Food Aversions in Children Receiving
Chemotherapy for Cancer

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Pediatric patients receiving cancer chemotherapy formed aversions to familiar foods in their usual diet when these foods were consumed prior to drug treatments. These aversions were evidently learned due to the association of these foods with the symptoms of drug treatment. Some simple intervention procedures may prove effective in preventing the development of these aversions.


APPETITE loss and food aversions are common in patients treated for neoplastic diseases.1-3 A factor which may contribute to these symptoms is the development of learned food aversions in patients receiving chemotherapy. Learned food aversions are aversions to specific foods or tastes which develop as a result of the association of those foods with unpleasant internal symptoms such as nausea. This learning, originally described in laboratory animals by Garcia et al.,4 has been viewed as a variant of classical conditioning with subjects learning to associate a conditioned stimulus (the taste) with an unconditioned stimulus (the illness) and subsequently rejecting previously acceptable and preferred foods.5 Unusual features of food aversion learning include the fact that it can occur in a single trial and is often quite long lasting.

In a controlled examination of learned food aversions in cancer patients, children were exposed to an unusual ice cream shortly before receiving chemotherapy.6 Patients receiving drugs which cause nausea and vomiting were significantly less likely to choose that ice cream again than controls. Thus, children avoided eating a novel food which had previously been associated with gastrointestinal toxic chemotherapy. The present study extends those results by finding that patients also form aversions to familiar foods in their usual diet when these foods are consumed prior to gastrointestinal (GI) toxic chemotherapy treatments. Additionally, the development of aversions to familiar diet items was less evident in subjects exposed to the test ice cream before their chemotherapy than in those exposed only to drugs. This latter observation suggests that novel taste exposures may be an effective intervention approach for preventing or blocking the formation of learned aversions to familiar diet items.

Method

Eighty-four pediatric patients ranging in age from two to 18 years participated in the study. They were informed that the study concerned “taste preferences of patients in this treatment program” but were not informed of the specific hypothesis being tested. All were being treated as outpatients at the Children’s Orthopedic Hospital Hematology Clinic in Seattle, with the most frequent diagnoses being ALL, lymphomas, ANLL, Wilm’s tumor, Ewings sarcoma and Hodgkin’s disease. Patients with advanced or refractory disease were excluded, as were patients receiving radiation therapy. Drugs known to cause nausea and vomiting at the doses given patients in this study were classified as GI toxic, e.g., Adriamycin (doxorubicin), cyclophosphamide, nitrogen mustard. Although the mechanism responsible for these symptoms is probably central and not located in the GI tract7 these drugs will be referred to as “GI toxic” in this report. Vincristine, a chemotherapeutic agent not associated with these symptoms, served as a non-GI toxic control drug.

This study determines whether pediatric patients form aversions to familiar foods in their routine diet when these foods are consumed before GI toxic drug treat-
ments. Patients' food preferences, usual menus and specific items eaten before arriving at the clinic were determined by means of questionnaires. Patients (or their parents) completed these questionnaires during an initial treatment session, and again at a subsequent evaluation session at least a week later. A brief interview regarding changes in food choices generally occurred during the evaluation session.

The questionnaires request patients to list (1) current favorite foods; (2) foods they are reluctant to eat; (3) two typical breakfast, lunch and dinner menus; and (4) specific foods eaten in the previous four to five hours (pre-therapy items). Specific items eaten prior to therapy were considered potential targets for the development of aversions. To assess aversions the two questionnaire forms from each patient were compared and scored by a rater blind to group membership of subjects; an aversion was scored when a specific food eaten before therapy (pre-therapy food) was no longer preferred; became actively disliked or was no longer listed in usual menus. Based on this scoring patients were classified as either showing an aversion or not.

In addition, patients were classified into three groups based on their scheduled clinic treatment. Patients scheduled for GI toxic chemotherapy were randomly assigned to either receive ice cream exposure (Group 1) or not (Group 2), as previously described. Patients receiving chemotherapy not associated with GI symptoms (vincristine) or no drug at this clinic visit composed the control group (Group 3). This allowed us to compare changes in food preferences in our experimental groups (Group 1 and 2) to a group not experiencing GI symptoms. Five patients reported that they had eaten no foods before therapy and were excluded from the analysis.

Multiple regression analyses were performed using the SPSS subprogram REGRESSION. Initially, variables such as treatment group; severity of drug symptoms; number of foods on pretherapy lists; age and delay between sessions were considered in the analysis to determine which variables best predicted the incidence of aversions. A stepwise analysis was employed which entered variables into the final equation only if their contribution to the variance approached significance.

**Results**

The number of patients in the GI toxic and control groups showing aversions to specific foods eaten before drug treatments is presented in Table 1. Aversions occurred in patients receiving chemotherapy associated with GI discomfort (patients in Groups 1 and 2 combined) significantly more often than in patients in the control group ($P < 0.02$).

Results of the multiple regression analysis indicated that the number of pretherapy foods listed made the greatest contribution to the variance in incidence of aversions ($F_{3,75} = 12.92; P < 0.001$). Importantly, when the number of pretherapy items was controlled for in the analysis an interesting relationship between treatment group and incidence of aversions emerged. Namely, when the two experimental groups were individually compared to controls, GI toxic drug treatment alone (Group 2) was significantly associated with the incidence of aversions ($F_{1,75} = 6.93; P < 0.01$); but, when similar drug treatments were combined with ice cream exposure (Group 1) the incidence of aversions was not significantly greater than in controls ($F_{1,75} = 1.15; P = 0.29$). These results suggest that exposure to a novel food (Mapletoff ice cream) before drug treatments may have had a protective effect since significant aversions to food in the normal diet were not formed in Group 1, in spite of GI toxic drug exposure. None of the other variables we evaluated contributed significantly to the incidence of aversions.

A significant interaction between treatment and the number of pre-therapy items consumed was also observed. Specifically, eating a greater number of foods before therapy was significantly associated with the incidence of aversions in Group 2 ($t$ test, $P < 0.001$) but not in Groups 1 or 3. Thus, the relationship between number of pretherapy items and aversions may not merely reflect an artifact of our method of detecting aversions since this would affect all groups equally. Rather, it suggests that patients receiving GI toxic chemotherapy and not exposed to an interfering taste (novel ice cream) are more likely to develop diet aversions if they eat more foods before their treatment.

**Discussion**

Learned taste aversions have been reported in both children and adults when a novelty flavored food was consumed before GI toxic chemotherapy. The present study found that similar aversions often occur to foods that are toxic to the GI tract.
in patients’ usual diets which happen to have been eaten up to several hours before treatment. A number of these aversions were confirmed by interviews with patients or their parents, and many proved to be quite persistent, lasting for several months. This study was confined to chemotherapy treatments given in a single clinic visit. Since cancer patients actually receive many such treatments the development of learned food aversions may be a significant etiologic factor in the frequent reports of capricious and frustrating changes in food preferences experienced by these patients. It is also possible that learned food aversions are of significance in the development of anorexia and weight loss in patients with cancer.

In addition to documenting a frequent incidence of learned food aversions associated with chemotherapy, this study pointed to two intervention approaches which may prove useful in preventing these aversions. Patients exposed to a novel taste (Mapletoff ice cream) before treatment did not show a significantly higher incidence of aversions than controls. These patients were randomly selected from those scheduled for GI toxic therapy, and in fact reported somewhat more severe drug symptoms (nausea; vomiting) than patients not exposed to the ice cream. The observation that this treatment was not significantly associated with the formation of diet aversions suggests that the ice cream may have blocked the development of aversions to foods in the diet. Similar effects have been observed in studies of learned taste aversions in animals. A novel taste, presented in association with toxic drug treatments, acts as an interference stimulus and prevents or attenuates aversions to target foods or drinks. Perhaps deliberate exposure in the clinic to novel, “scapegoat” tastes prior to chemotherapy treatments would protect normal diet items from becoming targets for learned food aversions.

Patients in Group 2 (no ice cream exposure) who reported eating only one or two items in the hours preceding treatment were far less likely to show learned food aversions than those eating three to five items. Obviously then, another potential way of preventing learned food aversions is to recommend to patients that they eat little before their treatments.

Food aversion learning has evolved in rats and many other species enabling them to learn to select needed nutrients and avoid toxins. This mechanism is clearly adaptive in that it allows organisms to associate the delayed internal effects of toxins and imbalanced nutrients with the taste of consumed foods and to adjust their intake accordingly. However, this mechanism may be triggered under inappropriate circumstances, as in the case of patients receiving cancer treatment. Food aversions which develop as a consequence of chemotherapy are likely to be only one of a number of factors which contribute to appetite loss in cancer patients. Unlike many other contributing factors, however, these food aversions may prove to be largely preventable by simple intervention procedures such as those suggested by the current study.

REFERENCES