Aspartame: Artifice and the Science of Sweet

by

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B.A. (Honours) English and Life Sciences
Queen's University, 2010

Submitted to the Program in Writing and Humanistic Studies
in Partial Fulfillment of the Requirements for the Degree of

Master of Science in Science Writing
at the
Massachusetts Institute of Technology

September 2011

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ABSTRACT

Aspartame has become an extremely popular artificial sweetener since its entry into the American market in 1981. Humans have an evolutionary preference for sweet tastes, and artificial sweeteners became a mainstream alternative to cane sugar in the 20th century for people looking to cut calories. Saccharin and cyclamates, both discovered accidentally in early chemistry labs, set the scientific precedent for low-calorie sweeteners and also built the consumer base that would lead to aspartame's rise after its own accidental discovery in 1965. This thesis takes a journalistic look at how artifice came to satisfy the human sweet tooth. Drawing on expert interviews, scientific papers, historical accounts and congressional records, it also examines some of the health complaints like headaches and seizures that have been attributed to aspartame's breakdown products, such as phenylalanine. Even after extensive FDA testing has found little scientific proof for many of these claims, controversy and uncertainty about aspartame persist. There are also new challenges: researchers are now investigating the idea that consuming diet drinks may actually contribute to weight gain. At the same time, as obesity rates climb and schools and cities look to ban calorie-dense sodas, many public health experts welcome aspartame because it poses a less clear-cut risk than sugar.

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ASPARTAME: ARTIFICE AND THE SCIENCE OF SWEET

The first of August 1985 dawned foggy and grey in the District of Columbia. Stepping out into the humid summer streets, a Senator by the name of Howard Metzenbaum was about to begin a day that would define his career. At 68 years old, the Ohio representative was no stranger to argument. Known for his fierce resolve, Senator Metzenbaum was nine years into his nineteen-year stint on Capitol Hill and already living up to his nickname "Senator No," so given because of a nearly flawless track record of arguing down legislation he opposed.

Later described by the *Los Angeles Times* in his obituary as "a firebrand who didn't need a microphone to hold a full auditorium spellbound," Senator Metzenbaum was known as an ardent advocate for workers' rights and gun control. But on this summer morning in 1985, the feisty senator had his sights set on a different, more delicate cause. His target was a fine white powder called aspartame that was known to pack an unusual punch of sweetness.

With a head of ivory hair and square glasses like picture frames around his artful eyes, he sought the Senate's attention. Routine budget talk aside, the floor belonged to Metzenbaum. Around him, the Senate Chamber was grand and airy. Yolk-yellow walls and royal blue carpeting enclosed a space accented with marble and a semicircle of rich mahogany desks. "Mr. President," he started. "Today I am introducing a bill called 'the Aspartame Safety Act of 1985.' I consider this legislation the absolute minimum that Congress needs to do to in order to protect the health and safety of the 100 million American consumers who are using this chemical sweetener."

Metzenbaum's bill called for further studies on the safety of the low-calorie chemical that sweetened the twenty billion cans of diet drinks he predicted Americans would consume that year. He wanted independent lab tests to get to the bottom of the headaches, seizures and memory loss that consumers claimed, in their letters to the Food and Drug Administration (FDA), were the result of an aspartame habit. He wanted these health complaints chronicled,

and he pushed for aspartame content to be labeled. Any new uses of the sweetener, Metzenbaum proposed, should be put on hold for one year or until the results of new tests could provide some comforting conclusions. Believing the original studies buttressing aspartame's approval were flawed and insufficient, he delivered his plea to the Senate: "We had better be sure that the questions which have been raised about the safety of this product are answered."

Despite his flair for debate, Metzenbaum was not the first person to take argument with aspartame. This Cleveland native who had built his career from humble beginnings, peddling flowers, magazines and razor blades to pay his way through college, just happened to have a Congressional soapbox from which to share his skepticism. Metzenbaum was stepping into a fight that, like the morning's storm, had been brewing over Washington for some time already.

Metzenbaum, who passed away in 2008, never did get the Aspartame Safety Act of 1985 approved. In an unusual turn of events, "Senator No" didn't get his way and his bill died in the Senate that summer. Two years after this failed attempt to curb aspartame's unbridled rise, Metzenbaum pushed one more time. On the third of November 1987, he chaired a Senate hearing, inviting consumers, scientists and FDA officials to share their views on the sweetener's safety. But at the end of the day, the hearing left the aspartame case back where Metzenbaum had found it, and where it remains today—shrouded in controversy, with opposing views on the evidence at hand and no satisfactory answers. The 1987 hearing was the last major attention aspartame was given in the United States Congress, but our appetite for the sweetener hasn't faded yet.

This is the story of sweetness: a craving that lies at the basis of the human diet, and a genetic quirk that played a key role in helping our early ancestors decide which foods were good to eat. Today, a taste for sweets is more universal than any other food preference among mammals. At first, humans satisfied the sweet tooth with cane sugar and had no interest in artifice. Then we did something odd: through a series of accidents starting in the late nineteenth century, chemists discovered that the pure, pleasant taste from cane fields could also be synthesized in chemistry labs at a lower calorie cost. Sweetness went artificial. Playing off the evolution of nutrition science and the country's response to one president's

heart attack, the dietary sweetener industry reached its apex with aspartame. Best in taste and in business savvy, aspartame was also met with the most vigorous public scrutiny. Today, artificial sweeteners comprise a giant industry built on mimicking the taste of sugar and are widely advertised to consumers as a way to keep thin. But it's easy to see they haven't helped—or maybe they've made matters worse. Today, an obesity epidemic coincides with a culture of calorie-free sweetness more pervasive than ever. How did we get here?

Nearly a quarter century after Metzenbaum raised the aspartame question in the United States Senate, people across the globe turn to it for sweetness. First introduced by the NutraSweet Company of Chicago in 1981, aspartame is now approved in over a hundred countries and used in some 6,000 food, beverage and pharmaceutical products. In America alone, two-thirds of the population use artificial sweeteners in daily life. But weight statistics clearly indicate we are no skinnier, despite having sipped diet sodas for decades. Some evidence suggests that using aspartame might even contribute to weight gain and still, accusations of ill health effects crop up, aided by support from new Internet communities. These anti-aspartame advocates tend to exist mainly on the fringe of a growing populace that doesn't pause to question artificial sweetness, but feeds a frequent craving for it.

Scientific research on aspartame has waned in recent years, but not because the safety debate has been neatly resolved. Questions and fears still linger, even after Metzenbaum's failed bill has been filed quietly away into Senate history. His concerns were dismissed, but through a look back at aspartame's story of sweetness and skepticism, it becomes clear that Metzenbaum was no lone wolf. His struggle represents the tangle of uncertainty and ambiguity that has shrouded artificial sweetness from the beginning. Through the knot of yet-unraveled questions, one wonder about Metzenbaum remains: maybe he was right.

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Across the campus of Yale University, November trees stand half-naked between redbrick buildings that slowly swell with people. Journalists, teachers and business professionals have come to this corner of New Haven, Connecticut to hear about the latest research at *New Horizons in Science.* At the front of one small room stands Dr. Leslie Curry, a blonde, fast-talking Research Scientist with the Yale School of Public Health. Her audience for the intimate lunchtime session is a group of well-dressed women who have come to hear

about heart health. Dr. Curry boots up her PowerPoint, shuts the door as the last straggler takes a seat, and surveys her thirteen attendees. Twelve women open Diet Coke cans in near synchrony. The seminar begins.

In the modern, middle-class hunt for pesticide-free produce, fair-trade coffee, organic dairy products and grain-fed, free-range chicken, the tabs on diet soda cans are cracking open more frequently than ever before. Twenty years ago, 101 million Americans drank artificially sweetened beverages. By 2007, that figure had nearly doubled to 194 million, notes Carolyn De La Peña, a cultural historian at the University of California, Davis and author of *Empty Pleasures.* But in this period of preoccupation with our food's origins and ingredients, aspartame remains relatively unconsidered by the millions of people who feed vending machines every day for a fizzy, calorie-free thirst quencher. It's oddly inconsistent that many health-conscious people, like Dr. Curry's crowd of educated women, flock to organic grocers and farmers' markets for the promise of something local or natural, but are generally content to sip aspartame-sweetened Diet Cokes, in the name of health or image, without much idea of what's inside or where it came from.

Diet drinks are perhaps the sweetener's most recognized use, but aspartame also lends sweetness to syrups, puddings, yogurt, chewing gum and tiny blue tabletop packets (labeled *Equal*) for tea and coffee. Aspartame is an attractive alternative to sugar because it's marketed as a zero-calorie sweetener. But it actually contains plenty of calories—exactly as many as sugar. If you were to place a pound of white sugar on one side of a balance scale and a pound of aspartame on the other, you would be looking at an equal 1,500 calories on each side. The reason we think of aspartame as being calorie-free has to do with the quantity used. Since aspartame is about two hundred times sweeter than sugar, manufacturers can achieve the same sweetness by using only a miniscule quantity. As such, virtually zero calories enter the equation.

The pound of sugar on the balance scale divides up into 96 teaspoons, 22 of which an average American consumes in one day, according to the American Heart Association. This sounds like a lot, until you tally up the sugar content of products like jam, orange juice, cereal, bread, raisins, yogurt and tomato sauce that fill even the healthiest shopping carts. Add in an

occasional candy bar or soda and you've hit 22 teaspoons, or flown straight by into higher digits.

At this rate, the American Heart Association estimates that it takes a typical person only four and a half days to plow through that pound of sugar. By contrast, it would take nearly six months for an extreme aspartame user to get through a pound of the chemical sweetener. And that's assuming they're consuming a whopping 75 packets of *Equal* per day, or 20 cans of diet soda. For the average user, it would probably take years to get through the pound of powder.

Both intensely sweet and calorically cheap, aspartame is a common example of an artificial sweetener that people turn to when looking to stave off weight gain or shed pounds. Aspartame's promise of sweetness without calories is counterintuitive, given that sugars found in nature tend to deliver sweet pleasure only at a caloric cost. Robert B. Shapiro, past President of the NutraSweet Company, used this idiosyncrasy to market aspartame as something revolutionary. In 1987, shortly after aspartame hit the shelves in the United States, he pointed out: "What we are saying to people is, 'you can have the pleasure without paying the price.' That's like saying there is such a thing as a free lunch."

It's as if aspartame gives the consumer a free pass, an invisible placard that reads: "This may be sweet, but I am not indulgent; I am making healthy, guilt-free choices." To be absolved of any guilt while indulging a craving is powerful, perhaps so powerful that we are easily won over—so enamored with aspartame's calorie-free, consequence-free idiosyncrasies that we fail to ask the questions we would of other foods. We forget to wonder where it came from, if it grows in nature, and if it can be found anywhere in the earth within a hundred miles of home.

Now a professor of American Studies, De La Peña once worked in the branding department for Coca Cola while finishing her doctoral degree. Her corporate work involved conducting market research, interviewing people—mostly female, she notes—who drank upwards of ten Diet Cokes every day. By figuring out what drove this extreme loyalty to the product, Coca Cola's marketing executives could use the knowledge to draw others in. "It was fascinating," She recalls. "Aspartame was a guiltless luxury for these women." Calorie-free sweetness offered a feeling of indulgent restraint that many found irresistible.

As De La Peña points out, this love affair was carefully crafted. It was no accident that aspartame came to have a stronghold on our fragile, self-conscious culture. We crave sweetness and desire thinness, but we are also wary of artifice. Man's relationship with artificial sweeteners started out shaky until threads as divergent as chemistry, war, body image and corporate savvy coincided to cement the match. Today, the market for aspartame is massive, it's growing, and it's pulsing to the beat of Coca Cola's latest ad campaign.

A cityscape, a spine-tingling rhythm, a beat that builds anticipation and an ice-cold bottle of Diet Coke: we're in a noisy bar among friends. Suddenly, we're painting graffiti in bold colors on the street, in the next second, being photographed by paparazzi, then bending over a newborn baby, listening to his heartbeat. Lyrics punctuate the action: *a moment, a love, a dream.* Soon we're in the outback: filming a massive explosion, hearing the melody build, *a laugh, a kiss, a cry,* taking a quick sip of that Coke. Between the applause, the lights and the laughter, snapshots of life have unrolled in the space of a moment.

This is "Sweet Disposition," the 2010 Oscar telecast commercial for Diet Coke. It is the modern face of artificial sweeteners: pervasive and proud, in hand at each of life's vivid moments and all the mundane ones in between. Far from sacrifice, "Sweet Disposition" is loud, it's salient, and it's rich. For Diet Coke, it captures a universal kind of desire.

The irony of such campaigns is that sweetness is just about the last thing on earth that needs advertising. Humans have a deeply ingrained affinity for sweets that dates back to early history, explains Johns Hopkins University anthropologist Sidney Mintz. "Since any normal human being can apparently experience sweetness, and since all the societies we know of recognize it," he notes, "something about sweetness must be linked to our character as a species." Academics are split on the specifics of the issue: some believe that our sweet tooth came about through biological evolution, and others think it's cultural.

The evolutionary story points to our ancient ancestors, hunter-gatherers who relied on fruit and honey for sustenance, and suggests we inherited genes from them that confer a liking for sweets. To our foraging ancestors, the sweetness of fruits and honey indicated these foods were edible and rich in valuable calories. Bitter or sour flavors, on the other hand, served as a sign that a plant or herb was poisonous. On the sparse savannah, humans who weren't genetically programmed to prefer sweetness would be less aware of the distinction between

edibility and danger. And without a craving for sweets, they would miss out on concentrated sources of good food energy. The survival advantage would pass to their sweet-toothed counterparts who would survive, eat fruits and multiply. Nearly all species of mammals alive today—like bears, foxes and mice—prefer sweet tastes. Human infants also show a liking for sweetness, suggesting the sweet tooth might appear even before our teeth do.

Harvard biological anthropologist Richard Wrangham found support for the evolutionary side of sweetness while living in Tanzania in 1972. He decided to follow a chimpanzee diet, foraging and eating whatever he found. "It left me extremely hungry," he later told *The New York Times.* On a couple of occasions, he recalls tasting raw monkey meat his chimp companions had left behind after a meal. He observed that these evolutionary ancestors of ours also tend to show a preference for sweetness: the chimps readily eat red Colobus monkey meat, which has a sugary taste, and tend to avoid the "very tough and unpleasant" black and white Colobus.

Evolution doesn't tell the whole story: social status and economics have also played a role in our taste for sweetness. Mintz comes down on the side of culture and argues that the drive for sweetness is born more out of "what are in fact culturally conventionalized norms, not biological imperatives." When Caribbean sugar plantations were first established in the 1400s as what Mintz calls the "overseas experiments of Europe," they provided a relatively unknown commodity. Two hundred years later, England's noble class began to consume cane sugar in coffee, tea and chocolate. When sugar's price began to drop as a result of free trade, commoners saw access to sweetness as a status symbol and started spooning it into tea almost universally. At the same time, sugar provided a valuable source of calories to the working poor. "It became the high-octane fuel of our diets," notes MIT anthropologist Heather Paxson, adding that sugar was at once a practical commodity and a symbol of desire. By the dawn of the nineteenth century, sugar was a staple in mainstream diets and Mintz estimates that British sugar consumption had increased by 2,500 per cent over the previous 150 years! From there, he concludes, the sugar industry grew to provide "a single source of satisfaction...for what appears to be a widespread, even universal, human liking for sweetness."

Science also has a hand in Mintz's view that sugar penetrated our food preferences over time. The more we feed our sweetness receptors and stimulate the brain's pleasure

centers as a result, the more we crave that response again. In other words, sweetness is mildly addictive. This is according to Dr. Gary Beauchamp, a taste researcher at the Monell Chemical Senses Center in Philadelphia. His work has shown that people are trained by repeated exposure to prefer certain flavors, like sweetness, even when this exposure happens as early as in utero. Fetuses have been shown to prefer flavors from their mothers' diets that have been passed on through amniotic fluid. "We believe these early experiences really set the stage for long term preferences," says Beauchamp.

In later life too, most of our preferences depend on how we condition our taste buds. "Each individual person out there perceives the flavor world differently," notes Beauchamp, adding that our predilection for sweetness can shrink or grow depending on how frequently we feed it. Many cola drinkers comment that, after switching to a low-calorie version for some time, they find the full-sugar version sickeningly sweet. What we choose, then, can actually change our taste buds. But the idea that our food preferences impact us more broadly is not new. As Jean-Anthelme Savarin famously said two hundred years ago: "Tell me what you eat; I will tell you what you are."

Whether genetic or cultural, or most likely some combination of the two, a taste for sweets runs deep in human societies. It's surprising, then, that the mechanism behind how we process sweetness on the tongue and in the brain is still poorly understood. Dr. Jane Leland has spent the past thirty years researching flavor at Kraft Foods, and says that sweetness isn't simple. What we perceive as a single taste, she explains, is really a "complex interplay" between smell, taste and texture. Together, these create a "sensation identity" we have come to call sweetness.

When a sip of soda lands on the tongue, specialized cells in the nose and mouth are there to receive it. Taste buds protrude as tiny islands called papillae on the surface of the tongue. Here, each molecule signaling sweetness locks into a socket. The sweetness receptor, identified in 2002, is spectacular. Like a single glove that fits several sizes and shapes of hands, this one receptor binds with an enormous diversity of molecules. Sweet-tasting chemicals don't tend to have a shape in common: some contain rings, others are straight chains; some are riddled with double bonds and others, mostly single. As Leland puts it,

"Sweetness corresponds to a pretty broad structural diversity." Yet somehow, one type of receptor recognizes them all.

Each molecule of a sweet substance, whether natural or artificial, comes with "recognition points" in its chemical structure. These are like tags that help the receptor identify what to cling onto. The single sweetness receptor has eight separate docking sites, each of which tends to bind with a specific recognition point—for example, ammonia or hydroxyl groups. The receptor is made of only two proteins, each encoded by one gene. A mutation in either of these genes can compromise the ability to taste. Cats, for instance, have a sequence of 247 letters missing from their genetic code, meaning they don't express one of the proteins needed to form the receptor. As a result, cats cannot taste sweetness.

Researchers who study sweetness compare the receptor to a Venus flytrap, the carnivorous plant that snaps insects inside of it with a quick fold of leaves when they land. Like a Venus flytrap, the sweetness receptor hinges closed around a tagged molecule when it makes contact. This binding sends a dizzying signal cascade—catalyzing, closing ion channels, changing charges and releasing chemical messengers—through the nervous system. The signal ends up at the brain's thalamus, a command center that integrates messages and dispatches them in all directions.

The thalamus forwards its message from the mouth and nose onto one of the brain's hotbeds of emotion and reward, called the orbitofrontal cortex. Here, the sweet signal spurs the release of dopamine—a chemical messenger that registers a feeling of pleasure. As Leland points out, dopamine is key: it's "crucial for the hedonic feeling of satisfaction following ingesting food with pleasant tastes." When we seek out sweetness, she emphasizes, we are really feeding our craving for dopamine. In the end, it is uncomplicated: sweetness simply makes us happy.

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Across the plains of Guanacaste Province, Costa Rica, windy roads slice like fissures through a crust of sugar cane fields. Stalks of cane extend as far as the eye can see, like a single carpet reaching from both sides of most roads and ending at the horizon. The plants stand at attention in tall rows, green tops swaying like graceful fingers in the breeze.

This sweet, grainy cane is one of the province's major exports. One by one, stalks will be cut at the root by field workers, men who rise early and retire late to harvest sweetness for money. After they axe the stalks by hand, bronze-skinned workers toss their cane into trucks whose open-air backs wait to be filled. The stalks stick out between each truck's metal ribs at odd angles, like tufts of hair left untamable by wind. The cane sighs a constant rustle as it rides down narrow roads to factories, where stalks are crushed and their juices extracted, liquid eventually evaporating away to leave crystals called sugar. After sunset on harvest days, cane fields are set quietly ablaze. Each field's surface returns to an empty state, roots ready to grow again.

Sugar cane's life cycle represents what many consider the natural side of sweetness. Cane is born from the earth and lives on soil, water and sunshine until the dry-season harvest. When its ashes settle into fertilizer and the rains return, the cycle begins anew. Here there is only photosynthesis, the sun's design and field workers with bare backs, lending calloused hands to a cycle that nature has sung for thousands of years.

The processes associated with preparing sugar for human consumption are ancient and simple: grinding, pressing, heating. But there is a great deal about the growth of the sugar empire that can't rightfully be labeled "natural." In the seventeenth and eighteenth centuries, African slaves were shipped like human cargo to booming sugar colonies in the West Indies, which needed more labor to sweeten teatime in Britain. The land most cane was grown on had been settled first by aboriginal people, who were forced to leave for the rise of sweetness. The powdery white commodity we know as sugar is also a far cry from the raw, brown shape the crystals take before they are refined. Here lies a new ambiguity: although it is born from the earth, sugar does not really equate to purity or goodness.

Regardless, through the early twentieth century, purity and goodness were the buzzwords of marketing sweetness. Sugar was considered natural and even healthy: a valuable source of earthy energy, like vegetables. With the sugar industry's focus on pleasure and vitality, extra calories and cavities weren't a concern. In their advertisements, Domino and Franklin sugar brands both proclaim their product as "100% pure," touting sugar's natural origins as a reason to view it as wholesome. Artificial alternatives were not on any chemist's radar.

One serendipitous day in 1879, that changed. Ira Remsen, the first chemistry professor at Johns Hopkins University, spent the thirty-third year of his life buried deep into his research on coal tar: a thick, black by-product of burning coal for energy. In the late nineteenth century, coal tar was a material with substantial promise. From it, chemists could derive tools for modern living that ranged from dyes and antiseptics to explosives and war gases. Since then, coal tar has also given way to paint, perfume, laxatives and aspirin.

Remsen was interested in the shape of organic molecules, especially groups containing sulfur, and wanted to know which chemical elements would shift and change when a compound called orthotoluene sulfamide was exposed to oxygen. Remsen suggested this experiment to a guest researcher in his lab, Constantin Fahlberg, who conducted the test and ended up with the residue of the result on his fingers. Soon after absentmindedly putting his hands to his mouth, Fahlberg noticed the result of his experiment, called benzoic sulfanide, was intensely sweet.

Neither Remsen nor Fahlberg had set out to synthesize a sweetener, but they took the discovery and ran with it—or at least, Fahlberg did. He went on to patent benzoic sulfanide as the world's first artificial sweetener, which he dubbed saccharin. Remsen, however, had a less entrepreneurial spirit. His biographers point out that, despite receiving a telegraph from a colleague overseas that read: "I warn you of Fahlberg," Remsen remained unconcerned with Fahlberg's dreams of turning the lab's discovery into something commercial. Fahlberg's name stands alone in crisp, tar-colored cursive on saccharin's 1884 patent.

Although derived against a basic backdrop of wooden lab benches and cabinets lined with shapely glass vials, saccharin went on to have far more impact than the stuff of an old-time apothecary. In the grainy lab photographs where Remsen's team of suit-clad men live on, 1879 looks like just another year on the job. But to the rest of the world, an important new door linking science, business and sweetness had opened.

Saccharin is not calorie-free, but because it is about 500 times sweeter than sugar, very little of it is needed to flavor a food or drink. Five grams of saccharin, for example, have the sweetening power of five pounds of sugar. This potency of flavor also translates into sweet economics. When the Monsanto Chemical Corporation first manufactured saccharin on an industrial scale in 1902, it cost only four cents to make enough saccharin to pack the same

flavor punch as thirty cents' worth of sugar. Each of the thousand-tablet tins was sold with the label: "little lumps of sweetness."

At the time, saccharin was not marketed as something healthy people would consume by choice. It was sold in pharmacies and targeted toward diabetics, because it could provide sweetness without driving up blood sugar levels. But since saccharin was cheap to produce and more easily soluble than sugar, manufacturers looking to cut costs often slipped it into canned fruits and drinks. This was easy to get away with because food labeling wasn't mandated in the early twentieth century, explains Xaq Frohlich, a PhD candidate in MIT's department of Science, Technology and Society whose research focuses on food labels. When the public found out about this surreptitious saccharin, however, they quickly called out the artificial sweetener as an adulterant. The *New York Times* picked up on this line of thought in the summer of 1911, with an article that labeled saccharin an "impurity" and a headline that asserted: "Saccharin Lowers the Quality of Food."

In the decades that followed, unadulterated natural sugar held its ground as a nutritious source of wholesome energy. Increasingly, sugar consumption was seen as an important factor in raising healthy children. "Sugar is a vital fuel in this little motor," reads one 1938 Domino Sugar advertisement. The "motor" the ad refers to is a dimple-cheeked boy, smiling as he bites into a piece of bread presumably baked by his mother from "safe, sealed, Domino pure cane sugars." By 1941, Domino's message was less subtle. "SUGAR FOR NUTRITIOUS MEALS!" reads one capital-letter advertisement.

Through the war years, sugar was routinely rationed on the home front so it could be available to soldiers on the battlefield. "Sugar helps the diet that points to victory," advises one poster from wartime. Thought to give men the energy they needed to secure victory, sugar was seen as the staple of heroes. At home, sweetness was sorely missed. Cutting back on sugar was "regarded as among the most painful and immediate of the petty hardships caused by war," Mintz notes in his book *Sweetness and Power.*

Rationing marks the first large-scale instance of Americans having to look beyond sugar for sweetness. "Perhaps sugar was seen as a kind of unpatriotic indulgence," suggests Yoshi Kukuchi, a postdoctoral fellow in the History of Science at MIT. In a political climate of patriotism and sacrifice, cutting back on traditional sweets was regarded as a help to the

war effort. Searching for a substitute, women on the home front got creative. Without adequate sugar for baking during World War II, they turned to the saccharin tablets that lined the shelves of pharmacies. The "little lumps of sweetness" saw a 30-fold increase in sales only a few months after the Food Rationing Program began in 1942. No longer used only among diabetics, saccharin tablets began to sweeten dishes from sponge cake to chili in wartime kitchens across America. Like sock darning and victory gardens, artificial sweetness had gained a reputation as a noble habit.

As wartime wore on, the next iteration of an artificial sweetener was in the works. Michael Sveda, a graduate student at the University of Illinois, had been experimenting with ring-structured salts in 1937 when he took a cigarette break. Putting his lips to the space on his cigarette where his science-stained fingers had been, he noticed an unusually sweet taste and concluded it must have been residue from his experiment. Dubbed cyclamates, Sveda's ring salts went on to be commercialized as an artificial sweetener in soft drinks and tabletop packets. Although 50 times sweeter than sugar, cyclamates are built up of many sodium ions. This gives them a slightly bitter and salty taste, making them better in blends with other sweeteners. Fourteen years after their accidental discovery, cyclamates were approved for use in diabetic foods. Seven years after that, the FDA officially recognized the new sweetener as safe for general use.

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On September 24, 1955 Dwight D. Eisenhower was taking a vacation in Denver. He wrapped up his game of golf for the day—27 holes—and retired to barbeque hamburgers with onion for lunch. In the early hours of the following morning, Eisenhower awoke with significant and increasingly severe chest pains. The 64-year old president was suffering a heart attack.

Eisenhower was the first sitting president to have a heart attack, and his condition made America noticeably anxious. Two days after the incident, Wall Street slumped and interest in health journalism spiked as the public cried out for daily updates on their president's condition. During the month it took for Eisenhower to recover to the point of being able to walk again, press conferences on his progress were held twice daily. The doctor flown in to care for the president, Harvard cardiologist Dr. Paul Dudley White, was a staunch

advocate of diet and weight control for managing and preventing heart disease. He became prominent immediately, and his medical views hit the mainstream with the media barrage that closely followed Eisenhower's health status.

When Eisenhower recovered and was re-elected to office in 1956, there was a new public awareness that heart attacks didn't have to be fatal. Altering the diet and restricting calories, it seemed, could make a real difference. "The heart attack really had an enormous effect on public opinion and preventative steps," recalls Victor McElheny, a science reporter who entered the field in the immediate wake of Eisenhower's illness. Around the same time, McElheny notes, the public was becoming more aware of the link between smoking and lung cancer and the polio vaccine's efficacy was also announced, sparking a major vaccination campaign. Nationwide organizations like the American Heart Association sprung up, making the American public newly conscious of preventative strategies for health. "This was a time of very dramatically heightened concern about health in general," McElheny remembers.

In the years that followed Eisenhower's heart attack, the trend toward "reducing" or cutting calories was broadly reflected in the media: the "ten-day miracle diet" and "sensational one-week reducing plan" filled the pages of American newspapers. In addition, the commercial market for artificial sweeteners began to boom. Cookbooks like Ruth West's 1956 *Stop Dieting! Start Losing!* laud saccharin and cyclamates as "pure gold," important tools for any lady looking to trim her waistline. In this climate of reduction where advertisements praised "trim hips, small waist, flat abdomen, shapely legs, [and] a streamlined figure," sugar was suffering.

By the 1960s, it was clear that the idea of artificial sweetness had hit a nerve and achieved a certain vogue. Saccharin and cyclamates were being used in mainstream diet products, labeled and advertised to broader audiences. Frohlich notes that artificial sweetness was "increasingly being marketed beyond patients" to a mass market rather than just diabetics. Cyclamate-sweetened tinned peaches and apricots flew off the shelves, increasing their sales by over a million dollars every year in the 1960s. Artificial sweetness had grown beyond cheap canning and pharmacy shelves, and had found its place in the public eye. Pleasure was key to this industry's success: heart-healthy diets didn't have to mean complete deprivation, so long as there was sweetness.

In October 1969, the glory days of artificial sweeteners came to a crushing halt. The FDA had received data from a new scientific study on cyclamates, and the results weren't good. Tests had found a high incidence of bladder cancer in rats that had been fed cyclamates. Although only a single study, it caused widespread concern. At the time, a tide of alarm was rising as science began to show that aspects of the environment could cause cancer. A decade prior, Congress had passed the Delaney Clause, banning any food additive "found to induce cancer in man or animal." When the clause was passed, it wasn't yet clear that virtually any system could be forced to produce a cancer, if inundated by enough chemicals. The FDA had originally argued against the clause but as it stood in 1969, the Association had no choice but to strike cyclamates from their list of foods "generally recognized as safe." A ban on the sweetener was drawn up, effective by the first of February.

Since then, mice, rats, dogs and monkeys have sipped on cyclamates in numerous testing efforts to have the sweetener re-approved in the United States. None of these studies have been able to replicate any cause for alarm. "As a result of all this very large body of work," notes Grant Dubois of the Coca-Cola Company, "it is now uniformly accepted that cyclamates are not carcinogens." This conclusion may be uniformly accepted by scientists and industry professionals, but government regulatory bodies are another story. Countries around the world are split down the middle when it comes to permitting the use of cyclamates: Belgium, Switzerland and the UK accept them, but Japan, Singapore and the United States do not. In Canada, cyclamates are not permitted in foods and beverages, but tabletop packets are widely available under the brand name *Sweet'N Low*. For a product so ubiquitous, cyclamates come with a puzzling small-print warning: "This sweetener should only be used on the advice of a physician."

A cyclamate-free market in 1970s America meant consumers were thirsty for other options. For the moment, saccharin reigned as the only artificial sweetener available. With diet soda enjoying large profits in the 1970s and a gaping hole in the competition where cyclamates had been, the stage was set for aspartame's entry. "In many ways," cultural historian De La Peña notes, "it was ideally positioned for success."

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The story really starts in Skokie. Now a town of 65,000 on the northern fringe of Chicago, Skokie was once home to the headquarters of a major pharmaceutical company called G. D. Searle. Known for the development of motion sickness pills and Metamucil, Searle focused on drugs that would improve the average American's quality of life. A quarter of a century after settling in Skokie, Searle made waves in 1965 when one of its young bench scientists stumbled upon a sweet piece of accidental success.

James M. Schlatter, aged 23, was working in the lab to develop an anti-ulcer medication. That December, he was on the hunt for a chemical that could inhibit gastrin, a hormone that normally drives stomach acid secretion and was thought to cause ulcers in overdrive. Schlatter was in charge of synthesizing one part of gastrin's large and complex structure so that his team could study its effects closely. One of the intermediates in the chemical process, like a stepping-stone on the way to the other riverbank, was a protein fragment known as aspartame. To Schlatter at the time, the piece was insignificant by itself, simply another standard substance to re-crystallize on the way to a more important goal.

"I was heating the aspartame in a flask with methanol when the mixture bumped onto the outside of the flask," Schlatter recalls. "As a result, some of the powder got onto my fingers. At a slightly later stage, when licking my finger to pick up a piece of paper, I noticed a very strong, sweet taste." But the clean, barely bitter sweetness that Schlatter encountered didn't initially faze him. "I thought that I must have still had some sugar on my hands from earlier in the day," he continues. "However, I quickly realized this could not be so, since I had washed my hands in the meantime." He traced the source of the powder back to the flask in which he had heated aspartame, and confirmed his suspicion with a taste test. "I felt that this...was not likely to be toxic and I therefore tasted a little of it," he continues, "and found that it was the substance which I had previously tasted on my finger."

Unknowingly, the young chemist had synthesized what would soon become America's favorite sugar substitute. It's logical that Schlatter would not have known to expect sweetness out of aspartame because, as his supervisor Dr. Robert Mazur later pointed out, its constituent parts are all either tasteless or bitter when taken alone. And since scientists still haven't pinned down a firm link between the chemical shape of a substance and the taste it registers, it is very difficult to plan the synthesis of new sweeteners. Aspartame's kite-like structure, with

its hexagon and tail, has little in common with table sugar, whose double-ring structure looks more like a pair of eyeglasses.

As the winter of 1965 faded into the spring of 1966, Searle's higher-ups recognized a new opportunity for success. Turning their attention away from ulcer treatments, Searle invested instead in aspartame as a sweetener. Over the next decade the company's executives commissioned a slate of safety studies on aspartame, aiming to gain the FDA approval they needed to bring their sweet discovery to the mass market. When Searle submitted a standard petition for aspartame's approval in 1974, it was thick with 15 major studies evidencing no cause for alarm. Dreaming of the smashing business success their sweetener would achieve when it entered the market upon approval, Searle stacked its staff with powerful minds, adding lawyers and salesmen to the team. One of Searle's new additions in 1977 was CEO Donald Rumsfeld, former congressman and Secretary of Defense. Lawyer Robert B. Shapiro was hired on as an attorney in 1979 and was later appointed President of the new NutraSweet initiative.

From the beginning, Searle was conscious that it wouldn't be good enough to slide under the wire where safety studies were concerned. The company wanted perfectly persuasive evidence to convince the FDA and the public, without a shadow of a doubt, that aspartame was safe. This part of Searle's business plan was born more out of confidence than anxiety. Aspartame was the latest in a growing line of sweet efforts being trounced by health scares, and Searle's executives believed they had witnessed enough failures to know what kind of message it took to achieve success.

The latest scare among sweeteners was saccharin. In 1977, as NutraSweet's petition was pending, the FDA received results from a study that had found high rates of bladder cancer in rats exposed to large doses of saccharin. It was like a déjà-vu of the cyclamate story, except this time the offspring of the saccharin sippers had developed cancer. Once again, cause for human concern was fairly low: in their press announcement for the ban, the FDA acknowledged the rats had been given "in excess of the amount a consumer would receive from drinking 800 sodas daily."

This time around, the public was crushed. Letters of complaint flooded the FDA's mailbox from across the country, totaling 6,000 alone in the first week after the ban was

announced. By Christmas, the complaint tally had reached one million. De La Peña points out that this extreme consumer revolt indicates how much the general public had come to rely on the sole artificial sweetener available at the time. "People did it like a drug," she recalls. "They were dependent on it, because they would be fat without it." Or at least, people *thought* they would be fat without saccharin. In the years since, with artificial sweeteners readily available, the American population is no slimmer. Perhaps what the protesters really clung onto was the powerful, paradoxical feeling of indulgent restraint that chemical sweeteners seem uniquely able to deliver.

Due to the backlash of letters, Congress intervened and postponed the saccharin ban's start date to allow for more testing. The date was rescheduled seven times, edging into the 1990s. Finally, Congress dropped the idea of a ban and settled on mandatory warning labels instead. Until 2000, the labels read: "This product contains saccharin which has been determined to cause cancer in laboratory animals." In the decades since the original saccharin scare, scientists have found that the sweetener appears to be carcinogenic only in rats, and not in other test animals. Experts generally agree that the problem relates to idiosyncrasies of the way rat urine is produced and has no relation to humans. The saccharin safety scare, however, made aspartame's entry all the more timely.

On the 26th of July 1974, G. D. Searle and Company got the good news they had been waiting for. The FDA had read Searle's petition and signed off on their scientific studies: aspartame had been approved for foods. The new sweetener was a simple compound with three parts. The first is aspartate, a basic chain of carbon atoms with branches made up of oxygen, nitrogen and hydrogen sprouting off the sides. The chain gives way to a piece with a hexagonal ring structure, called phenylalanine. Finally, the compound has a small tail on the end called methanol, the simplest alcohol. Aspartame's ingredients are amino acids, known as the microscopic building blocks of protein, and contain only basic parts: carbon, hydrogen, oxygen and nitrogen.

The celebration in 1974 didn't last long, however. The following year, two members of the public filed formal objections against the FDA's decision. James Turner, a consumer lawyer, and Dr. John Olney, a professor at Washington University School of Medicine, both feared that aspartame might be toxic to the brain after breaking down in the body. Olney had

conducted some of his own studies on rats, and found that seven out of 160 rats fed frequent doses of aspartame grew brain tumors, while none of his 120 unexposed rats developed any growths. Olney's studies were not meant to be a precise measure of hazard in humans: the amount of aspartame to which he exposed the rats every day is the equivalent, to a 170-pound man, of about two and a half *thousand* cans of diet soda. Rather, Olney had designed his tests as the canary in the coalmine, meant to signal any early danger and gauge the need for further testing. He concluded that aspartame was worth further investigation, and wanted the FDA to know it.

A circuitous dance followed in which the FDA reviewed the original Searle studies at length. In the meantime, aspartame's path to market was put on hold. Finally, in 1980, the FDA concluded once again that the science behind aspartame's safety was trustworthy. As one last measure, they convened a committee of three outside scientists who would hear testimony and review the safety evidence for aspartame at a Public Board of Inquiry. These scientists agreed that the sweetener's breakdown products were no cause for concern. However, the available data "did not rule out the possibility" that aspartame could cause brain tumors in rats. No abnormal growths had ever been observed in humans, but under the Delaney clause—prohibiting any food additives that cause cancer in animals—members of the Board could not support Searle's sweetener.

The FDA then reviewed the old data a third time and evaluated new studies. Dr. Michael Jacobson, head of the Center for Science in the Public Interest, the country's oldest nutrition watchdog group, recalls that FDA staff then concluded that Olney's rat brain samples had been misinterpreted. "[The FDA] persuaded the committee that those weren't brain tumors they were looking at," Jacobson relates. Even though Olney's tissue samples were debatable and the aspartame doses he had used were extreme, the study left a lasting mark on the sweetener's reputation. Says Jacobson, "It raised the cancer question that's been lingering ever since."

By the summer of 1981, newcomer FDA Commissioner Dr. Arthur Hull Hayes, Jr. ruled that sufficient evaluations had been done to prove aspartame's safety. Dismissing any lingering concerns about the brain tumor question, his tenure saw Searle's petition approved once and for all. That year, aspartame appeared on the market in dry goods like tabletop

sweetener packets. Two years later, aspartame had also been approved for use in soft drinks. By 1986, Searle had sold upwards of $600 million worth of aspartame and had built a new manufacturing plant to accommodate their booming business. In a few short years, aspartame had become the most thoroughly studied food additive the FDA had ever approved. But even so, the controversy hadn't been put to rest.

Conspiracy theories persist: some believe that Searle tried to camouflage unfavorable results in order to push the sweetener through approval in the name of quick profits. Some argue it's problematic that Dr. Hayes later went on to work as senior medical advisor at Searle. More persuasively, others take issue with the fact that Searle CEO Donald Rumsfeld also served as an advisor to President Ronald Reagan, and had helped to put Dr. Hayes in his appointed FDA position the same year aspartame was finally approved.

As the third artificial sweetener met with the cancer question, aspartame was not unique in this regard. But rather than sit still and anticipate bad publicity, NutraSweet's executives took a new and aggressive approach with marketing: they played up the natural aspects of their artificial sweetener. In an advertising blitz that has since been used as a case study in successful branding, the NutraSweet Company mailed small packages of aspartame-sweetened gumballs to houses across the country in 1984. Enclosed pamphlets focused on aspartame's ingredients, all derivatives of protein, and the strategic company name: *Nutra*Sweet. They also played up aspartame's sense of fun. Gumballs gave the product a youthful, carefree image and the all-important sense of guiltless indulgence. Finally, the promotional material drew a stark contrast between aspartame and saccharin. "Aspartame created this whole campaign: we're not saccharin," De La Peña notes. "Simply by not being saccharin, NutraSweet was good. For consumers tired of two decades of chemical controversy, a pleasant story about proteins may have been a welcome respite."

Advertising campaigns for aspartame also focused on its clear, natural taste. One 1986 television commercial for Diet Pepsi, made with NutraSweet, features a young Billy Crystal. "I'll tell you something, darling. You look marvelous," he croons to an icy can. "And not only do you look marvelous, my little twelve-ounce darling, but you taste marvelous." A female voice chimes in with song: "No other taste attracts so much attention."

Taste was where aspartame triumphed over its predecessors, and where it captured market share despite the doubts Senator Metzenbaum had begun to cast publicly on the sweetener at the time. "The problem with diet drinks was the taste," recalls Hank Cardello, who worked as the marketing director for Coca Cola in the 1980s, when the company first started sweetening Diet Coke with aspartame. Saccharin and cyclamates tasted sweet, but metallic and distinctly artificial. "Flavor never really broke through in offering something consumers would want," he says. "Aspartame offered that." With aspartame's entry into the soft drink market came a rise in the popularity of diet products, simply because they tasted more like natural sugar. In 1984 alone, Americans consumed about 800 million pounds of aspartame. Five years later, diet drinks made up a quarter of the $43 billion soft drink industry. Both Coke and Pepsi switched to 100 per cent aspartame formulas in their diet drinks by the end of 1989, settling on the taste their customers knew and loved. As Cardello puts it, "Aspartame was in essence the savior to the diet drink category."

Coming up with such an ideal sweetener isn't easy, according to Lyn O'Brien Nabors, editor of the trade manual *Alternative Sweeteners*. It needs to be colorless, odorless and at least as sweet as table sugar; it must dissolve in water and be stable in conditions that are acidic, basic, warm or cool. It should possess "a clean, pleasant taste" that onsets immediately but doesn't linger too long. It must be non-toxic, either broken down safely in the body or excreted unchanged. It also should not cause cavities, nor should it be difficult or expensive to store or transport. And it should be easy to produce, preferably with some of the same methods or machines as sugar so it can use existing equipment. The more of these criteria a sweetener meets, Nabors explains, "the greater the consumer acceptability" and "the more desirable it is to industry." Nabors's list reads like a dreamer's description of her perfect mate: it's idealistic, it's demanding, and it leaves a lingering wonder if anything artificial could ever fit the bill and truly imitate sugar.

Cane sugar's fibrous layers start out firm and unforgiving, like celery. After anchoring your teeth in the tough stalk, it only takes about ten seconds to suck out all of the dilute, sweet water. Sugar cane's flesh is left dry like cotton baton. Indigestible and spent, it is spit into a ditch or tossed back to the fields. This original source of raw, earthy sweetness delivers a taste that aspartame can mimic only after a complicated song called synthesis.

For just about every can of aspartame-sweetened soda in the world, this process takes place at one of two production plants, one in the state of Georgia and the other in Japan. Making aspartame requires precision because two of its component parts, phenylalanine and aspartate, are like devious twins. Both are chiral, a term chemists use to describe compounds that are the mirror image of each other on a molecular level. Like human hands, pairs of chiral compounds reflect each other's shape, but show their difference when you try to lay one on top of the other. If the wrong version of each starting material is used, the final molecule will have an imperfect layout, like a body designed with a left hand where the right one should be. Aspartame's overall shape is important because only one configuration confers sweetness.

To separate the desired form of phenylalanine (called "L") out of a mixture containing both it and its partner (called "D"), manufacturers break up the two with a digesting enzyme derived from pig kidneys. Then, they apply an acid that divides the resulting mixture into two easily identifiable layers, like oil and vinegar. Once the correct form of phenylalanine is isolated, chemists mix it with the simple alcohol methanol. Adding a strong acid helps to bind the methanol tail onto phenylalanine, and makes the aspartame molecule two-thirds complete. Finally, the chain called aspartate is added, releasing a water molecule as it binds to finalize the sweetener. The end result: a white powder, looking clean and crisp as snow, ready to be packaged into products.

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Aspartame's phenomenal industrial success and rise to popularity suggests this sweetener met Nabors's criteria and hit the mark. But as synthesis and marketing ramped up through the 1980s, something was not right. A small rumbling of protest against aspartame slowly gained momentum, and NutraSweet syndrome was born.

NutraSweet syndrome is the single name given to the sprawling constellation of health problems that some consumers have attributed to their aspartame habit. These activists spread their gospel in self-published books and on websites, offering flaming indictments of the FDA's original approval of aspartame. They warn of brain tumors and serve up anecdotes like cocktails: colorful, easy to swallow and prone to make you lose your sensibilities if you take in too many and the effects start to run together. The mainstream medical community sees

these advocates as dubious; they see themselves as crusaders for precisely the causes most physicians are afraid they're obscuring: health, truth and clarity.

One such figure is Cori Brackett, a radio host and documentary filmmaker from Tucson, Arizona. In her struggle against weight gain, Brackett recalls seeing aspartame as an ally. "I was a Shakespearean actor for awhile," she says, remembering that the joy of playing a part was often offset by the constant pressure to stay thin. "I was trying to keep my figure," she explains, "so I had been drinking a six-pack of diet soda a day for about twenty years."

Ten years ago, Brackett received a wake-up call. She began to feel a frequent tingling sensation in her hands and feet, and visited her doctor for a brain scan. "I was diagnosed with multiple sclerosis, which really threw me for a loop," she recalls. "I was thirty-four years old and trying to get my life together, and then all of a sudden this bombshell hit." Not long after the diagnosis, Brackett says she lost her ability to walk and began to use a wheelchair. Eventually, she was unable to talk. "Almost everything shut down in me except my desire to live and my basic functions," she recalls.

Even though she had begun to cut back her aspartame habit around the same time she was diagnosed with neurological problems, Brackett remains convinced that the sweetener is to blame. Early into her illness, she began to do her own research into the cause of her multiple sclerosis. Her curiosity started with small-scale Internet searches at home and grew into an ambitious cross-country documentary project. In her 2004 film *Sweet Misery: A Poisoned World*, Brackett takes an investigative look at aspartame through interviews with several patients, physicians and researchers who are firmly opposed to the sweetener. The thrust of the film is her claim that aspartame gives "subtle toxic effects over many years" and wreaks havoc on biological systems.

In the film, we meet an emergency medical technician, a traveling salesman and a homemaker. Each was formerly a heavy aspartame consumer until a disorder struck. For Rob Mehl, it was lupus. For Ed Johnson, it was Lou Gherig's disease. For Lorena Murray, it was vision problems and hearing loss. Each claims that giving up aspartame made their serious symptoms disappear almost immediately. "I really felt like I needed to get the word out about aspartame and my own experiences, to spare other folks from going through what I went through," Brackett explains of her motivation for the film. Today, she is recognized as one of

the most prominent anti-aspartame advocates and notes that many people concerned about the sweetener now contact her for advice.

The odd part about Brackett's story is the ending. "Today, I'm walking four miles pretty much every day, loving life and feeling great," she relates. "No problems, not even a pinprick in my fingers and they used to be numb." When she speaks of her seemingly miraculous recovery and her conversion to the firm belief that aspartame is harmful, Brackett's language has a religious zeal to it. "One of the hardest things is getting people to understand, to fully believe, because you have to jump off the building with both feet and faith," she says. You don't know until you try [cutting out aspartame] and you find out, hey, I feel better."

Brackett says that at the time of her diagnosis with multiple sclerosis, she was overweight, smoked regularly and drank at least five cans of diet soda every day. This is in line with cultural historian De La Peña's observation that many anti-aspartame advocates are simply searching for a scapegoat. "Aspartame is a really good place to put the blame for generally unhealthy lives," she notes, adding that people also tend to fault aspartame when a loved one suffers from a serious illness or a death that can be linked to the sweetener in any way. To those looking for solace, the aspartame industry is an easy, impersonal target at which to channel the sadness of loss. And to people who take these grievances and publish them online, tying a sweetener the world holds dear into the mix, maybe it feels like someone out there is listening.

As for Brackett, she is still troubled when it comes to sweetness. Despite her health concerns with aspartame, she hasn't gone back to white sugar. In her fridge she keeps a large container of "Just Like Sugar," which lists ingredients like chicory root, dietary fiber, vitamin C and crystalline maltodextrin, a starch. Even after all her trouble, she still craves the guilt-free pleasure of artificial sweetness. "It doesn't dissolve well in coffee," Brackett admits of her new go-to sweetener. "But it's alright in baking. I made a batch of brownies that were perfectly fine. They were sweet."

Dr. Michael Jacobson, head of the CSPI, falls on the opposite end of the spectrum from these anti-sweetener soldiers who spread their conspiracy theories online. Hank Cardello, the ex-Coca Cola marketing executive, calls Jacobson "the top cop of the food police"—a trim vegetarian who favors rational and educated criticism of health research. Jacobson's rigor is a

good thing, because he has a whole country to consider when gauging how healthy or harmful food additives are. From his downtown office in Washington, DC, Jacobson criticizes the emotional stance some online communities take against aspartame. "The Internet is filled with rubbish about aspartame," he says. "Some people have dedicated their lives to proving that it is evil incarnate." If you ask Jacobson, evil is irrelevant. He prefers sticking to science.

The website Jacobson oversees at the CSPI also advises steering clear of aspartame, but he is plainly unemotional and far from stubborn about his stake in the issue. Actually, Jacobson says he is looking to change it. "I'm considering making our rating of aspartame a little less bleak," he says, explaining that the current warning is based mainly on the results of a 2005 study from Italy that found high cancer rates in aspartame-fed rats. Matter-of-factly, Jacobson shares his suspicion that these results came about because the experimental rats were kept for close to three years. "This is very unusual," Jacobson points out. "Usually, they're slaughtered at 24 months, sometimes 30. Almost never three years." A two-year-old rat is about the equivalent of a 65-year-old person in age, and keeping rats one extra year adds the equivalent of 33 human years. In other words, the Italian study was charting cancer rates in the rough equivalent of century-old humans. "In one way, the longer you keep them alive, the more likely they are to get cancer," Jacobson notes. "The longer a study lasts, the more likely you are to find a problem. That kind of muddies the water a little."

While the muddy waters that continue to swill around aspartame studies cause Jacobson to reconsider his opinions, MIT neuroscientist Dr. Richard Wurtman has taken a different approach and fled the floodplain. Wurtman doesn't talk about aspartame anymore. Perched in a shiny new office on Vassar Street in the building that houses MIT's Brain and Cognitive Sciences Department, he will expound happily on just about anything else. He will also, occasionally, crack open a Diet Coke. But to this towering, broad-smiled professor emeritus with the voice of a radio announcer, murky and uncertain waters leave too much room to have your words twisted when you warn, however mildly, about aspartame.

Dr. Wurtman authored several studies on aspartame in the 1980s and, as an expert on proteins in neuroscience, spent a great deal of time investigating the sweetener's effects on the brain. He also testified in front of the FDA's Board of Inquiry on aspartame in 1980. The message his body of papers puts forward, however, was not a sensational plea for aspartame

abstinence. Instead, it remains a simple narrative of human diversity that suggests the need to proceed with caution.

The blood-brain barrier is like a backyard fence, where only some things can pass through the tight cracks. Like free-moving ants and stray cats in a garden, particles like oxygen and anesthetics can diffuse from veins and arteries into the fluid that bathes the brain. Other substances are left to exist on one side or the other, without the right to pass. When aspartame is digested in the small intestine, it is broken down into its three simple parts: methanol, phenylalanine and aspartic acid. Since aspartic acid cannot cross the selective frontier into the brain, it doesn't cause much concern as a by-product in the body. Methanol, the tail end of aspartame, is known to be toxic in high doses. But it enters the body in such miniscule amounts through the sweetener—the established toxic level equates to about a thousand cans of diet soda—that it is not generally a concern.

Aspartame's final metabolite, phenylalanine, is the focus of Wurtman's work. The FDA has set an "Allowable Daily Intake" (ADI) for aspartame of 50 milligrams per kilogram of body weight, which equates to around 25 cans of soda in a 170-pound man. An ADI represents the amount a person could theoretically consume every day over the course of a lifetime with no risk. After a dose of this size, Wurtman's studies have found that blood phenylalanine levels spike up to about 300 per cent. This is because phenylalanine competes with other compounds of its class, called large neutral amino acids, to gain access to channels that will carry them across the blood-brain barrier. With more phenylalanine in the blood, it can more easily knock its competitors out of the running for the gateways to the brain.

Wurtman has also found that if aspartame is digested at the same time as carbohydrates— for instance, drinking an afternoon can of Diet Coke with a cookie or a lunchtime soda with a sandwich—this 300 per cent rise in phenylalanine nearly doubles. Carbohydrates invite an onslaught of insulin, which in turn eliminates more of those large neutral amino acid competitors, filing them away into muscle. Phenylalanine, dominant in number and facing diffusion channels like empty goal posts, is well positioned to enter the brain. When phenylalanine does get to the brain in extreme concentrations, it can slow the production of hormones called catecholamines, things like serotonin that mediate depression and alertness.

There's about eight times more phenylalanine in a quarter-pound burger than in a can of diet soda, and there's also a considerable amount in milk and bananas. But the difference, Wurtman's papers point out, is that consuming phenylalanine in foods means it's digested with several other components of protein. In a hamburger, phenylalanine is just one piece of the larger protein package the body receives. Entering the body with its competitors—fighters with show names like valine, leucine and tryptophan—phenylalanine is at more of a disadvantage in foods when it comes to accessing the brain.

About one in every 15,000 babies is born with an unusual genetic condition called phenylketonuria (PKU). These people are missing the enzyme that breaks down phenylalanine, causing any ingested to build up in the brain like a snowdrift accumulating into clunky snow banks. Eventually, a phenylalanine overload has tragic results like seizures and severe brain damage. Consuming aspartame is known to be extremely dangerous and even life threatening for this population. Today, doctors prescribe strict, lifelong phenylalanine-free diets to help these patients manage their condition. This intervention is only possible because PKU can be screened for: since the 1960s, American infants have been given routine blood tests to detect the condition within a few days after birth. It's important to detect PKU right away because breast milk is full of phenylalanine.

Since PKU is a recessive disorder, a child has to receive a copy of the PKU gene from both of his parents in order to have the condition. But an estimated two per cent of the general population carries only one copy of the gene, meaning they don't express PKU but they are likely more sensitive to phenylalanine. Wurtman's body of work cautions that these people are among the "symptomless but susceptible people" who are probably more sensitive to aspartame, and might actually experience things like headaches and seizures if they consume the sweetener by the gallon. But because they are only carriers, these people have no way of knowing about their sensitivity until they try aspartame with adverse effects. Dr. Reuben Matalon, previous head of the PKU clinic at the University of Illinois, once put it this way: "We don't know them and they don't know themselves."

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American food laws require that additives, sweeteners included, should not impact any body system other than the ones they directly mean to. If a compound does affect systems

beyond things like digestion or sensation, the FDA switches its official perception of the substance. It's no longer a food; it's a drug. Once something is classified as a drug, the stakes are raised. FDA regulation of drugs is stringent, and their safety has to be continually monitored in order for their use to be allowed. Food additives, with their seal of physiological ineffect, are like teenagers who scrape by to pass a driving test: once approved, there's no requirement that their safety ever be monitored again.

This odd state of affairs is one reason why, despite the body of complaints, aspartame isn't slated to drop out of the market anytime soon. There's no onus on physicians to keep a running tally of the sweetener-related health complaints they receive, nor are they required to ask about aspartame habits when considering other lifestyle aspects of medical history, like smoking, caffeine use and exercise. According to people as divergent in background and methods as ex-actress Brackett and neuroscientist Wurtman, adding this single query to a physician's checklist would do a great deal to gauge the truth and the extent of aspartame's alleged effects.

Questions about aspartame are all the more essential right now from a public health standpoint. While the popularity of sugar-laden foods grows, Americans' waistlines are also seeing a marked increase. Ex-Coca Cola executive Cardello, who recently authored *Stuffed: An Insider's Look at Who's Really Making America Fat,* notes that the nation's hundred million overweight or obese people constitute "a panethnic, pancultural and paneconomic problem" that's leading to other health consequences like heart disease and diabetes. In the large quantities that we guzzle liquid calories in sweetened drinks, sugar becomes problematic. During the 1950s and 60s, a standard bottle of Coca Cola contained 6.5 ounces. Today, a single-serving bottle is 20 ounces. "They've morphed into what I like to call weapons of mass consumption, and they're out of control," Cardello says. Adding pounds from sugar is a simple law of accretion: "We don't have to take advanced calculus to figure this out."

The calculus of artificial sweetness, however, might be a little more complex and counterintuitive than scientists first imagined. In an office standing tall on Science Hill at Yale University, Ph.D. Student Qing Yang is studying a new aspartame hypothesis. A small and wiry neuroscientist-in-training, she is clad in a bright pink t-shirt and baggy denim

overalls as she talks about her research. After attending Yale's Neuroscience 2010 symposium, Yang was inspired to put together a review paper on the recent idea that zero-calorie artificial sweeteners actually contribute to weight gain.

This hypothesis has spread through the scientific community as well as the general public over the past decade. The idea, Yang explains, is that artificial sweeteners might not incite the same pleasurable dopamine rush that sugar usually sparks. Some early brain scan evidence supports the idea that aspartame doesn't complete this reward loop: pleasure areas aren't activated to the same extent by aspartame as they are after consuming sugar. Without satisfaction, the hypothesis goes, a person will only seek more sweets and as a result, they will likely gain weight.

Yang points to another roadblock with aspartame, called the "substitution effect." Feeling healthy after picking an artificial sweetener, we have a tendency to validate other unhealthy diet choices because of it. This is like justifying a second helping of food or a large dessert, Yang explains, because you opted for diet soda. This type of behavior can also backlash and end up causing weight gain.

The rest of the argument for aspartame causing weight gain mostly rests on a loose correlation between rising obesity rates and the more widespread use of artificially sweetened products. If you plot both on the same set of axes, the resulting lines climb upward at a roughly similar rate. One American Cancer Society study of 78,694 women found that, over the course of one year, up to seven per cent of regular aspartame users gained weight, compared to non-users. In a similarly massive study of health metrics in 11,564 children, Harvard University researchers noted that boys who regularly drank artificially sweetened sodas had a higher body mass index (BMI), a measure of body fat, than their peers.

But the idea that a correlation between the two firmly implies that one causes the other is the same fallacy Brackett's documentary falls into at one point, when it declares that aspartame's 1983 entry into the soda market sparked the ten per cent rise in brain cancer cases that also occurred that year (notably, right when MRI scans entered mainstream diagnostics). As A. Raines neatly summarized in a letter to the editor of the *Washington Post* in 1987, "As aspartame is estimated to be consumed by about half the US population, one need not be an epidemiologist to grasp the problem of establishing a cause-and-effect relationship. Half the

headaches in America would be expected to occur in aspartame users, as would half the seizures and half the purchases of Chevrolets." The link between aspartame and weight gain is still early and largely unproven. It presents an interesting possibility, but many more studies are needed before it can be taken as fact.

Today, as many schools move ahead with new initiatives to ban sugary sodas, some embrace artificial sweeteners as being healthy. Others prefer to steer students away from sweeteners entirely, presenting either kind as an unhealthy choice. Umana Middle School Academy in East Boston is one of the latter. When the lunch bell rings and students flock to the cafeteria for offerings like macaroni and cheese with steamed broccoli, they can choose milk, water or juice to drink. "If we did sell soda, we do not any longer," says Principal Alexandra Montes McNeil.

In 2008, the year before Principal McNeil arrived at Umana, the city of Boston launched a public health campaign to get sugar soda out of schools, and Umana was one of their experimental targets. Psychologists and physicians from Northeastern University, Boston Medical Center and Boston University School of Medicine collaborated with the municipal government to launch a project that would help 3,500 students make better beverage choices.

"Sugar-sweetened beverages, defined as drinks with added sugars, such as nondiet carbonated soft drinks...are one factor thought to be related to the rise in childhood obesity," notes Northeastern psychologist Dr. Jessica Blom-Hoffman. As part of the project, she and her colleagues encouraged popular convenience stores near six Boston middle schools to market milk, water and juice more aggressively to students than any kind of soda. The six-month campaign involved classroom lessons, prominently displayed posters and a raffle for an iPod that students could enter if they accumulated enough healthy drink credits on special punch cards. It was a grand plan, but it didn't work.

In sample observations of 142 middle school students before the campaign, 97 per cent were buying juices and sodas. After the campaign, a follow-up observation of 176 students still showed 93 per cent choosing a sugary drink. Despite a complex and well-organized plan, kids still weren't motivated to change their behavior. This failed outcome was predictable, if you ask Cardello, because artificial sweeteners weren't part of the solution. He argues that chemicals like aspartame are the best way to substitute sugar, "taking calories off the street"

without making people feel like they have to change their ways too much. If you can choose a large soda without calories, he says, you still get sweetness and satisfaction. Since wartime, many consumers have seen artificial sweeteners as a healthy indulgence, rather than a deprivation. Although the American Beverage Association only permits aspartame-sweetened soda to be sold in high schools, Cardello believes it's important to let kids choose them, too. "In marketing terminology, these are captive audiences," he says. "What a great laboratory to teach better eating habits."

Beyond schools, a similar initiative is taking shape on a national scale. Following initiatives in San Francisco and New York, Boston officials have begun formulating a plan to ban sugary sodas from city buildings. This is a movement that Cardello supports: he notes that consuming sugary sodas has "rock solid proof of harm," but with regard to artificial sweeteners being dangerous, "the evidence is not definitive enough."

Jacobson, who says the CSPI is "vehemently opposed" to sugary sodas being sold in schools, echoes Cardello's words almost exactly. "My feeling is that the risk of sugary soda is clear cut: they contribute to obesity, they contribute to tooth decay, and obesity contributes to a lot of other things. Either you're getting more calories, or you're replacing potentially healthier foods with sugar," he says. "And I guess I come down to, having an occasional diet soda is just a very small risk, considering the evidence of harm is not clear cut."

Science hasn't yet turned up any convincing proof of aspartame's danger to the mainstream population. However, the jury is still out: Wurtman and colleagues once wrote that with aspartame, "the absence of proof cannot be taken as proof of absence." Even after having probed the question in laboratories and Congress hearings, there is no simple answer. This particular story of sweetness remains rife with ambiguity and uncertainty.

Our taste for sweetness may be simple, but aspartame has always been a complicated hybrid. It's pleasure and restraint; it's artifice played up in advertising as natural. It's the result of an unplanned chemical blip and a meticulously plotted business strategy. This artificial sweetener—the most thoroughly tested in history—is officially recognized as safe, but also the most contested.

One of the issues is the reality that safety testing on aspartame is, and always has been, largely completed by industry professionals with a financial interest in proving no harm. This

clouds the legitimacy of any scientific study, and was one of Senator Metzenbaum's main concerns back in 1985. He was adamant that anyone other than G.D. Searle conduct another round of aspartame safety tests, and announced to the Senate: "We do not need the people who are making millions of dollars on aspartame telling us it's safe."

Alongside this uncertainty about trusting the results of safety studies, there's also an ambiguity when it comes to nutrition. Cardello points out that aspartame is widely accepted by mainstream science: "The bottom line is, no one's screaming 'get rid of it.' That's only true if you hit the Internet." But he also points out that aspartame will probably never get a "ringing endorsement" from the nutrition community because it provides nothing good. "It's empty calories," he says. With no nutritive value of its own, aspartame-sweetened soda will never be the gold-standard beverage for health. Is aspartame safe? Is it healthy? As Cardello explains, it's unlikely that any community—science, public health, nutrition, or medicine—will weigh in on this unequivocally.

Nearly half a century after Schlatter's lucky mistake and a quarter century after Metzenbaum's fight, aspartame is still a symbol of not knowing. Schlatter didn't know he was synthesizing sweetness, and it took the FDA several years and testimonies to know what to make of aspartame's safety studies. Brackett doesn't know how or even if aspartame made her sick. Based on the scientific studies he has seen, Jacobson doesn't know quite what to advise the public. Still, as we sip on it, we don't know what it is doing to us. We keep at it because that simple sweetness makes us happy.

One of the frustrations inherent to science is that it never gives final answers. Uncertainties are built into the practice. Some of the most illuminating concepts of our time, like evolution and relativity, are amalgams of evidence that we count on as being real. Science has shown the conclusions behind these theories to be plentiful, logical, even beautiful—but always with a tiny, unuttered caveat. It's in the nature of scientific theories to leave the possibility that some yet-unexplored avenue could turn all we think we know on its tail.

In its own way, aspartame's simple sweetness is like a microcosm of this scientific anxiety. Logic and science, government and bureaucracy have lined up to tell us that this fine, white powder doesn't merit any more worry. The simple, sensible answer is to believe these words, and I am inclined to. The problem is that we humans are not always sensible, but

messy and emotional creatures who remember. We think back to the cyclamate ban, the saccharin scare and the cancer question, and these pieces of memory build our fears. Even though we may know better, we still have anxieties about this sweetness.

Risk theorists agree that humans are idiosyncratic with fear: often we worry about the wrong things, and do so to our detriment. On an earth that is slowly warming beneath our feet, many stand worrying not about fossil fuels, but about nuclear power. As a growing population decides against vaccination, fearing improbable effects like autism or mercury poisoning, rates of preventable infectious diseases are rising. On American soil after the terrorist attacks of September 11, 2001, a newfound fear of air travel made many more people hit the highways. But statistically, driving by car is much more dangerous than flying, notes Boston-area risk consultant David Ropeik. "Death tolls on American highways rose significantly in those first 3 months [after 9/11]," he relates. "That's what killed them—their fear."

In an age where bureaucracies make most of the rules, risk theorists suggest people tend to favor emotional conclusions over rational ones. We consider ourselves pioneers of rightness, railing against the system and thinking we know better than science because as humans, we can intuit. Aspartame and artificial sweetness are tangled in the same messy knot of emotion and reason. Except perhaps it's harder to recognize that, because this is more commonplace than a vaccine, more mundane even than boarding an airplane or taking a stance on global warming. It's a canned drink or a piece of chewing gum, a daily reality that seems to merit little other attention. Without any reasonable evidence of harm, I don't think aspartame is going to hurt us. But I feel that it might.

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It's a rainy October night in Cambridge, Massachusetts—the kind where stripes of water chase each other down glass storefront windows, never seeming to tire. At dusk, River Street is quiet save for the sound of raindrops. Inside one cookie-cutter, box-shaped Rite-Aid pharmacy, a mother and her young son take refuge from the drizzle. Her jacket hangs loosely from her shoulders, leaving empty spaces inside the faded corduroy.

Her son, maybe ten years old, stands beside her with shoelaces untied and an untamed crop of carrot-orange hair on his head. As they wait in line to pay for a cheap Halloween costume, the boy surveys the wall of snacks lining the checkout counter. A far cry from

rationing of the 1940s or the reducing vogue of the decade that followed, sweets here are plentiful. In colorful packages, they cry out for his attention. At last his eyes settle on the refrigerator. He looks to his mother, busy consulting her worn leather wallet. "Can I have a soda?" he asks, desire in his eyes. She shakes her head no, signifying an old routine.

The boy is quiet, perhaps considering his options, planning a strategy. With one more glance toward the refrigerator, he knows what it takes to get what he wants. He turns back to his mother, and tries: "Diet?"

She considers this for a moment, and then nods in acquiescence. As the mother of a young son, she is no stranger to argument, but tonight she looks too downtrodden for debate. Passing the cashier a soft twenty, she receives a Spiderman costume and a can of Diet Dr. Pepper in return. And suddenly somewhere between the carbonated water, the aspartame, the caffeine and the caramel color, a dreary night and the sadness of a cheap, last-minute costume matter less. Her son is happy.

Outside of the pharmacy, in the Senate and around school vending machines, in histories and hospitals and on the Internet, in laboratories and local governments, this kind of transaction is studied and debated, anticipated and warned against. In all of those places too, Senator Metzenbaum's storm still rages on. "On the issue of aspartame...there are those of us in Congress who will not rest until this agency meets its responsibilities to the American consumer. That, I can promise," he said to his fellow Senators that August day in 1985. A quarter-century later some still haven't rested, determined to prove Metzenbaum was right. For now, we are stuck at a crossroads in the story of sweetness. As new sweeteners enter the market, Splenda and stevia among them, the industry is moving forward. But it is clear that aspartame, with all of its arguments, is not a story we can put behind us just yet.

Between ring salts and a slew of sacrificed rats, decades of debate and a serendipitous spill, the larger story of aspartame is broad in its reach across decades and laboratories. But if you look into just about any small corner of the world, like a New England pharmacy one rainy evening, something mundane happens, something ordinary that continues to drive an entire scientific and cultural movement toward artifice and consequence-free indulgence. People make a choice. And because of it tonight, one lanky little redhead gets a single, simple wish: sweet satisfaction.

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