THIS WAY IN

Hope in a Glass?

Doctors question whether "medical foods" marketed to improve symptoms of neurologic conditions such as dementia are worth the money.

BY STEPHANIE CAJIGAL

When Gregory T. Martini stopped by his father's house one evening three years ago, he expected to do most of the talking. His father, a former engineer, had been diagnosed with Alzheimer's disease (AD) two years prior, a condition that had reduced his conversations to little more than "Hi, how are you?" So Martini was especially surprised when during this particular visit, his father initiated what turned into an 30-minute dialogue.

"I was amazed," says Martini, 51, an attorney from Miami, FL. "It's one of those things that when you think back, you ask yourself, 'Did it really happen?'"

What could have caused the 88-year-old to start acting like his old self again? According to Martini—and his father's doctor—the only factor that could account for the change was that his father had been prescribed a product called Axona two weeks earlier. Axona is a "medical food" manufactured by Accera and marketed for people with mild to moderate AD as improving cognitive function.

Martini, however, never had the chance to see any long-term improvement; three days after his visit, his father fell and broke his hip. It was an injury from which he never fully recovered before passing away last year.

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>
> —WILLIAM H. THIES, PH.D., CHIEF MEDICAL AND SCIENTIFIC OFFICER FOR THE ALZHEIMER'S ASSOCIATION

While Martini remains a believer, the medical community has mixed feelings about whether Axona should be prescribed to people with AD. And with few effective treatments available for the symptoms of the disease, consumers may be particularly vulnerable to unsubstantiated marketing claims.

MEDICAL FOODS VS. PHARMACEUTICALS

Alzheimer's disease causes the brain to become less efficient at converting sugar (glucose) into energy. Some scientists believe this inefficiency may contribute to cognitive decline, although the research supporting this theory is preliminary. One animal study, for example, found that dogs fed an alternate form of glucose performed better on visual-spatial memory tasks and short-term memory tests. Axona counteracts the glucose-deprivation process, or so the theory goes, by providing caprylic triglyceride, an ingredient that the brain can use as an alternate energy source. The food comes in the form of a packet containing 20 g of powder that is mixed with 4-8 oz of water.

Introduced in 2009, Axona is currently the only medical food in the United States marketed for people with AD, although others are in development. Since the product is sold as a medical food and not a pharmaceutical drug, the manufacturer wasn't required to submit results from the same rigorous clinical trials that pharmaceutical companies must submit when seeking approval from the U.S. Food and Drug Administration (FDA) for a new drug. (Axona is not sold as a supplement either; even if it was, the FDA does not approve supplements.)

"The amount of evidence needed to sell a product as a medical food is considerably less than that needed to get approval for a pharmaceutical," says William H. Thies, Ph.D., chief medical and scientific officer for the Alzheimer's Association. "If I wanted to create a medical food, I would formulate and test a theory about how the ingredients would work in the body. As long as the medical food is based on ingredients found in a regular diet, the FDA won't require evidence of effectiveness in advance of it going on the market."

Accera published its research results in 2009 in the journal *Nutrition & Metab-*

LAURA FLUGGA/ISTOCKPHOTO

olism. The study reported that of 152 people with mild to moderate AD, those who consumed the shake showed slightly better scores on cognitive tests than those who were given a placebo. The differences in scores were statistically significant.

However, the results of this study can be misleading for patients and neurologists alike, according to Gary Gronseth, M.D., professor and vice chairman of neurology at the University of Kansas and Fellow of the American Academy of Neurology (AAN). The reason is that while researchers followed the rules of good study design by randomly assigning patients to two groups—one taking Axona and one taking placebo—they also added patients toward the end of the study without randomizing them, Dr. Gronseth notes. The addition of these patients could very well have skewed the results.

Randomly assigning patients to treatment groups (for example, by flipping a coin) is an essential feature of good study design because each patient is unique. Without randomization, patients receiving Axona may, on average, be different than patients receiving placebo: They may have more slowly progressing dementia, as an example. This difference, rather than any effect of Axona, might explain why patients taking Axona do better.

"Adding patients without randomization is a frankly bizarre and unscientific way to conduct a study. When the researchers analyzed the results with just the patients who were randomized to the Axona or placebo groups, they found the treatment had no effect," Dr. Gronseth says. "That's not to say that if people keep doing these studies they may find that medical foods such as Axona actually work, but properly performed research needs to be done."

Dr. Thies says that in order to help patients and doctors make better decisions, medical food companies should voluntarily commit to doing the same amount of research that they would need to submit if they were seeking drug approval.

Raj C. Shah, M.D., associate professor of family medicine and medical director of the Rush Memory Clinic at the Rush Alzheimer's Disease Center in Chicago, IL, says that patients, advocacy groups, researchers, regulators, and companies should come together to determine what the appropriate pathway is for developing medical foods.

"Currently, there is not a significant demand for the FDA to alter the regulations for bringing medical foods to market," says Dr. Shah, who has consulted for Accera and has written a review paper on medical foods.

Representatives of Accera say the company is trying to produce better evidence. Holger Kunze, CEO, tells *Neurology Now* that the company hopes to enroll about 500 patients from 50 to 60 sites throughout the United States for a clinical trial that will test Axona's effectiveness. The trial is set to launch in a few months, he says, but enrollment has not yet begun.

DICE: JOACHIM ANGELTUN/ISTOCKPHOTO

MEMORY LANGUAGE AUDIO SPATIAL **LOGIC** NUMBER

NEUROBICS

Total Perfection

This puzzle tests your ability to reason about numbers.

Suppose you roll three dice. The three numbers might be all different, or some numbers might be the same. Let's say you find that when you multiply the three top numbers together, you get a result that is the same as when you add the three numbers together. What three numbers did you roll? There is only one solution.

For instance, if you roll the numbers 1, 3, 4, then multiplying the three numbers gives you 12, while adding the numbers gives you 8. The numbers 12 and 8 are not the same, so we know that 1, 3, 4 is not the answer.

Hint: this puzzle does take a little while to solve, but it is not as hard as it looks. Try different combinations of numbers until you find one that works, starting with small numbers.

Bonus puzzle: Once again you roll three dice. This time you find that when you multiply the three top numbers together, you get a result that is twice as large as when you add the three numbers together. What three numbers did you roll? There are two different solutions to this puzzle.

These puzzles were adapted from the book *The Playful Brain: The Surprising Science of How Puzzles Improve Your Mind*, by Richard Restak and Scott Kim (Riverhead Books 2010). For more information, visit theplayfulbrain.com. —*Scott Kim*, scott@scottkim.com

ANSWERS ON P. 14

COST-BENEFIT RATIO

For the time being, is Axona, which sells for approximately $75 for a month's supply and isn't covered by insurance, worth the money?

Probably not, says Nikos Scarmeas, M.D., associate professor of neurology at Columbia University Medical Center. "There are some hints of efficacy, but the appropriate thresholds—those used for FDA medication approval—need to be reached in order to have high certainty about efficacy," he says.

Dr. Isaacson, who treated Martini's father, says he has seen firsthand how patients can improve on Axona. "As long as it's safe and grounded in scientific evidence, and patients are doing better on it, then I'm ok with that," he says.

Dr. Thies offers this common-sense approach: "If you can afford the product and it makes you feel better, there is probably little chance of harm in trying it," he says. "If, on the other hand, you're deciding between buying a medical food or a pharmaceutical drug, the evidence is in favor of buying the drug."

DESTINATIONS

Morgan's Wonderland, San Antonio's Accessible Amusement Park

After months of planning and saving, one father's long journey from Maine to San Antonio, TX, was worth every difficult mile. For the first time, he and his son, who has severe cerebral palsy, rode a carousel together.

This is the kind of story that Gordon Hartman hears all the time from guests at Morgan's Wonderland, the ultra-accessible amusement park that he created. Hartman is the founder of the Gordon Hartman Family Foundation, a non-profit that provides funding and consulting

services to agencies that assist families with special-needs children. Driven by a desire to create an inclusive place where people of all abilities could play together, Hartman built a 25-acre park named for his 17-year-old daughter, who has cognitive delays and physical challenges due to autism spectrum disorder.

Morgan's Wonderland operates as a nonprofit, which allows Hartman to keep the cost of admission low. People with special needs are admitted free, as are children age two and under. General admission for adults is $15 and $10 for children.

When planning the park, Hartman consulted physicians, physical therapists, people with special needs, and caregivers. "Sometimes amusement parks are built for people without taking into consideration people with special-needs, and it's only afterwards that park developers think about how to comply with the *Americans With Disabilities Act*. I wanted to put special needs first."

For example, the specially designed carousel is level with the ground so that no one has to step up to board. Many of the animals on the carousel have a unique saddle—shaped like the back of a chair—to lend additional support to the rider, and some don't move up and down at all. The dragon is designed to accommodate a person in a wheelchair, and a bench allows a family member to go along for the ride.

Kids can hop aboard a miniature train that circles the eight-acre lake. Three playgrounds on top of composite rubber surfaces are located under awnings where water misters help keep everyone cool. Adapted and traditional swings allow guests—even those in a wheelchair—to soar. Over in the Sensory Village, children can shop in a grocery store, catch animated butterflies in an interactive theater, and announce the weather in a simulated TV station. And if children become overstimulated, they can rest in the Garden Sanctuary.

Safety is paramount at the park, which has eight-foot tall perimeter fencing, a public address system, and video surveillance. All guests wear radio frequency identification wristbands. If a child becomes separated from his or her group, other group members can scan their wristbands at one of the location station monitors to find the child.

Since Morgan's Wonderland opened two years ago, more than 200,000 people from all 50 states and 30 countries have visited. With inquiries from more than 20 cities globally about building a Morgan's Wonderland in their community, Hartman says, "This is only the beginning of something bigger."

—Barbara and Jim Twardowski, R.N.

ADVOCACY

The Huntington's Disease Youth Organization

When Matt Ellison witnessed the progression of Huntington's disease (HD) in his father, he also discovered a lack of resources for affected families—particularly young people. "The impact of HD on your life can be huge, but the support available to young people is miniscule," says Ellison, a 23-year-old from England.

So he created the Huntington's Disease Youth Organization (HDYO). Huntington's disease is a devastating, hereditary, degenerative brain disorder that affects an individual's ability to walk, talk, and reason. Currently, HD has no cure and limited treatment options. Children have a 50-percent chance of inheriting the fatal gene if they have a parent with the disease. The goal of HDYO is to empower youth with knowledge about HD and provide a supportive community to help one another cope with realities of the disease.

The organization recently launched its website, **HDYO.org**. "The website is a remarkable effort by Matt and many other young people who are dedicated to this cause," says BJ Viau, HDYO's U.S. board member.

To read the new guideline for patients and caregivers from the American Academy of Neurology on treating involuntary movements in HD, go to **bit.ly/OH4hWt**.

NEUROBICS ANSWERS CONTINUED FROM P. 13

The three numbers are 1, 2, and 3, because multiplying 1+2+3 gives you 6, as does adding 1x2x3

The bonus puzzle has two answers. One answer is 1, 4, and 5, because multiplying 1x4x5 gives you 20, which is twice as big as 1+4+5=10. The other answer is 2, 2, and 4, because multiplying 2x2x4 gives you 16, which is twice as big as 2+2+4=8.

BARBARA AND JIM TWARDOWSKI; DICE: JOACHIM ANGELTUN/ISTOCKPHOTO