69) there were 2 peaks and a 'shoulder', each corresponding to 1 of the 3 peaks in the graph of the younger group (males and females combined), but in the

[1] Based on a report accepted by the Israel Ministry of Education in partial fulfillment of matriculation requirements of LEA REZNIK, and constituting an extension of the work of HENRY TABE.

[2] G. P. BAKER, Lancet *2*, 373 (1960).

[3] H. HARRIS and H. KALMUS, Ann. Eugen. *15*, 24 (1949).

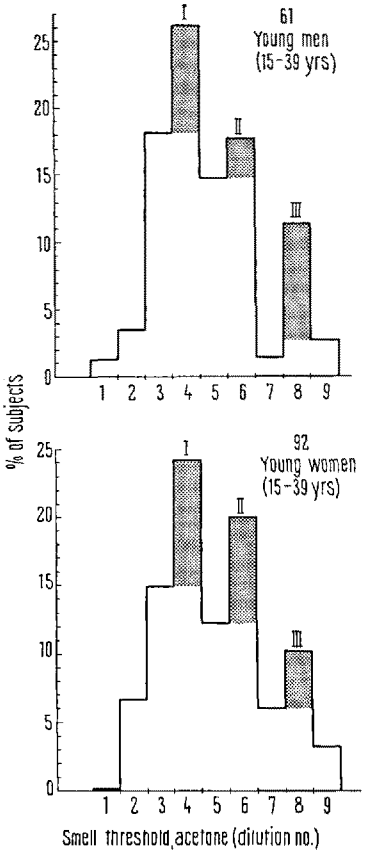

Fig. 1. Percent distribution of thresholds for the smell of acetone among young men and women. Dilutions numbered 1–9 correspond to aqueous acetone concentrations of 8.0, 4.0, 2.0, 1.0, 0.5, 0.25, 0.10, 0.05 and 0.01%, respectively.

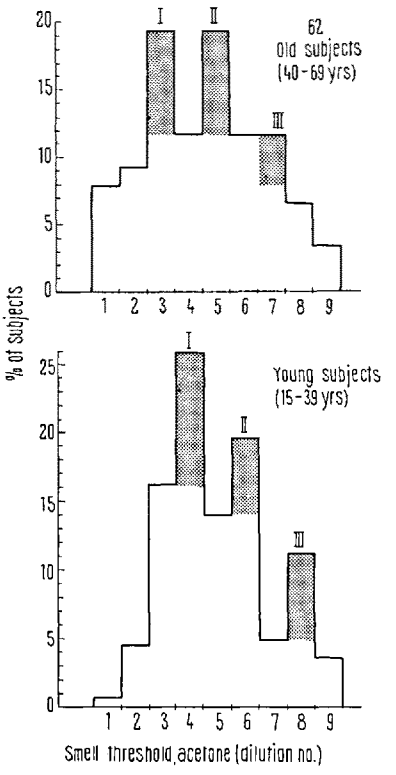

Fig. 2. Percent distribution of thresholds for the smell of acetone among older subjects as compared with younger subjects. Dilutions as in Figure 1. Note decreased sensitivity of older subjects.

younger group the peaks were lower in concentration by 1 dilution step (Figure 2).

Of our total population studied 15.5% were non-tasters of PTC, in accord with the findings of SHEBA et al.[4] in Israel, as applied to a mixed group of Ashkenazim and Sephardim such as ours. There were no non-tasters among the 42 subjects whose sense of smell for acteone was most acute (thresholds 7, 8 and 9, Figure 2). The difference in the ability of these subjects to taste PTC as compared with the rest of the population tested was significant ($\chi_2 = 9.6$, $p < 0.002$). Among the 56 subjects least sensitive to the smell of acetone (thresholds 1, 2 and 3) 26.2% were non-tasters, a significantly higher proportion than in the rest of the population tested ($\chi_2 = 5.2$, $p < 0.025$).

FORRAI et al.[5], whose work appeared while this study was in progress, found a bimodal distribution of acetone thresholds, rather than a trimodal distribution as we did. However, the range of thresholds they used may possibly not have been wide enough to identify a peak among their most sensitive subjects. The absolute thresholds they found are not comparable with ours. This may be due to the fact that we used water as the diluent for the acetone, while they chose silicone oil because of its lack of vapor pressure. They also used a finer gradation of concentrations than we did, with differences of one half log units between solutions. A standardized technique is apparently of prime importance for studies in this field, and since among our older subjects there was evidence of presbyosmia for the smell of acetone, the populations studied should be carefully matched for age.

The trimodal distribution found for the threshold for the smell of acetone suggests a genetic basis, similar to that for the trimodal distribution of INH inactivation[6] or pseudocholinesterase activity (dibucaine number)[7], among others. The correlation between sensitivity to the smell of acetone and ability to taste PTC, whose genetic basis is so well established, tends to support this assumption, and in addition, suggests genetic linkage.

Zusammenfassung. Individuelle Geruchsschwellenwerte für Azeton folgen einer trimodalen Kurve und stehen in Beziehung zur Fähigkeit, PTC zu schmecken. Diese Befunde deuten darauf hin, dass die Geruchsempfindlichkeit für Azeton eine genetische Grundlage hat.

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