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From: Mark Gold [mgold@shelltown.net]
Sent: Sunday, January 12, 2003 11:12 PM
To: fdadockets@oc.fda.gov
Subject: Docket # 02P-0317 Recall Aspartame as a Neurotoxic Drug: File #4: Reported Aspartame Toxicity Reactions

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To: FDA Dockets Submittal

From: Mark D. Gold
Aspartame Toxicity Information Center
12 East Side Dr., Suite 2-18
Concord, NH 03301
603-225-2110

Date: January 12, 2002

Please find below Evidence File #4: Reported Aspartame Toxicity Effects

Reported Aspartame Toxicity Effects

Q. What are the reported reactions to aspartame ingestion?

How often are such effects seen?

Answer

==> What are the reported reactions to aspartame ingestion?

We will limit our discussion in this FAQ to reported toxicity reactions to aspartame ingestion. Controlled studies showing problems with aspartame ingestion will be discussed in another FAQ. Toxicity reactions to aspartame can be divided into three types:

1. Acute toxicity reactions occuring within 48 hours of ingestion of an aspartame-containing product.

2. Chronic toxicity effects occuring anywhere from several days of use to appearing a number of years (i.e., 1-20+ years) after the beginning of aspartame use.

3. Potential toxicity effects that would be nearly impossible for the user to recognize the link to aspartame.

In an epidemiological survey which appeared in the Journal of Applied Nutrition (Roberts 1988), 551 persons who have reported toxicity effects from aspartame ingestion were surveyed. The adverse effects found cover a subset of reported acute and chronic toxicity effects from aspartame. What follows is a listing of the adverse health effects which were found.

	# of people	(%)

Eye		
- Decreased vision and/or other eye problems (blurring, "bright flashes," tunnel vision)	140	(25%)
- Pain (or or both eyes)	51	(9%)
- Decreased tears, trouble with contact lens, or both	46	(8%)
- Blindness (one or both eyes)	14	(3%)
Ear		
- Tinnitus ("ringing," "buzzing")	73	(13%)
- Severe intolerance for noise	47	(9%)
- Marked impairment of hearing	25	(5%)
Neurologic		
- Headaches	249	(45%)
- Dizziness, unsteadiness, or both	217	(39%)
- Confusion, memory loss, or both	157	(29%)
- Severe drowsiness and sleepiness	93	(17%)
- Paresthesias ("pins and needles," "tingling") or numbness of the limbs	82	(15%)
- Convulsions (grand mal epileptic attacks)	80	(15%)
- Petit mal attacks and "absences"	18	(3%)
- Severe slurring of speech	64	(12%)
- Severe tremors	51	(9%)
- Severe "hyperactivity" and "restless legs"	43	(8%)
- Atypical facial pain	38	(7%)
Psychologic-Psychiatric		
- Severe depression	139	(25%)
- "Extreme irritability"	125	(23%)
- "Severe anixiety attacks"	105	(19%)
- "Marked personality changes"	88	(16%)
- Recent "severe insomnia"	76	(14%)
- "Severe aggravation of phobias"	41	(7%)
Chest		
- Palpitations, tachycardia (rapid heart action), of both	88	(16%)
- "Shortness of breath"	54	(10%)
- Atypical chest pain	44	(8%)
- Recent hypertension (high blood pressure)	34	(6%)
Gastrointestinal		
- Nausea	79	(14%)
- Diarrhea	70	(13%)
Associated gross blood in the stools (12)		
- Abdominal pain	70	(13%)
- Pain on swallowing	28	(5%)
Skin and Allergies		
- Severe itching without a rash	44	(8%)
- Severe lip and mouth reactions	29	(5%)
- Urticaria (hives)	25	(5%)
- Other eruptions	48	(9%)
- Aggravation of respiratory allergies	10	(2%)
Endocrine and Metabolic		
- Problems with diabetes: loss of control; precipitation of clinical diabetes; aggravation or simulation of diabetic complications	60	(11%)
- Menstrual changes	45	(6%)
Severe reduction or cessation of periods (22)		

- Paradoxic weight gain	34	(5%)
- Marked weight loss	26	(6%)
- Marked thinning or loss of the hair	32	(6%)
- Aggravated hypoglycemia (low blood sugar attacks)	25	(5%)
Other		
- Frequency of voiding (day and night), burning on urination (dysuria), or both	69	(13%)
- Excessive thirst	65	(12%)
- Severe joint pains	58	(11%)
- "Bloat"	57	(10%)
- Fluid retention and leg swelling	20	(4%)
- Increased susceptibility to infection	7	(1%)

There are other clinical reports in the scientific literature of aspartame-caused toxicity reactions including Blumenthal (1997), Drake (1986), Johns (1986), Lipton (1989), McCauliffe (1991), Novick (1985), Watts (1991), Walton (1986, 1988), and Wurtman (1985).

Many pilots appear to be particularly susceptible to the effects of aspartame ingestion. They have reported numerous serious toxicity effects including grand mal seizures in the cockpit (Stoddard 1995). Nearly 1,000 cases of pilot reactions have been reported to the Aspartame Consumer Safety Network Pilot Hotline (Stoddard 1995). This susceptibility may be related to ingesting methanol at altitude as suggested in a letter from Dr. Phil Moskal, Professor of Microbiology, Biochemistry, and Pathology, Chairman of the Department of Pathology, Director of Public Health Laboratories (Moskal 1990), or it may simply be that some pilots tend to ingest large quantities of aspartame during a flight. Whatever the case, numerous warnings about aspartame dangers have appeared in piloting journals including The Aviation Consumer (1988), Aviation Medical Bulliten (1988), Pacific Flyer (1988), CAA General Aviation (1989), Aviation Safety Digest (1989), General Aviation News (1989), Plane & Pilot (1990), Canadian General Aviation News (1990), National Business Aircraft Association Digest (NBAA Digest 1993), International Council of Air Shows (ICAS 1995), and the Pacific Flyer (1995). Both the U.S. Air Force's magazine "Flying Safety" and the U.S. Navy's magazine, "Navy Physiology" published articles warning about the many dangers of aspartame including the cumlative deliterious effects of methanol and the greater likelihood of birth defects. The articles note that the ingestion of aspartame may make pilots more susceptible to seizures and vertigo (US Air Force 1992).

Countless other toxicity effects have been reported to the FDA (DHHS 1995), other independent organizations (Mission Possible 1996, Stoddard 1995), and independent scientists (e.g., 80 cases of seizures were reported to Dr. Richard Wurtman, Food (1986)). Samples of some aspartame toxicity reactions reported on the Internet can be found on the Aspartame (NutraSweet) Toxicity Info Center web page:

http://www.tiac.net/users/mgold/aspartame/

Frequently, aspartame toxicity is misdiagnosed as a specific disease. This has yet to be reported in the scientific literature, yet it has been reported countless times to independent organizations and scientists (Mission Possible 1994, Stoddard 1995). In other cases, it has been reported that chronic aspartame ingestion has triggered

or worsened certain chronic illnesses. Nearly 100% of the time, the patient and physician assume that these worsening conditions are simply a normal progression of the illness. Sometimes that may be the case, but many times it is chronic aspartame poisoning.

According to researchers and physicians studying the adverse effects of aspartame, the following list contains a selection of chronic illnesses which may be caused or worsened by the chronic, long-term ingestion of aspartame. (Mission Possible 1994, Stoddard 1995)*:

Brain tumors	Multiple sclerosis
Epilepsy	Chronic faigue syndrome
Parkinson's Disease	Alzheimer's
Mental retardation	Lymphoma
Birth defects	Fibromyalgia
Diabetes	Arthritis (including Rheumatoid)
Chemical Sensitivities	Attention Deficit Disorder

*Note: In some cases such as MS, the severe symptoms mimic the illness or exacerbate the illness, but do not cause the disease.

Also, please note that this is an incomplete list. Clearly, ingestion of a very slow poison (as discussed in other FAQs) is not beneficial to anyone who has a chronic illness.

Finally, potential toxicity effects from aspartame including brain cancer (as seen in pre-approval research) and effects on fetal brain and nervous system development will be discussed in other FAQs.

==> How often are such effects seen?

Until recently approximately 90% of aspartame sales were in the United States (Monsanto 1994). Other countries are now being inundated with aspartame, but it will be some time until they begin to feel the full effects of aspartame toxicity on the general population. Since the U.S. has some history of significant use, we will limit the discussion to the frequency of effects in the U.S.

There have been well over 7,000 aspartame toxicity reactions officially received by the U.S. Food and Drug Administration between 1982 (after aspartame was first approved) until 1995 (DHHS 1993, DHHS 1995). From this figure, we can estimate the number of actual toxicity reactions observed.

FDA officials believe that as little as 1% of the serious adverse drug reactions are reported to the FDA (Kessler 1993). Using a reported rate of 1%, we would estimate that there have been 700,000 recognized aspartame toxicity reactions in the U.S. since 1982. However, there are a number of significant adjustments that must be made before we can accept this estimate.

1. Most physicians are aware of the Adverse Reaction Monitoring System (ARMS) and are encouraged by the FDA to report serious adverse drug reactions (Kessler 1993). Physicians are not encouraged by the FDA to report aspartame toxicity reactions to the FDA (Food 1995). The lay public is generally unaware of ARMS and much less likely to report adverse reactions to the FDA. Therefore, this would lower the estimated reporting rate below 1%. Let us make a small adjustment and estimate a 0.88% reporting rate.

2. It was pointed out by James Turner, Esq. in a letter to the then FDA Commissioner Frank Young that no program to monitor aspartame toxicity reactions was created until February 1984, two years after aspartame approval began (Turner 1984). This would probably add at least 1,200 reported reactions (probably much more), so that we should use 8,200 toxicity reaction reports. In addition, a Freedom of Information act request determined that the regional FDA offices had been told that only "serious" complaints should be forwarded to the FDA headquarters (Turner 1984). "Serious" complaints were complaints where the illness was severe enough to require the attention of a physician. Since this happened between 1984 (when the monitoring system began) and 1985, we can estimate an additional 300 toxicity reactions would have been reported for a total of 8,500.

3. In 1987, it was brought out at U.S. Congressional Hearings that the FDA had been transferring aspartame toxicity reaction calls to the AIDS Hotline (Turner 1987). In addition, it was reported by James Turner, Esq. of Community Nutrition Institute (CNI) that there were numerous cases of people calling the FDA to report toxicity reaction and they were told that there was no connection between aspartame and adverse reactions and no other information was taken by the FDA. While this may not effect the reporting rate after the start of 1988, it would significantly effect the reporting rate before that time. Let us make another small adjustment and estimate a 0.78% reporting rate.

4. Perhaps the biggest reduction in the reporting rate comes from the fact that Commissioner Kessler's estimated 1% reporting rate for adverse drug reactions involves only "serious" adverse reactions. The rate for reporting *all* drug reactions (if such reporting were done) would almost certainly be no more than 0.5%. Therefore, if we cut our current estimated reporting rate of 0.78% in half, the estimated reporting rate for *all* toxicity reactions to aspartame (including serious or mild) would be no more than 0.39%.

During the first couple of years that aspartame was on the market, there was publicity that would likely have increased the reporting rate. However, since the FDA did not have a monitoring system in place until February 1984, the estimated increased number of reports will not be that much. I will reduce the number of reports by 1,000 to 7,500 to take this into account.

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We now have approximately 7,500 reports at an estimated reporting rate of 0.39%. This totals approximately 1.9 million *recognized* aspartame toxicity reactions in the U.S. between 1982 and 1995. These reactions run anywhere from mild to very serious illnesses.

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It is very important to understand, however, that 1.9 million represents only those toxicity reactions that have been discovered by users and/or healthcare practitioners. Quite often, I encounter case histories were people suffered for long time and did not make the connection. For example:

"I have suffered from Migraines for years. As soon as I gave up Nutrasweet my migraines disappeared. All those Cat Scans, MRI's.....for nothing."

"Since I last wrote my brother has been off nutrisweet since then. My brothers lupus type of symptoms completely went

> away. My brother has been a physician for over 10 years .. his doctor (a specialist) who has been treating him has seen the significant difference and wants to write a research paper on this .. my brothers physician has now started prescribing getting off nutrisweet for his other patients."

Therefore, I believe that in addition to the estimated 1.9 million people in the U.S. who have recognized aspartame toxicity reactions in themselves (from serious to mild), there are many times that number who are suffering from some of the symptoms mentioned above and that they do not recognize that chronic aspartame use is the cause or at least a contribuatory factor. I would estimate that *at least* 7.6 million others are suffering from some symptoms related to aspartame use (many mild symptoms, but many serious ones as well) and do not recognize the connection.

In addition to the estimated 1.9 million recognized reactions and 7.6 million unrecognized reactions in the U.S., it is very important to note that aspartame has been used in significant amounts in the U.S. for a relatively short time. A U.S. Department of Agriculture report noted that it wasn't until approximately 1987 that aspartame was used in significant amounts in the U.S. (USDA 1988). Therefore, aspartame had been used for only nine (9) years in signficant amounts through 1995. When one considers that the damage from aspartame is often silent and cumulative (much like chain-smoking cigarettes), one can see that a couple of generations of aspartame use might be disasterous!

The FDA and NutraSweet have claimed that the number of reported adverse reactions have declined substantially since the mid-1980s (Pauli 1995, Butchko 1994). In addition, the FDA recently claimed that the number of reported toxicity reactions for 1995 was only 11 (WSJ 1996)! It is important to realize that during the mid-1970s the FDA was investigating wrong-doings of the aspartame manufacturer and stated the facts exactly as they found them:

> "[The manufacturer] lied and they didn't submit the real nature of their observations because had they done that it is more than likely that a great number of these studies would have been rejected simply for adequacy. What Searle did, they took great pains to camouflage these shortcomings of the study. As I say filter and just present to the FDA what they wished the FDA to know and they did other terrible things for instance animals would develop tumors while they were under study. Well they would remove these tumors from the animals." [FDA Toxicologist and Task Force member, Dr. Andrian Gross (Wilson 1985)]

During the late 1970s and early 1980s, a number of key government and FDA officials left their jobs to work with companies related to the aspartame industry (GAO 1986). This included key FDA officials such as the head of the FDA Bureau of Foods becoming a Vice President of the National Drink Association and the FDA Commissioner becoming a high-paid consultant for the manufacturer's PR firm, Burston Marsteller (Gordon 1987). After this period of time, there was no scientific evidence and no amount of serious toxicity reports that could get the FDA to seriously consider funding independent, properly-conducted (e.g., chronic exposure) research. That appearance of the FDA being under the total control of the manufacturer, Monsanto, continues to this day.

I include these comments about the FDA to demonstrate why no independent scientist familiar with the aspartame issue takes statements from the FDA such as "11 reported reactions in 1995" seriously. There are many people, including myself who have received that many toxicity reaction reports in a single day during 1995. The reality is that independent organizations have noted that aspartame toxicity reaction reports given to them have *increased* every year since the late 1980s (Stoddard 1995). It is also important to note that in mid-1995, the FDA admited that it had stopped recording aspartame toxicity reactions (Food 1995). That may have something to do with why the numbers that the FDA reported to the Wall Street Journal (WSJ 1996) were so small!

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