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Pharmacologic Agents in Food

Some investigators hold that food-induced migraine is the result of chemical agents found in foods. Tyramine is the most commonly incriminated migraine provoker; however, phenylethylamine, nitrites, alcohol, and aspartame have also been reported to precipitate symptoms.

Tyramine: As a vasoactive amine, Tyramine may provoke vascular headache. Foods rich in tyramine are aged cheeses, fermented sausages, sour cream, wines, pickled herring, and pods of broad beans. Although tyramine is often touted as an important provoker of headache, controlled studies yield conflicting results.

Hanington in 1967, using placebo-controlled challenges with 100 mg of tyramine, reproduced migraine symptoms in four of four subjects with a history of food-induced migraine. Four patients without history of food-induced migraine had no symptoms with tyramine while two of four who were unsure of the role of food in their headaches reported migraine with tyramine. Smith and colleagues used multiple double-blind challenges in 45 patients with food-induced migraine. Ninety-four tyramine challenges (125 mg) precipitated migraine on 75 occasions whereas 60 placebo challenges led to migraine in only 5 instances.

A number of other studies, however, have not demonstrated an important role for tyramine. Moffett and associates, in a double-blind, placebo-controlled trial, studied 10 patients with migraine alone, with migraine and epilepsy, and 8 who felt tyramine-containing foods provoked headache. Patients ingested 125 mg of tyramine or placebo and recorded symptoms for 48 hours. None of the subjects with migraine alone reported headache with tyramine. Tyramine produced headache in one patient with migraine and epilepsy. In subjects with presumed tyramine-induced migraine, headaches were as common with placebo as with tyramine. Ziegler studied 80 patients with migraine using 200 mg of tyramine in a double-blind, placebo-controlled trial. Forty-nine had no symptoms with either active or placebo challenge, 12 had migraine with both, 11 had headache with placebo alone, and only 8 had migraine with tyramine alone. Finally, Forsythe and Redmond challenged 62 children in a blinded fashion with 100 mg of tyramine. Only 12 reported headache after tyramine. In a second trial with 38 children, only 5 had migraine with tyramine. From the above data, it appears that tyramine may precipitate headaches in a few individuals, but is **not** a major cause of migraine.

Phenylethylamine: Phenylethylamine, another vasoactive amine, is found in certain cheese, red wines, and chocolates. Sandler and coworkers reported 36 subjects who felt chocolate provoked migraine. They were challenged in single blind fashion with either 3 mg of phenylethylamine or placebo in capsules. Eighteen reported migraine with phenylethylamine, while six had migraine with placebo. Peatfield reported open challenges with 10 g of plain chocolate in six patients felt to have chocolate-induced migraine. Five reported migraine within 8 hours after the ingestion.

However, Moffett and colleagues studied 25 subjects with a history of chocolate or cocoa-induced migraine with double blind, placebo-controlled challenges. Eight reported headache only with chocolate, 5 only with placebo, 1 with both, and 11 with neither. Fifteen repeated the challenges and only five reported headache with chocolate alone. Interestingly, of those participating in both trials, only two consistently reported migraine after chocolate alone. Again, divergent results are seen between studies; however, dose may play a role. Scheitzer and coworkers analyzed a number of chocolate preparations and found approximately 150 times less phenylethylamine than was used in the challenges by Sandler. They concluded that either migraine possibly associated with the ingestion of chocolate is not due to phenylethylamine, or migraine patients are sensitive to extremely low levels of this substance.

Nitrites: Potassium and sodium nitrites have been used as food preservatives for years. Foods with the highest concentrations of nitrites include hot dogs, bacon, ham, lunchmeats, smoked fish, and some imported cheese. Headaches following the ingestion of frankfurters or other cured meats have been reported and are pulsatile approximately 50% of the time.

Ethyl Alcohol: Migraine patients often mention alcohol as a provoker of headaches, typically beginning 30 to 45 minutes after ingestion. Certain red wines may contain tyramine or phenylethylamine. Well-controlled studies addressing the precipitant in alcoholic beverages are lacking.

Aspartame: In 1984 the Centers For Disease Control interviewed 517 subjects who had reported symptoms with the ingestion of aspartame-containing products. Of these, 346 reported neurological or behavioral symptoms including headache, dizziness, and mood alterations. Aspartame as a provoker of migraine had been described in a single case report. When 40 subjects with a history of aspartame-induced headache were studied with double blind, placebo-controlled challenges, no difference in headache frequency was observed when aspartame was given versus placebo. However, a more recent study, using a different double blind challenge protocol, demonstrated different results.