“Good Medicine Always Has a Bitter Taste”

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In 1994, Nelson et al. provided an insightful review of possible etiologies of the cancer anorexia-cachexia (AC) syndrome. This syndrome, with its classical clinical picture of anorexia, wasting, poor performance status, is a major cause of morbidity and mortality in cancer patients. The reported frequency of anorexia varies from 15% to 40% at presentation and close to 80% with advanced disease. Hallmarks of this AC syndrome include:

- Equal mobilization of fat and skeletal muscle;
- Normal or increased basal metabolic rate;
- Increased liver size and metabolic activity;
- Reduced lipoprotein lipase activity; acute phase protein reaction; increased Cori cycle activity;
- Normal or increased glucose turnover; and
- Increased protein breakdown.

Weight loss may be due to factors that decrease food intake including nausea and vomiting, early satiety, direct tumor encroachment on the gastrointestinal tract, influence of radiation therapy and chemotherapy, pain, and emotional distress. Nelson et al. defined anorexia as a loss of desire to eat and speculated on the role of lack of taste and learned food aversions in this syndrome.

Much scientific interest has been generated regarding this problem. In a large multicenter study, the Eastern Cooperative Oncology Group (ECOG) studied the prognostic effect of weight loss before chemotherapy in 3,047 patients enrolled in 12 chemotherapy protocols. The frequency of weight loss ranged from 31% for lymphomas and 87% for gastric carcinoma. The survival was significantly shorter in nine protocols for patients with weight loss compared to patients with no weight loss. Response rates were lower in patients with weight loss, but this difference was significant only in breast cancer patients. Thus the ECOG study identified the importance of weight loss as a prognostic factor across multiple institutions.

Recently, Boltong and Keast published a masterful review of taste and the influence of chemotherapy. To understand this review, the terminology used must first be explored. Taste is the foundation of flavor and is the sensation derived when chemical molecules stimulate the taste receptor cells in the oral cavity. Multiple peripheral and cognitive functions are responsible for the perceived flavor of food and drinks. Taste is only one component of flavor but provides important information about food, including pleasure and displeasure.

The taste system detects five qualities of food:

- Sweetness elicited by sugars reflecting carbohydrates;
- Soursness elicited by free hydrogen ions reflecting excessive acid;
- Umami or savory taste elicited by glutamic and other amino acids denoting protein content;
- Saltiness elicited by sodium and other ions reflecting mineral content;
- Bitterness reflecting potential toxins in foods.

Taste is perceived when certain soluble chemicals in saliva contact taste receptors on taste buds on the tongue, soft palate, and oropharyngeal areas. After the taste receptors are activated, afferent signals are sent to the taste processing center in the brain and the appropriate taste quality is experienced.

Hedonics is a term referring to psychological determination of the extent to which a life experience is pleasurable. In relation to eating and drinking, hedonics encompasses food liking. Liking is defined as the immediate experience or anticipation of pleasure from the oral stimulation of food. On the other hand, food aversion is the result of unpleasant food experience often influenced by factors such as appetite, hunger, and learned food aversions.

In 1978, Bernstein reported learned taste aversions in children receiving chemotherapy linked to the side effect of nausea. A total of 41 patients ranging in age from 2 to 16 years participated in this study. Patients treated with gastrointestinal (GI) toxic drugs were stratified by age and the number of prior GI toxic drug regimens. Then they were randomly assigned to one of two groups: the experimental group (Group 1), which received a paired association between an unusual ice cream and GI toxicity; the control group (Group 2), which experienced GI toxicity without receiving ice cream. The unusual ice cream was a novel flavor of maple and black walnut flavor extracts (Mapletonoff). The results showed that the consumption of the ice cream before GI toxic chemotherapy resulted in a diminished

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likelihood of a subsequent choice of that ice cream. Thus
this aversion to Mapleoff ice cream appeared to be a spe-
cific, learned response and not an effect of the GI toxic
drugs alone, since Group 2 patients were not averse to eat-
ing the ice cream. As noted by the author, this demonstra-
tion of an acquired aversion to a novel flavor in children receiv-
ing chemotherapy is important to physicians who adminis-
ter treatments that cause nausea and vomiting. Such taste
aversions may be one of many factors contributing to the
anorexia and weight loss seen in pediatric cancer patients.
Indeed, chemotherapy taste changes are related to altered
number or structure of taste cell receptors, interruption of
neural coding, neurotoxicity from systemic chemotherapy, or
detection of drug secretion in saliva.3

Without an understanding of the clinical manifestations
of altered taste and hedonics experiences of food in patients
receiving chemotherapy, there is no framework to develop
appropriate interventions to manage this unpleasant impact
of treatment. To address this problem, the authors3 conducted
a systematic literature review on the influence of chemother-
apy on taste perception and hedonic experiences. They spe-
cifically examined the following outcome measures:

- Sensitivity to the five taste qualities;
- Perceived intensity of the five taste qualities;
- Food liking;
- Food aversion; and
- Appetite.

A two-armed review of multiple databases of published
studies in English examining taste perception and hedonics
was conducted. For both study arms, strict agreed on inclusion/ex-
clusion criteria were followed. One hundred and sixty-three
papers were screened in the taste arm and eight (5%) met
inclusion criteria. Nine hundred and seventy-two papers
were screened in the hedonics arm of which only 25 (3%)
met inclusion criteria. Two papers were included in both the
taste and hedonics arm. These 31 articles included in the sys-
tematic review more often reported observational rather than
experimentally designed studies.

The most commonly reported aversive food items with
the associated taste quality were

- Coffee—Bitter;
- Red Meat—Umami;
- Tea—Bitter;
- Chocolate—Sweet/Bitter; and
- Citrus (Fruit or Juice)—Sour.

The results of this systematic literature review failed to
provide sufficient evidence suggesting that chemotherapy
influenced taste in a significant and uniform way. Most stud-
ies focused on the taste qualities of sweet and salt rather than
bitter, sour, or umami. The authors speculated that it may not
be dramatic shifts in the sensitivity to and intensity of quality
of taste, but rather the hedonic elements of food, flavor, or
patient symptoms, which exert the greatest effect on the
perception of food and drinks consumed during or after
chemotherapy. Furthermore, the incorrect understanding of
taste is responsible for the belief that this altered sense is a
problem for patients undergoing chemotherapy. This mis-
understanding results from using the word “taste” when the
more appropriate term is “flavor.”

In regard to the hedonics of food, there was a consistent,
small body of evidence indicating food liking and appetite
are adversely affected by chemotherapy, and some evidence
these changes are reversed over time. Aversive changes to
liking and appetite generally occur during the first 6 months
of chemotherapy. Symptoms do not uniformly resolve with
time and there is the possibility that these changes in liking
and appetite may be transient. This review found no evi-
dence that appetite or liking and the sense of taste were
simultaneously influenced by chemotherapy.

The practical implications for patient care of this exten-
sive review, as noted by the authors, include the following:

- Avoid familiar foods immediately prior to chemother-
apy to reduce the chance of developing learned
food aversions if chemotherapy causes a negative
or nausea inducing experience.
- Avoid commonly consumed foods such as coffee,
tea, chocolate, red meat, and citrus fruit or juice.

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