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## Complications of Treatment

## Metallic taste in cancer patients treated with chemotherapy

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## ABSTRACT

**Background:** Metallic taste is a taste alteration frequently reported by cancer patients treated with chemotherapy. Attention to this side effect of chemotherapy is limited. This review addresses the definition, assessment methods, prevalence, duration, etiology, and management strategies of metallic taste in chemotherapy treated cancer patients.

**Methods:** Literature search for metallic taste and chemotherapy was performed in PubMed up to September 2014, resulting in 184 articles of which 13 articles fulfilled the inclusion criteria: English publications addressing metallic taste in cancer patients treated with FDA-approved chemotherapy. An additional search in Google Scholar, in related articles of both search engines, and subsequent in the reference lists, resulted in 13 additional articles included in this review. Cancer patient forums were visited to explore management strategies.

**Findings:** Prevalence of metallic taste ranged from 9.7% to 78% among patients with various cancers, chemotherapy treatments, and treatment phases. No studies have been performed to investigate the influence of metallic taste on dietary intake, body weight, and quality of life. Several management strategies can be recommended for cancer patients: using plastic utensils, eating cold or frozen foods, adding strong herbs, spices, sweetener or acid to foods, eating sweet and sour foods, using 'miracle fruit' supplements, and rinsing with chelating agents.

**Interpretation:** Although metallic taste is a frequent side effect of chemotherapy and a much discussed topic on cancer patient forums, literature regarding metallic taste among chemotherapy treated cancer patients is scarce. More awareness for this side effect can improve the support for these patients.

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## Introduction

The majority of patients with cancer will be treated with chemotherapy during the course of their disease. Remarkably, several side effects of chemotherapy seem to be accepted, whereas suitable management strategies are often not provided. Taste changes, particularly the occurrence of metallic taste, is one of these neglected side effects. Taste changes are common in 45–84% of

the cancer patients treated with chemotherapy [1]. These taste changes refer to an absence of taste perception (ageusia), a decreased or increased taste sensitivity (hypogeusia or hypergeusia), a distorted taste perception (dysgeusia), or a taste perception without an external stimulus (phantogeusia) [2]. Taste alterations have been associated with a poor appetite, a decreased energy and nutrient intake, changes in food preference, and a decreased quality of life [3–9]. Cancer patients can experience taste changes during chemotherapy treatment, which can last for a few hours, weeks, or several months after chemotherapy discontinuation [3,10,11].

A metallic taste is a typical taste alteration reported by cancer patients. In a study among patients with various cancer types, 29 of 37 (78%) patients described their perceived taste change as metallic after at least two cycles of various chemotherapy treatments [12]. Another study reported physical and psychosocial complaints in 204 cancer patients [13]. The medical oncologists of these patients were also asked to specify which complaints they knew their patients encountered. A metallic taste was reported by

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approximately one-third of the patients, whereas the medical oncologists perceived this symptom only in one-tenth of these patients.

Although, a metallic taste seems to be a frequent side effect of chemotherapy, literature on this subject is scarce. For this review all available studies regarding metallic taste in cancer patients treated with Food and Drug Administration (FDA) approved chemotherapy were analyzed. This review addresses the definition of metallic taste, assessment methods, prevalence, duration, possible causes due to chemotherapy, and management strategies.

### Search strategy

The electronic database PubMed was used to conduct a comprehensive search on metallic taste and chemotherapy up to September 2014. The following strategy was adapted across the database: (“Antineoplastic Agents” [Mesh] OR “Antineoplastic Agents” [Pharmacological Action] OR cancer OR chemotherapy\*) AND (“Olfaction Disorders/chemically induced” [Mesh] OR “Taste Disorders/chemically induced” [Mesh] OR ((metal OR metals OR metallic) AND taste\*)). This search resulted in 184 articles, of which 13 articles were included [2,12,14–24]. Articles not related to metallic taste in cancer patients treated with FDA-approved chemotherapy, without English translation or abstract, and animal studies were excluded. Many studies do not have metallic taste as their primary focus. As a consequence, relevant articles can be missed in a PubMed search based on titles and abstracts. Therefore, the search was expanded with a Google Scholar search on ‘metallic taste AND chemotherapy’ in full texts instead of titles and abstracts only. Furthermore, related articles of both search engines were examined and subsequent reference list searches were carried out. This search resulted in 13 additional articles, which addressed aspects of metallic taste in cancer patients treated with chemotherapy and articles that investigated characteristics of metal salts eliciting a metallic sensation in healthy participants [10,13,25–35]. Fig. 1 shows the flow diagram of the selection procedure of the articles. Cancer patient forums were visited to explore management strategies.

### Definition of metallic taste

Cancer patients treated with chemotherapy report sensations, such as a ‘metallic taste’, ‘chemical taste’, ‘drug taste’, ‘blood taste’ and ‘bitter taste’ [14,15]. Of these sensations, a metallic taste is most commonly reported by patients treated with chemotherapy [10,12,16,17]. It is unclear whether all these tastes refer to the same sensation. Probably, these sensations are hard to explain for patients, since it is often the first experience with this kind of taste. Therefore, a metallic taste is difficult to recognize as compared to the primary tastes sweet, sour, salty, and bitter. Metallic taste has been described as a phantogeusia [2,18]. However, it is unclear whether this metallic taste is a true taste phantom or whether external cues are involved. In food science, metallic taste has been characterized as ‘a peculiar mouthfeel, which is similar to that observed when an iron nail or metal foil is placed in the mouth’ [36]. Metallic sensations are also reported as a side effect of drugs [37], specific foods [38], artificial sweeteners [39], electrical stimulation of the tongue or chorda tympani nerve [40,41], burning mouth syndrome [42], during pregnancy [43], and as a result of damage by stapedectomy or anesthesia of the chorda tympani nerve [44,45]. Furthermore, the evoked sensations of metal salts, such as iron, copper and zinc, have been described as metallic [25,26]. Especially ferrous sulfate ( $\text{FeSO}_4$ ) has been proposed as a distinctive metallic compound and is used as a reference standard in food sensory evaluation [46].

### Assessment of metallic taste

Questionnaires, interviews, and stimulation with metal salts eliciting a metallic sensation have been used to assess metallic taste. These methods will be described hereafter.

#### Questionnaires

Several questionnaires regarding taste changes have been used to assess metallic taste in cancer patients. A study used a self-developed 33-item questionnaire, which included an alternative ‘other’ response option next to the options of change in sweet, salty, sour, and bitter taste, where patients could report metallic taste [32]. Another study used a questionnaire on 12 physical symptoms associated with chemotherapy [13]. Patients had to report if and on how many days they experienced the symptoms during the preceding week. One item in this questionnaire was ‘metallic taste in mouth’. No other questions regarding taste changes were included. The questionnaires used in two studies could not be retrieved [12,16]. To our knowledge, no questionnaire has been developed specifically focusing on metallic taste.

#### Interviews

In three studies, metallic taste in chemotherapy treated cancer patients was studied by an interview [10,15,27]. Two of these studies performed a 30-min telephone interview using a self-developed Sensory Information Questionnaire (SIQ) [10,27]. The SIQ contains open-ended as well as focused questions related to taste, smell, touch, hearing, and vision. In a third study, interviews on general health, medication use, oral symptoms, taste changes, smoking, and oral hygiene habits were held [15]. Taste changes were determined by asking the patients whether they experienced taste changes (yes/no). Next, patients with taste changes were asked regarding the type of taste change (hypogeusia, hypergeusia, dysgeusia or ageusia) and to give a specific subjective description of the experienced taste changes.

#### Stimulation with metal salts eliciting a metallic taste

No studies have compared the metallic taste reported by cancer patients treated with chemotherapy with the metallic sensation evoked by metal salts. The following studies give insight into the characteristics of metal salts and factors associated with the reported metallic taste evoked by these metal salts in healthy participants.

A study performed in 18 healthy participants (eight men; age 19–33 years) investigated the detection thresholds of three iron salts: ferrous sulfate ( $\text{FeSO}_4$ ), ferrous chloride ( $\text{FeCl}_2$ ), and ferrous gluconate ( $\text{FeGlu}$ ) [28]. For each stimulus, serial dilutions were made by a factor of 2.5, with 0.0125 mol/L as the highest concentration. A triangle test including the stimulus and two blanks (water) was carried out at each selected concentration, starting at the lowest concentration. The test was finished when participants made three correct discriminations in a series or when all concentrations were evaluated. The best estimated threshold for each participant was considered as the geometric mean of the concentration including the last error and the next higher concentration. Wide ranges of detection thresholds were found with median detection thresholds of 202, 81, and 13  $\mu\text{mol/L}$  for  $\text{FeSO}_4$ ,  $\text{FeCl}_2$ , and  $\text{FeGlu}$  respectively. Furthermore, ten of these 18 participants and three other participants (six men; age 20–42 years) were asked to describe the taste of each stimulus as sweet, sour, salty, bitter, metallic, astringent or they could describe another taste. The proportion of participants who described the iron compounds as a metallic taste decreased as the concentration increased ( $F(2,24) = 8.23$ ,  $P = 0.0019$ ). Higher concentrations of  $\text{FeSO}_4$  and  $\text{FeCl}_2$  were more frequently described as bitter and a higher concentration of  $\text{FeGlu}$  as sour. Metallic taste was more

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