

# Diet and Headache: Part 1

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**Background.**—The role of diet in the management of the headache patient is a controversial topic in the headache field.

**Objectives.**—To review the evidence supporting the hypothesis that specific foods or ingredients within foods and beverages trigger attacks of headache and/or migraine and to discuss the use of elimination diets in the prevention of headache disorders

**Methods.**—This represents part 1 of a narrative review of the role of diet in the prevention of migraine and other headache disorders. A PubMed search was performed with the following search terms: “monosodium glutamate,” “caffeine,” “aspartame,” “sucralose,” “histamine intolerance syndrome,” “tyramine,” “alcohol,” “chocolate,” “nitrites,” “IgG elimination diets,” and “gluten.” Each of these search terms was then cross-referenced with “headache” and “migraine” to identify relevant studies. Only studies that were written in English were included in this review.

**Results.**—Caffeine withdrawal and administration of MSG (dissolved in liquid) has the strongest evidence for triggering attacks of headache as evidenced by multiple positive provocation studies. Aspartame has conflicting evidence with two positive and two negative provocation studies. Observational studies provide modest evidence that gluten- and histamine-containing foods as well as alcohol may precipitate headaches in subgroups of patients. Two of three randomized controlled trials reported that an elimination diet of IgG positive foods significantly decreased frequency of headache/migraine during the treatment as compared to baseline time period.

**Conclusions.**—Certain foods, beverages, and ingredients within foods may trigger attacks of headache and/or migraine in susceptible individuals. Elimination diets can prevent headaches in subgroups of persons with headache disorders.

*Key words:* diet, headache, migraine, monosodium glutamate, nitrates, aspartame, sucralose, alcohol, tyramine, wine, beer, histamine, citrus, caffeine, folate, omega-6 fatty acid, omega-3 fatty acid, gluten

*Abbreviations:* ASA aspirin, CI confidence interval, DAO diamine oxidase, MSG monosodium glutamate, NCGS non celiac gluten sensitivity, OR odds ratio, RCT randomized controlled trials, TTG tissue transglutaminase

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Headache

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## INTRODUCTION

The role of diet in the treatment of headache disorders is one of the most controversial topics in the field of headache medicine. There have been a number of diets purported to decrease the frequency of headache, but few of the diets have been rigorously studied and most lack an adequate control group. Some diets require elimination of specific foods or beverages that trigger attacks of headache while others require more comprehensive diets that prevent headaches.

This represents the first of a two part review of diet and headache. In Part 1 of the review we will present the evidence supporting the hypothesis that specific foods, ingredients within foods and beverages trigger attacks of headache and/or migraine. We will also discuss the use of elimination diets in the prevention of headache disorders. In Part 2 of the review we will review the use of comprehensive diets for the preventive treatment of headache as well as the possible mechanisms through which foods might trigger headache.

## METHODS

A PubMed search was performed with the following search terms: “monosodium glutamate,” “caffeine,” “aspartame,” “sucralose,” “histamine intolerance syndrome,” “tyramine,” “alcohol,” “chocolate,” “nitrites,” “IgG elimination diets,” and “gluten.” Each of these search terms was then cross-referenced with “headache” and “migraine” to identify relevant studies. Only studies that were written in English were included in this review.

## SPECIFIC FOODS, INGREDIENTS WITHIN FOODS AND BEVERAGES

Twenty-seven to thirty percent of migraineurs self-report that foods trigger attacks of migraine.<sup>1,2</sup> The most common foods and beverages that have been self-reported to trigger migraine include chocolate, coffee, nuts, salami, alcoholic beverages, milk, citrus fruits, and cheese while the most frequent ingredients were caffeine, monosodium glutamate (MSG), artificial sweeteners, nitrites, gluten, and biogenic amines (eg, histamine, tyramine, and phenylethylamine)<sup>3-6</sup> (Table 1).

The dietary patterns of persons with migraine and non-migraine headache differ from those with no headache.<sup>7</sup> Those with migraine or non-migraine headaches have a lower intake of alcoholic beverages. Persons with migraine with aura consume less chocolate, ice cream, hot dogs, and processed

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**Table 1.—Self-Reported Foods, Ingredients Within Foods and Beverages That Have Been Associated With Headache**

	Examples
Foods	Chocolate, Citrus fruits, Nuts, Ice Cream, Tomatoes, Onions, Dairy Products
Beverages	Alcoholic Beverages, Coffee
Ingredients	Caffeine, Monosodium Glutamate, Histamine, Tyramine, Phenylethylamine, Nitrites, Aspartame, Sucralose, Gluten or Wheat

meats. A recent diary study examined the associations between trigger factors and migraine attacks within individuals and found that single dietary triggers were statistically associated with migraine attacks in <7% of persons.<sup>8</sup> We will next review the evidence linking specific foods, and ingredients within foods and beverages to attacks of headache and/or migraine.

### Monosodium Glutamate

MSG is the sodium salt of glutamate and a flavor enhancer that is used in a variety of processed foods including frozen or canned foods, soups, international foods, snack foods, salad dressing, seasoning salts, ketchup, and barbecue sauces.<sup>9</sup> MSG may not be specifically mentioned on food labels, but a number of other names may suggest its addition such as natural flavor, kombu extract, hydrolyzed plant protein, hydrolyzed vegetable protein, and flavoring. Kwok first coined the term “Chinese restaurant syndrome” for a group of symptoms (eg, headache, flushing, paresthesias, sweating, palpitations) that occurred after ingestion of Chinese food.<sup>10</sup> He postulated that these symptoms were caused by the large amounts of MSG that had been added to the food as a flavor enhancer.

There have been a number of randomized placebo-controlled studies that have been performed to determine whether MSG provokes the symptom complex associated with the Chinese restaurant syndrome. A recent systematic review of these studies was conducted to ascertain whether there was evidence that MSG provoked headache.<sup>11</sup> The authors divided studies into those in which MSG was added to food and others in which MSG was consumed as a liquid because the ingestion of food has been reported to decrease the absorption of MSG.<sup>12-21</sup> They found little evidence that MSG added to food triggered headache. Conversely, MSG dissolved in liquids at high concentrations (eg, >2%) precipitated headache in four of five provocation studies. They also noted that “blinding” of the studies may have been compromised as MSG has a distinctive flavor that may have been recognized by the study participants.

### Caffeine

Caffeine is the most commonly used stimulant across the globe. It is found in diet products such as tea, coffee, chocolate, soft drinks, and in some medications such as pain killers

and weight loss pills. Caffeine can effectively abort attacks of migraine when combined with aspirin and acetaminophen in combination analgesics, but can also provoke headache upon its withdrawal in habitual caffeine consumers.<sup>22-24</sup> A review of the effects of caffeine on brain health suggested that a moderate amount of caffeine (eg, 200 mg in one setting or up to 400 mg/day) does not precipitate any harmful effects, but rather may improve mood and reduce depression.<sup>25</sup> Higher dosages (>300-400 mg/day) can produce anxiety and panic disorder particularly in men.<sup>26,27</sup> Genetic polymorphisms of the adenosine A<sub>2A</sub> receptors may influence susceptibility to the side effects of caffeine such as insomnia or anxiety.<sup>28,29</sup>

Population-based studies reported conflicting results regarding the relationship between headache and caffeine consumption.<sup>30</sup> Most have reported a higher prevalence of headache, migraine, and chronic daily headache with caffeine consumption, while some have found no association whatsoever.<sup>31-37</sup> The Head-HUNT study found that higher caffeine consumption (>540 mg/day) was positively correlated with infrequent headaches (OR 1.16 [95% CI; 1.09, 1.23]) and negatively associated with chronic headaches (OR 0.82; [0.69, 0.98]).<sup>38</sup> Current and past use of caffeine-containing combination analgesics has also been positively associated with chronic headache.<sup>34,35,39</sup> In contrast, a 2015 study did not find an increased headache frequency in persons with migraine or tension headache that consumed of aspirin/caffeine combination tablets when compared to those that used aspirin (ASA) alone or other analgesics.<sup>40</sup> This study however did not control for the number of days that ASA/caffeine combination tablets was consumed in their analyses, which is one of the most important factors in the provocation of medication overuse headaches.

To our knowledge there have only been two studies that withdrew caffeine in patients with headache disorders and observed the effects of this intervention on headache. Hering-Hanit and Gadoth studied 36 children and adolescents with chronic daily headache with high caffeine intake (mean 196 mg/day of caffeine intake).<sup>41</sup> They gradually withdrew all caffeinated beverages from these patients and noted that 33 (92%) of them became completely headache free. In another study, investigators withdrew caffeine from 113 adult migraine patients and reported that the efficacy of abortive medications was improved in these patients.<sup>42</sup>

There is convincing evidence that abstinence from caffeine may precipitate headache in habitual caffeine users. These headaches have been termed “caffeine withdrawal headaches.” There have been ≥10 past studies demonstrating a significantly increased incidence of headache after withdrawal from caffeine in habitual users.<sup>43-54</sup> The median percentage of individuals that experience caffeine withdrawal headaches after abstinence is 47%.<sup>24</sup> Withdrawal symptoms that include

headache can start as early as 12-24 hours after abstinence from caffeine, peak at 20-51 hours, and last for 2-9 days.<sup>24</sup> It requires three consecutive days of caffeine consumption in a caffeine naïve patient to generate withdrawal symptoms.<sup>55</sup> Complete abstinence may not be necessary as a decreased amount of caffeine as compared to normal may also trigger headaches.<sup>55</sup> The withdrawal headaches are characterized as bilateral, throbbing, and can sometimes be associated with nausea.<sup>56</sup> The probability of withdrawal headaches increases with greater amounts of daily caffeine consumption, but as little as 100 mg/day of caffeine can produce headaches upon its withdrawal.<sup>55,57</sup>

Based on the above data we would make the following recommendations regarding caffeine use in the headache patient. First, we believe that it is reasonable to continue caffeinated beverages in the headache patient as long as they consume small to moderate dosages of caffeine (eg, <400-500 mg/day) and their daily dosage does not vary by substantial amounts. If patients cannot consume approximately the same dosage of caffeine per day and maintain a regular schedule of caffeine consumption then it might be best to decaffeinate them. Second, we would suggest that the dosing interval between caffeinated beverages not exceed 24 hours, as this gap may lead to caffeine withdrawal headaches. Third, we cannot rule out the possibility that daily dosages of caffeine exceeding 400-500 mg/day are associated with headache in some patients. In these patients we would either recommend a complete withdrawal of caffeine or a reduction in their daily consumption to <400-500 mg/day.

#### Artificial Sweeteners

Aspartame is an artificial sweetener that has been associated with headaches in several studies. Koehler and Glaros performed a two period crossover study of 11 migraine patients in which aspartame (300 mg capsules qid) or matching placebo (1 capsule qid) was administered for four week time periods with a one week washout period between treatment periods.<sup>58</sup> The frequency of migraine headaches was significantly higher in the aspartame than the placebo treatment period ( $P = .014$ ).

Van Den Eden et al conducted a two-treatment, four-period crossover study of 32 participants with self-reported headaches with ingestion of aspartame.<sup>59</sup> They were randomized to aspartame capsules (30 mg/kg/day) or matching placebo in three daily doses. Each treatment period was one week followed by with a washout day between treatment periods. The percentage of days with headache was significantly greater in the aspartame as compared to the placebo group across all treatment periods (33% vs 24%,  $P = .04$ ).

Schiffman et al completed a two-way crossover study of 40 persons with self-reported headaches with consumption of aspartame containing foods or beverages.<sup>60</sup> They were

administered three dosages of either aspartame (10 mg/kg with each dose) or placebo over a 4-hour time period in a two-period crossover study. There was no difference in the incidence of headache in the aspartame as compared to the placebo groups (35% vs 45%;  $P < .50$ ).

Lindseth et al performed a crossover study to determine whether there were neurobehavioral differences between those that consumed a low and high aspartame diet (25 mg/kg/day vs 10 mg/kg/day) during an eight-day treatment period.<sup>61</sup> Those receiving the high aspartame diet had more depression and irritability than the low aspartame diet, but the incidence of headache did not differ between the groups. Therefore, two of the four provocation studies found that aspartame treatment was associated with a greater frequency of headache and/or migraine as compared with placebo. It should be noted that dosages of aspartame used in these studies were quite high compared to that normally consumed in a typical diet.

Finally, in a case series, Newman and Lipton reported two persons whose migraines were thought to be triggered by the administration of rizatriptan melting tablets, which contain aspartame as an additive to the tablet.<sup>62</sup>

Sucralose has also been associated with headache attacks, but only in isolated case reports.<sup>63,64</sup> Bigal and Krymchantowski reported a case of a woman in which 90% of her attacks of migraine were precipitated by sucralose. The addition of either sucralose or sugar to orange juice demonstrated that migraine was triggered by 2/2 trials of sucralose and 0/3 trials of sugar.<sup>63</sup>

#### Biogenic Amines

Biogenic amines are synthesized by the decarboxylation of free amino acids and include histamine, tyramine, and phenylethylamine.<sup>65</sup> They occur naturally within foods, but may also be produced by bacteria as part of the fermentation process. The evidence supporting their role in the provocation of headache will be presented below.

Histamine intolerance syndrome is suspected when persons report flushing, pruritus, wheezing, hives, fatigue, or sneezing upon ingestion of foods that have high histamine content.<sup>66</sup> These foods include some fish, cheeses, processed meats, fruits including strawberries/tomatoes, fermented foods, and alcoholic beverages. Pretreatment with an oral antihistamine has been shown to decrease the frequency of headache after ingestion of foods and/or beverages with high histamine content in those with "histamine intolerance syndrome."<sup>67</sup>

Studies suggest that the histamine intolerance syndrome results from an imbalance of histamine intake and degradation. Foods with extremely high histamine content can produce symptoms of histamine intolerance as evidenced by scombroid poisoning that occurs after the ingestion of spoiled fish. Conversely, decreased degradation of histamine can also cause this syndrome. Diamine oxidase (DAO) is an enzyme

that degrades histamine in the gut and its activity is decreased in persons with histamine intolerance syndrome.<sup>68,69</sup> Decreased activity of DAO is common in persons with migraine, occurring in 87% of these individuals in one study.<sup>70</sup> Polymorphisms in DAO that decrease enzyme activity have also been associated with an increased prevalence and disability of migraine headache.<sup>71,72</sup> Therefore, decreased activity and/or certain polymorphisms of the DAO enzyme may identify persons that are predisposed to develop histamine intolerance and migraine.

Tyramine is found in a number of foods and beverages including cheese, wine, broad beans, sausage, and yeast extracts.<sup>73</sup> The enzymes that catabolize tyramine are monoamine oxidase (MAO) enzymes, diamine oxide, and enzymes that sulfoconjugate tyramine. Tyramine was first contemplated as a headache trigger as a result of case reports of hypertensive crises and severe headaches that developed in persons receiving MAO inhibitors that eat foods high in tyramine content.<sup>74</sup> Serum levels of tyramine are elevated in patients with chronic migraine as compared to controls and persons with other headache disorders.<sup>75</sup>

There have been six positive and four negative randomized controlled trials in which persons were challenged with either oral tyramine or placebo.<sup>76-85</sup> Most of the positive studies were from one group and there may have been methodological issues with many of these trials (eg, unequal allocation of tyramine vs placebo, period effect with crossover design).<sup>65</sup> There have been two clinical studies in which persons with migraine received either a low tyramine or placebo diet.<sup>86,87</sup> Neither study demonstrated any difference in the frequency of migraine and/or headache with a low tyramine diet as compared to placebo. Therefore, there is inconclusive evidence that tyramine precipitates attacks of headache or migraine.

#### Alcohol

Alcohol is one of the most commonly reported dietary trigger factors for migraine. In fact, 29-36% of migraineurs self-report that alcohol precipitates attacks of migraine.<sup>1,3,88</sup> Most cross-sectional studies have reported an inverse association between the prevalence of migraine and alcohol consumption, which likely reflects the fact that migraineurs tend to avoid alcoholic beverages. Peres et al<sup>8</sup> performed an electronic diary study and demonstrated that migraine attacks were associated with consumption of an alcoholic beverage in 2.5% of persons with migraine.<sup>89,90</sup> Wober et al found that beer consumption was actually associated with a decreased occurrence of migraine and headache attacks.<sup>91</sup> Another diary study found that alcohol was more likely to be a trigger factor for migraine when it was consumed during a stressful time period.<sup>92</sup> Thus epidemiological data suggest that alcohol is associated with an increased frequency of migraine attacks in some migraineurs and a decreased frequency in others.

There have been several provocation studies of wine in persons with migraine. Littlewood et al randomized 19 migraineurs that identified red wine as a trigger factor to drink either red wine or vodka.<sup>93</sup> They chilled the beverages to disguise their taste and participants drank from a dark straw so that they could not discern its color. Attacks of migraine headache were significantly more likely after consumption of red wine as compared to that of vodka (9/11 [82%] vs 0/8 [0%];  $P < .001$ ). However, it was unlikely that blinding was maintained as the consistency of wine and vodka are completely different. Trethewie reported that migraine was triggered in 5/17 provocation tests after consumption of a claret.<sup>94</sup> Wines with the highest histamine content were more likely to trigger migraine attacks.

#### Chocolate

Chocolate has been self-reported to be a precipitant for migraine headaches in 2-22% of persons with migraine.<sup>3,5,95-98</sup> A recent diary study found that migraine was more common on days with exposure to chocolate consumption as compared to those without exposure, but this occurred in only 2.5% of migraineurs.<sup>8</sup> Another diary study reported that an exposure to chocolate was more likely to be encountered on migraine than non-migraine headache days.<sup>99</sup> Therefore, epidemiological data might suggest an association between chocolate consumption and attacks of migraine, but only in a minority of persons with migraine.

There have been several double-blinded placebo-controlled provocation studies with chocolate. Gibb et al found that migraine was triggered in 5/12 (42%) subjects given chocolate, while 0/8 (0%) given placebo experienced an attack ( $P$  value = .051).<sup>100</sup>

Marcus et al performed a double-blinded cross-over study of 81 female subjects with chronic recurrent headache.<sup>101</sup> Each subject received four provocation trials, two with chocolate and two with carob. The incidence of headache did not differ between groups (22.7% with chocolate vs 20.5% with carob;  $P < .68$ ). Thus there are scant data that chocolate is a trigger factor for headache or migraine. We cannot rule out the possibility that chocolate is a trigger factor for a small percentage of persons with migraine or headache disorders.

#### Nitrites

Nitrites are preservatives found in processed meats such as bacon, sausage, ham, and lunch meats. They inhibit the growth of certain microbes such as *Clostridium botulinum*, and they preserve the color and flavor of meats. Nitrites were first implicated as migraine triggers based upon a case report in 1972 in which a patient reported headaches after ingestion of frankfurters, bacon, salami, and ham.<sup>102</sup> The patient later underwent a blinded challenge with an aqueous solution that contained either nitrites or sodium bicarbonate. The solution provoked a headache in 8/13 nitrite and 0/8 placebo challenges.

A later diary study found that 5% of persons with migraine were statistically more likely to have an attack on days in which they have consumed nitrites/nitrates.<sup>8</sup> There have been fewer reports of nitrites triggering headaches in recent years, which could be secondary to a government mandated reduction in the quantity of nitrites placed in foods for fear of carcinogenicity from nitrosamines.<sup>103</sup>

### **IgG Positive Foods**

The identification of IgG specific antibodies to foods is another method to identify foods that may trigger headache and/or migraine. There have been three randomized controlled trials (RCT) to determine whether identification of IgG-positive foods and their subsequent avoidance decreases the frequency of migraine.

Alpay et al performed a study in which 30 persons with migraine were tested for IgG antibodies to 266 food antigens.<sup>104</sup> They were randomized to a 6-week diet that either included or excluded foods that were positive for IgG antibodies. The group that excluded IgG positive foods had a statistically significant reduction in the frequency of headache compared to baseline (10.5 days to 7.5 days;  $P < .001$ ), while the group that included these foods had no change from baseline.

Mitchell et al randomized 167 individuals to a diet that excluded IgG positive foods or a sham diet.<sup>105</sup> As compared to baseline, they found a statistically significant reduction in the frequency of headache days in the group that excluded IgG positive food at 4 weeks (eg, 1-day reduction), but not at the 12-week time period, which was the primary outcome measure for the study. The main weakness of this study was that participants were simply mailed their diets with no verbal instruction on maintenance of their diets, which may have reduced compliance with their diets.

Aydinlar et al performed a study in which 21 patients with both migraine and irritable bowel syndrome received IgG food testing.<sup>106</sup> They were randomized to a diet that eliminated or included the IgG positive foods and then crossed over to the opposite diet. As compared with baseline there was a reduction in the frequency (4.8 vs 2.7;  $P < .001$ ), duration (1.8 vs 1.1 days), and severity (8.5 vs 6.6 on a visual analog scale;  $P < .01$ ) of attacks during the elimination diet and no change in these measures during the diet that included IgG positive foods. Therefore, two of the three randomized controlled trials suggest that diets that eliminate IgG positive foods provide a modest preventative benefit for migraine.

### **Gluten**

Gluten-free diets are a fad in today's culture and are most commonly used in patients with celiac sprue and non-celiac gluten sensitivity. Both of these disorders have extra-intestinal symptoms that include headache/migraine, and these symptoms have been reported to improve with a low gluten diet.<sup>107,108</sup>

Therefore, it is not uncommon for headache patients to inquire about the utility of a gluten free diet in the management of their headache disorders.

The prevalence of celiac sprue is 1% in the general population, but may approach 2-4% in persons with migraine or other headache disorders.<sup>107-109</sup> Likewise, its prevalence is 3-5% in patients with irritable bowel syndrome, particularly the diarrhea predominant subtype, which is a common comorbidity in persons with migraine.<sup>110,111</sup> Autoimmune disorders may also increase the risk for celiac sprue.<sup>112-114</sup> The intestinal symptoms of celiac sprue include abdominal pain, diarrhea, abdominal bloating, and flatus, while the extra-intestinal manifestations include ataxia, myopathy, encephalopathy, neuropathy, and migraine.<sup>115</sup> Patients with celiac sprue may also have white matter lesions on magnetic resonance imaging of the brain.<sup>116</sup>

Sprue pathogenesis is attributed to activation of T cells by gluten and formation of autoantibodies to tissue transglutaminase (TTG). The diagnosis is first suspected with positive IgA antibodies for TTG and/or gliadin. The diagnosis of celiac sprue is confirmed with a small bowel biopsy on upper endoscopy demonstrating villous atrophy. The treatment is a gluten free diet, which has also been shown to reduce the frequency of migraine in small case series.<sup>107,108,116</sup>

Non celiac gluten sensitivity (NCGS) is also a disorder in which gastrointestinal symptoms occur with exposure to wheat products, but this syndrome lacks the IgA antibodies to TTG that are characteristic of celiac sprue.<sup>117</sup> One study found that IgG anti-gliadin antibodies were positive in 57% of persons with NCGS.<sup>118</sup> Even though it is called NCGS, it has been theorized that gluten may not even be the protein responsible for this syndrome. Patients have similar gastrointestinal and extra-intestinal symptoms to celiac sprue.<sup>117</sup> The diagnosis is established by double-blinded gluten food challenge. A positive challenge test would be an improvement in gastrointestinal symptoms with the gluten-free diet followed by a recrudescence of symptoms after a double-blinded gluten food challenge. Small bowel biopsies do not demonstrated villous atrophy, but may be normal or only show a lymphocytic infiltrate. There are no specific studies to demonstrate that headaches improve with a gluten-free diet, but a recent study found a statistical significant reduction in "other" extra-intestinal symptoms with a gluten-free diet as compared to baseline in patients with documented NCGS.<sup>119</sup>

The above studies suggest that gluten might be associated with headache in patients with celiac sprue or possibly in those with NCGS. One might consider testing for celiac disorders in migraine patients with a history of diarrhea, ataxia, neuropathy, or autoimmune disorders. We would recommend testing for IgA antibodies against TTG and gliadin to screen for celiac disease and IgG antibodies against gliadin to screen

for NCGS. It may also be necessary to perform a small bowel biopsy to confirm the presence or absence of celiac sprue. There is no current evidence for use of a low gluten diet to treat headaches in persons that do not have one of these two disorders.

### Pro-Algesic Foods

The term “pro-algesic” foods was coined by Brian Cairns and refers to foods or ingredients within food that precipitate pain upon their ingestion or withdrawal.<sup>120</sup> Caffeine withdrawal and administration of MSG (dissolved in liquid) have the strongest evidence of being “proalgesic” for headache as evidenced by multiple positive provocation studies. Aspartame has conflicting evidence with two positive and two negative provocation studies. Observational studies provide modest evidence that alcohol, gluten, and histamine are pro-algesic for headache in subgroups of patients. There is little to no evidence that chocolate is a trigger for headache and/or migraine.

Several factors influence whether a given food or beverage might trigger headache. Some foods may precipitate headache upon exposure, while others may only cause headache upon withdrawal (eg, caffeine). High dosages of some foods or ingredients may be necessary to trigger a headache as evidenced by the studies involving MSG, caffeine, and aspartate. Some foods or ingredients precipitate headache only in subgroups of persons with very specific immunological responses to food, such as celiac sprue and in those positive for IgG antibodies. Others may require ingestion over days or weeks to precipitate headache, such as aspartame or MSG. Genetic factors may exist that render some individuals more vulnerable to the effects of one food, ingredient, or beverage as compared to another (eg, caffeine). The sheer number of factors that may have moderate response to a dietary trigger might explain the heterogeneity of dietary triggers encountered in headache patients.

### Elimination Diets

Elimination diets require the identification of provocative foods, beverages, or ingredients and their subsequent elimination from the diet. There are three different approaches to identify foods, beverages, or ingredients for an elimination diet. Persons may have noticed such a high frequency of headache or migraine upon exposure to the dietary trigger that there is no doubt that an association exists. In that case they may wish to avoid that food or beverage altogether. The risk with this approach is that it is entirely dependent on the ability of the observer to recognize the association and is subject to false positive and negative attributions.

A second approach for elimination diet intervention would be to use serological testing to identify foods to be eliminated. This would pertain to IgG food testing as well as serological testing for celiac disorders. Testing for celiac disorders might only be performed in those with higher risk of celiac

disorders, which includes those with irritable bowel disorder, peripheral neuropathy, ataxia, or other autoimmune diseases. A third approach would be to complete a food diary in which all food and beverages are recorded on a given day along with the presence or absence of headache or migraine. The patient and his/her treating physician would then need to identify if headaches were more common on exposed as compared to non-exposed days.

There are also a number of problems with interpretation of food diaries.<sup>4</sup> First, exposure to a given food may not always precipitate a headache, and the food effect may depend on the quantity consumed, which may be difficult to quantify. Second, there may also be a lag time of 1-2 days between exposure to a food trigger and the development of headache. Third, it is difficult to know what threshold to use to define an association between food and migraine. For example, should one consider a food to be a trigger if headache occurs 50%, 75%, or 90% of the time upon exposure? A past review of migraine trigger factors recommended that a food might be considered a trigger if headache occurred in  $\geq 50\%$  of instances within one day after exposure.<sup>4</sup> Fourth, there may be multiple trigger factors in a patient, and it may be difficult to define a single trigger among multiple triggers. Fifth, individual foods contain many different ingredients, and it may be virtually impossible to identify one specific ingredient as the trigger. For the above reasons it might be best to use a food diary as part of an app in which it can be determined statistically if headache is more common on exposed as compared to non-exposed days.

## CONCLUSIONS

There are a number of foods that have been demonstrated to trigger attacks of headache and/or migraine upon exposure or withdrawal to these substances. The response of a headache patient to a given dietary triggers may depend on the dosage and timing of exposure, as well as genetic factors. Identification of dietary triggers can be challenging given the numerous foods and ingredients consumed on a daily basis by the typical headache patient. Food diaries and/or specific serologic testing might be employed to identify and later eliminate these foods from their diets. Further studies are needed to define the precise role of elimination diets in the management of the headache patient.

## Statement of Authorship

### Category 1

#### A. Conception and Design

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#### B. Acquisition of Data

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**C. Analysis and Interpretation of Data**

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**Category 2****A. Drafting of Manuscript**

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**Category 3****A. Final Approval of the Completed Manuscript**

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