reduction was observed 4 to 9 hours later. "When calcitonin was given 1, 3, or 22 hours before, feeding was not substantially decreased." Increasing the period between the ingestion of a flavor and the induction of sickness decreases the conditioned taste aversion subsequently displayed (6). Delaying the injection of lithium chloride from 1.5 hours to 4.5 hours produced a fourfold decrease in the effectiveness of the injection as measured by intake suppression (7). Therefore, an amount of lithium chloride producing a similar decrease in food intake should have been injected at least 4 to 5 hours after a novel flavor had been presented. Should such a test still show no taste aversion, the conclusion that no sickness was present to cause the reduction in food intake would be made more plausible. However, some doubt would still remain because we do not know how the speed of onset of sickness influences the formation of conditioned taste aversion. Gradualness of onset may militate against the efficiency of a learned association.

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We used two flavors (black walnut and chocolate), one of which had previously been paired with the administration of calcitonin; the other had previously been paired with the administration of vehicle. When the animals were subsequently presented with a choice between the two flavors, neither flavor was significantly preferred (Fig. 1). There was, however, a nonsignificant tendency for a decreased consumption of black walnut extract in the animals for which black walnut extract had been paired with calcitonin. There was no apparent aversion when calcitonin had been paired with chocolate. Perhaps a significant conditioned aversion would be revealed by this procedure if large numbers of animals were tested.

In another experiment, we administered calcitonin 3 hours before the first exposure to saccharin (backward conditioning (3)) and we were again unable to demonstrate a conditioned aversion. Finally, we gave animals access to saccharin for a 6-hour period after they received calcitonin. When subsequently tested for their preference of saccharin as opposed to water the calcitonin-treated animals increased their consumption of saccharin, but not as much as did the controls. (None of the differences were statistically significant.) Our studies thus far lead us to conclude that, although it might be possible to produce a conditioned taste aversion by administration of calcitonin, such an effect would certainly not be robust and is not easily demonstrated. We also point out that food-deprived animals that had received calcitonin ate avidly; as we noted in our original study (4), the animals that received 12.5 units of calcitonin per kilogram of body weight invariably began to eat within 10 seconds of food being introduced into their cages. Also, although the maximum effect of calcitonin occurred between 4 and 9 hours with a small (12.5 U/kg) dosage, larger dosages were effective over an entire 24-hour period. We have always used the largest dosage (50 U/kg) for conditioned aversion studies.

Conditioned aversions can be produced by moderate dosages of a wide variety of drugs, such as chlormezazine, benzodiazepines, barbiturates, alcohol, ether, methaqualone, scopolamine, and the anorexogens amphetamine and cholecystokinin (2, 5). Illness and nausea are not prominent features of the clinical pharmacology of these drugs, and some of these drugs can produce conditioned taste aversions in animals but do not decrease eating. It thus appears likely that any disturbance of homeostasis can produce a conditioned taste aversion. Therefore, although such studies may be informative, it would probably be unwise to attribute any pharmacological effect of a drug to nausea or illness (in the usual sense) solely on the basis of conditioned taste-aversion studies.

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12 December 1979; revised 17 July 1980

Fig. 1. Amount of black walnut–flavored (BW) solution and chocolate (Ch) solution (McCormick extracts; diluted 40:1) drunk by animals given simultaneous access to both solutions for 60 minutes (mean ± standard error). The animals previously had been given access to each solution and had then been injected with either synthetic salmon calcitonin (CT) (Armour Pharmaceutical; 50 U/kg, subcutaneously) or vehicle (Veh), as indicated by the arrows. Thus calcitonin was paired with chocolate for group B, with black walnut for group C, and with neither solution for group A (N = 10 per group). Animals were tested while on a 23.5-hour schedule of fluid deprivation. A two-way analysis of variance for one repeated measure showed no significant effects (for groups, F(2, 27) = 1.02, P = 0.374; for chocolate versus black walnut, F(1, 27) = 0.68, P = 0.423; for interaction, F(2, 27) = 1.45, P = 0.251). A post hoc comparison for group C also did not achieve significance (P = 0.05, Scheffe). Finally, Wilcoxon matched-pairs signed-ranks tests were performed for each of the groups and none reached statistical significance (T = 18.5, N = 9; T = 25, N = 10; and T = 10, N = 10 for groups A, B, and C, respectively).

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Science 211 (4483), 734.
DOI: 10.1126/science.211.4483.734