A Trace of Arsenic

Minute levels of a notorious poison in rice-based foods raise a troubling question: Is any amount of arsenic safe to eat?

BY **DEBORAH BLUM**

The cans of baby formula invaded Brian Jackson's Dartmouth College lab late in 2010. His team picked up an armful of popular brands at the food co-op in Hanover, N.H. Then another armload. Eventually Jackson had a cabinet full of the brightly labeled canisters. Today, he still keeps a few in his office. Not as clutter — that's not his style. He just likes to keep his toxicology evidence close at hand.

A 47-year-old analytical chemist with sandy-gray hair and blue eyes, Jackson has a chemist's passion for the picky details of analysis, the skill his colleagues tapped when they asked him to investigate a disturbing possibility: that baby foods and formulas made with rice might contain arsenic, a known carcinogen. Ingested even at the trace levels the scientists suspected, devastating health outcomes could result.

Much of the U.S. rice crop is grown in fields that harbor arsenic-based pesticides once used on cotton crops.

In a first round of tests, arsenic levels in all the products Jackson's group studied fell within the 10 parts per billion safety limit the EPA sets for water. (There is no limit for arsenic for most foods.) But a short time later, while shopping at the co-op, Jackson noticed two brands of toddler formula, both high-end organic products, that his team had missed on the first sweep.

This time, to the team's surprise, the arsenic readings flew off the chart.

"My first thought," Jackson says, "was that I'd better reanalyze these samples in case I'd screwed up."

His second thought, after confirming the readings, was to wonder: What made the arsenic levels spike in those two cans? In answering that question, Jackson traced not just the story of the metal-loving rice plant, but also the tangled and troubling path of a notorious poison through our past and present.

A naturally occurring metallic element, arsenic permeates the Earth's crust. Glinting silver-gray in rocks and soils, it mixes with other minerals as it seeps into water supplies, drifts on the dusty plumes of volcanic eruptions and travels on the wind. It also spreads through industrial use, from mining to agriculture.

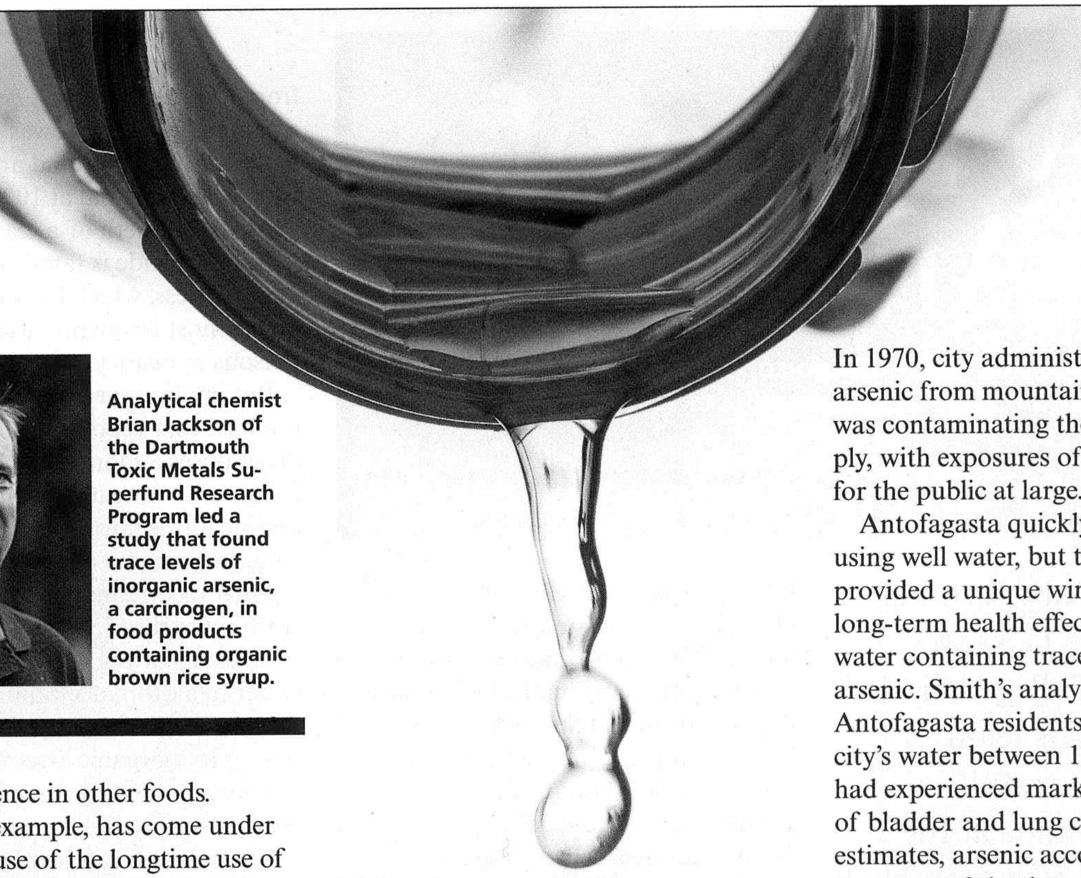
Arsenic coils like a dark smoke through our history. The word derives from the ancient Greek *arsenikon*, meaning "potent." It was used to describe the compound arsenic trioxide, which can be lethal at 100 milligrams, about one-fiftieth of a teaspoon. Arsenic trioxide is famously tasteless and odorless, which helped make it one of the most frequently used homicidal poisons in history.

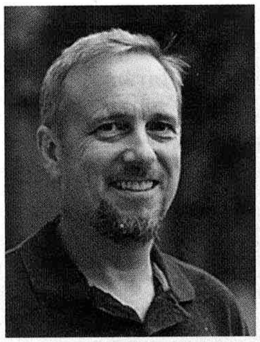
But in recent years, studies have revealed that exposure to far smaller doses poses a more subtle — but also insidious — threat. The pure element arsenic mixes into many compounds, either organic (in chemical lingo, meaning that it contains carbon) or inorganic (without carbon). And even at concentrations of parts per billion (ppb), closer to a drop in a swimming pool than a drop in a teacup, long-term exposure to inorganic arsenic — generally considered the most toxic form — has been linked to an increased risk of cancer and other life-threatening illnesses. Although arsenic hasn't been studied in as much detail as other toxins found in industrial materials, such as mercury or PCBs, scientists say it underscores the finding that minute exposures to such substances can do great harm.

At low doses, arsenic doesn't overwhelm body systems immediately or even cause death over the course of months. Rather, explains Dartmouth molecular toxicologist Joshua Hamilton, chronic exposure to trace arsenic inflicts damage at a cellular level, increasing the body's vulnerability to a wide array of sicknesses, including cancer, cardiovascular disease and diabetes. While trace arsenic won't kill on its own, he says, it "seems to make everything worse."

For decades, officials have focused on trace arsenic in drinking water as the chemical's primary public health threat; in 2001, the EPA dropped the limit for arsenic in water from 50 ppb to 10 ppb. But in the past few years, regulators have also begun to worry about exposure from foods and beverages. This summer, concerned about arsenic in pesticide residues found in imported juices, the FDA announced it will limit the amount of arsenic allowed in apple juice to 10 ppb, the same amount permitted in water.

The FDA has also investigated





Analytical chemist Brian Jackson of the Dartmouth Toxic Metals Superfund Research Program led a study that found trace levels of inorganic arsenic, a carcinogen, in food products containing organic brown rice syrup.

arsenic's presence in other foods. Chicken, for example, has come under scrutiny because of the longtime use of an arsenic additive in poultry feed. But the top-priority food on the list is rice, which became a focus when researchers realized that it takes up inorganic arsenic from soil far more efficiently than other grains. A July study revealed the first evidence directly linking consumption of rice containing arsenic to genetic damage in humans.

Such findings are especially alarming because rice is a major part of the diet in certain communities, such as those with an Asian heritage, and because rice is a staple for infants and young children, whose developing bodies and brains are especially vulnerable to harm.

It's that last concern that sparked the formula studies in Jackson's Dartmouth lab.

EVIDENCE OF HARM

The realization that trace amounts of arsenic might pose a health threat began with mysterious outbreaks of disease in Southeast Asia. In the 1960s, scientists in Taiwan traced an outbreak of blackfoot disease, caused when dying blood cells lead to gangrene, to arsenic-contaminated well water. In many wells, arsenic levels exceeded 800 ppb (80 times as high as today's EPA standards); some wells registered as high as 1 part per million.

Still, researchers didn't pay serious attention to the problem for decades, after a massive public health crisis came to light in Bangladesh. In the 1970s, villages began drilling wells to prevent the deadly infectious diseases that flourished in warm, sewage-tainted surface waters. As predicted, infectious disease rates dropped. What was not predicted was the insidious growth of other diseases: lung and bladder cancers, cardiovascular problems, diabetes and severe skin lesions. As part of a search for the cause, geologic tests revealed large deposits of arsenic-rich minerals steadily leaching into groundwater, causing levels in many wells to top 500 ppb.

After investigating the arsenic situation in Bangladesh at the request of the World Health Organization in the late 1990s, Allan Smith, an epidemiologist at the University of California in Berkeley, recommended that officials declare a public health emergency for what he considered "the largest mass poisoning of a population in history."

Smith had also investigated evidence of similar poisoning in Antofagasta, a Chilean port city that in 1958 had switched from well water to a cheaper supply sluicing down from the Andes. In 1970, city administrators realized arsenic from mountain mineral deposits was contaminating the city's water supply, with exposures of 500 to 800 ppb for the public at large.

Antofagasta quickly returned to using well water, but those dozen years provided a unique window into the long-term health effects of drinking water containing trace amounts of arsenic. Smith's analysis showed that Antofagasta residents exposed to the city's water between 1958 and 1970 had experienced markedly higher rates of bladder and lung cancer. By his estimates, arsenic accounted for about 7 percent of deaths among Antofagastans age 30 and older. "I believe arsenic poses the highest cancer and mortality risks we know of compared to any other environmental exposure," Smith says. "The only exposure we can compare it to is active smoking."

But researchers are also compiling evidence that arsenic poses a health threat at far lower doses than in such highly contaminated water supplies. New York University epidemiologist Yu Chen has followed up on both the Taiwan and Bangladesh findings by looking at water contaminated by arsenic levels of 50 ppb and below. At this trace exposure, she's found evidence of troubling changes in blood cells. And in tracking human disease patterns, she's established a clear link between such low-dose chronic exposure and increases in high blood pressure and heart disease. In one study, she estimated that among Bangladeshis whose drinking water contained as little as 50 ppb of arsenic, exposure accounted for some 29 percent of heart disease deaths.

Read the latest on the health risks of arsenic in food at *Discover* blogs: **DiscoverMagazine.com/arsenic**

TOP: SHUTTERSTOCK. INSET: DARTMOUTH COLLEGE

Animal studies strengthen the case. In one study, Dartmouth's Hamilton found that arsenic exposure at 10 ppb compromised the immune systems of mice so much that they could not fend off an ordinary influenza infection. In another study, his team found that mice given chow containing trace amounts of arsenic, then exposed to a standard daily dose of ultraviolet light, had higher rates of skin cancers than mice given untainted chow. "This is a very, very subtle poison at low doses," Hamilton says. "Each passing year, we've discovered health effects at lower and lower doses. There isn't any other toxicant that we know of that even comes close to arsenic in terms of the number of health effects at the doses we're seeing and the numbers of people worldwide who are potentially exposed."

THE RICE CONNECTION

As evidence of harm from low-dose arsenic in water mounted, scientists began to wonder about the food grown in that water and distributed to dinner tables worldwide.

The first person to tackle the issue was biogeochemist Andrew Meharg. In 1999, Meharg, then at the University of Aberdeen, Scotland, was studying the environmental effects of arsenic in Bangladesh when a student noted that rice was being irrigated with vast quantities of arsenic-contaminated water.

Could that raise the risk? The question was urgent because rice is a dietary staple — not only in the typical vegetarian Bangladeshi diet, but everywhere: in whole form and also in rice flour, malt, bran, pasta, noodles, breakfast cereals, cereal bars, crackers, rice cakes and more. "While a range of other foods may show arsenic elevation, we do not eat them two or three times a day, in a multitude of forms," says Meharg, now at Queen's University in Ireland. "In terms of importance: rice, rice and rice again. Nothing matches it."

Testing the rice paddies in Bangladesh, Meharg found his fears realized. Rice plants took up inorganic arsenic from water and soil with dismaying efficiency: at 10 times the rate of other grains. And the flooded fields — which turned out to foster the release of inorganic arsenic — only made things worse.

Later, comparing samples of multiple species of rice grown in numerous regions around the world, he found arsenic levels almost universally elevated, including in the U.S. Notably, much of the U.S. rice crop is grown in regions of the South where the soil is contaminated by old arsenic-based pesticides, once used by farmers to protect cotton crops from boll weevils. In a 2007 study, Meharg found that rice grown in some South-central states contained nearly twice as much arsenic (an average of 30 ppb) as rice grown in California (an average of 17 ppb).

HEALTH FOOD SURPRISE

The leap to early childhood exposure was straightforward. In 2008, Meharg reported that arsenic in baby rice cereal sold in the U.K. exceeded safety levels set for drinking water by both the U.S. and the European Union.

That finding caught the attention of scientists at Dartmouth's Toxic Metals Superfund Research Program, which tracks high-profile metallic elements, mainly arsenic and mercury, for the federal government. One Dartmouth scientist, epidemiologist Margaret Karagas, had already found that babies whose mothers relied on water from wells drilled in New Hampshire's arsenic-rich bedrock — with contamination measured at levels as high as 1 ppm (1,000 ppb) — were disproportionately likely to have low birth weight and might also be more vulnerable to childhood infections. But now the Dartmouth researchers decided to investigate food as well.

Baby foods were the starting point.

The Dartmouth researchers realized that all kinds of baby formulas and foods contained rice; many were thickened with rice starch. It was that awareness that prompted Jackson's investigation of formulas.

Although the team's initial tests found barely a trace of arsenic in baby formula and pureed baby food, later tests showed that two organic toddler

Secret Ingredients

New detection tools have helped public health officials gain better understanding of low-dose toxins and pathogenic bacteria and viruses in many foods, including this partial list:

Arsenic
Rice, apple juice, chicken, pet food

Melamine
Baby formula, pet food

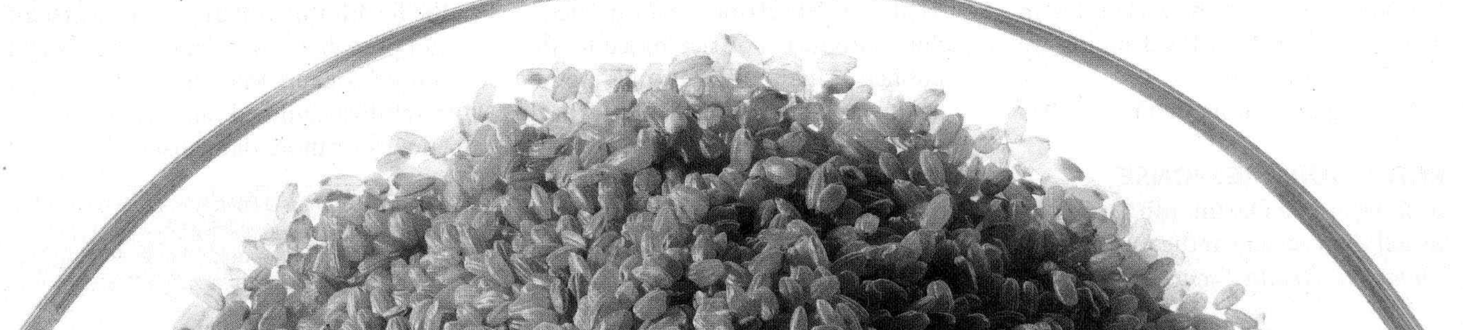
Mercury
Seafood

E. coli
Spinach, lettuce, sprouts, bologna, beef, hazelnuts, frozen cookie dough

Salmonella
Cucumbers, sprouts, tomatoes, mangoes, papayas, cantaloupe, chicken, beef, pistachios, Turkish pine nuts, wheat cereals, peanut butter, tahini paste, dog food, red and black pepper on some Italian-style meats

Listeria
Cantaloupe, ricotta cheese, deli meats, soft cheeses, smoked fish

Norovirus
Norovirus, responsible for almost half of all reported foodborne illnesses, is spread by human contact and by consuming tainted food and water. Foods commonly involved in norovirus outbreaks include leafy greens, fresh fruit and shellfish



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formulas contained up to 60 ppb of arsenic (adjusted for dilution) — six times the EPA safety limit for water.

Labels on the formula canisters told why: They were sweetened with organic brown rice syrup, considered a healthy alternative to corn syrup. And while brown rice syrup is rare in baby foods, it is common in crackers, cereals, snack bars, energy bars and many products marketed as health foods. "We didn't choose the syrup as a study subject," Jackson says. "The syrup chose us."

The Dartmouth team expanded their tests, analyzing 29 cereal bars and energy bars as well as three varieties of pure brown rice syrup. Rice-free bars, they found, had the lowest arsenic levels, as little as 8 ppb. Arsenic concentrations in the rice bars ranged from 23 to 128 ppb; those sweetened with brown rice syrup were at the high end. Organic brown rice syrups registered as high as 400 ppb of arsenic — mostly the more dangerous inorganic form.

It made sense that syrup, which concentrates sugars, would also concentrate other chemicals, including arsenic. But the Dartmouth team did not expect it to concentrate arsenic so intensely. So another member of the group, plant geneticist Mary Lou Guerinot, decided to take a closer look. Using a technique that creates high-resolution, three-dimensional images, Guerinot and her colleague Tracy Punshon, an expert at imaging metals moving through living systems, found arsenic concentrated in the grain's nutrient-rich outer layers, which are polished off in the processing of white rice but remain in brown rice.

As the data emerged in detail, Punshon stopped buying rice-based cereal bars and started making her own rice-free bars. Another researcher, a runner, had been a devotee of energy bars sweetened with rice syrup — until analyses showed she was taking in some five times the EPA drinking-water standard for arsenic.

She stopped eating them.

PATCHWORK RESPONSE

Still, when the Dartmouth team published their results in the journal *Environmental Health Perspectives* in February 2012, they were unprepared for the public outcry. Parents called, frightened they had been poisoning their children. Media outlets clamored for quotes. Some producers of rice-based foods publicly criticized the group's methods.

Bottom: Rice is particularly prone to accumulating arsenic because it confuses two forms of inorganic arsenic — arsenite and arsenate — with silicon and phosphorous compounds that are essential for the plant's structural integrity and health. Top: Inorganic arsenic accumulates in the outermost layers of the rice grain.

"It was a bit of a bother," says Jackson, characteristically understated. He doesn't gravitate to being onstage. "I don't want to get into a fight. I published what I published, I've gone through the whole peer review process. That was really enough for me." And in the end, even his industry critics accepted his point. The organic formula maker Nature's One, whose products were implicated in the research, announced a new zero-tolerance policy for the element.

Yet Jackson points out that a central problem remains: No one really knows how much rice is safe to eat. But recent research provides further evidence that a diet high in rice that contains arsenic is worth avoiding. In July, researchers in the U.K. and India reported that people who ate arsenic-tainted rice on a daily basis showed troubling signs of chromosomal damage — and that such damage increased with greater amounts of arsenic in the rice.

As such connections are made, Jackson and his colleagues argue that what's really needed isn't a patchwork of voluntary responses but an official safety standard for arsenic in all foods. That stance is affirmed by other public safety advocates as well, including scientists working with *Consumer Reports* who have recently reported elevated arsenic levels in both juice and rice.

The FDA's 10 ppb limit for apple juice, announced this summer, is widely regarded as a response to such concerns. The agency is now considering a limit for rice as well. Although FDA officials have not commented publicly on what a rice standard might look like, scientists working with the agency say one focus is on the most visible risk groups — infants, children and high-rice-consumption populations such as those on gluten-free diets and people of Asian and Hispanic descent, who often eat rice and rice products several times a day.

Whatever the regulatory future holds for arsenic, it is only one piece of a bigger issue of trace contamination, says Hamilton, who considers the arsenic story a cautionary tale. As we consider the health threat that low-dose arsenic can pose, he says, we must also consider other toxicants that have not yet been carefully examined but that might be equally or more dangerous. D

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JAY SMITH/DISCOVER, ADAPTED FROM TRACY PUNSHON, DEPARTMENT OF BIOLOGICAL SCIENCES, TOXIC METALS SUPERFUND RESEARCH PROGRAM, DARTMOUTH COLLEGE (RICE GRAIN) AND FROM ANDREW MEHARG, QUEEN'S UNIVERSITY (STRUCTURAL FORMULAS)

Food Radar

Detecting the Dangers

Importing Risk

Like our cars and our kids' toys and of course those designer bags, the food we eat often comes from overseas. Almost 15 percent of foods consumed in the U.S. come from outside the country. That includes about half our fruit, 20 percent of our vegetables and 80 percent of our seafood. Fully 90 percent of the shrimp that hits American tables hails from abroad, primarily from Southeast Asia, Ecuador and Mexico. Thousands of ingredients used in countless food products are imported from foreign lands; penetration from overseas is so vast and complex that a single product might contain ingredients from multiple countries, a fact you would never discern from labeling on the food itself.

The situation might sound exotic, but it puts us at risk. Technically, the U.S. asks foreign food producers to hew to the same standards as American counterparts. But in reality, no government-mandated system ensures that occurs. Some shrimp grown in Southeast Asian factory ponds, for instance, are doused with toxic antibiotics outlawed here, according to Michael Doyle, director of the University of Georgia's Center for Food Safety.

When it comes to food grown at home, the FDA and the U.S. Department of Agriculture (USDA) have greater reach to find problems and the teeth to clamp down. Every food factory in the U.S. is supposed to undergo rigorous inspection. On the local level, when a restaurant fails to meet standards for food safety and cleanliness, local inspectors can shut it down.

But when food comes from abroad, it is only as safe as the laws of the producer-nation can guarantee. And many of the countries our food comes from are far less vigilant or consumer-oriented than the U.S. Once imported foods reach our shores, they enter the distribution chain with little fanfare and scrutiny; some argue they are barely vetted at all. Instead, by and large, problems come to light when Americans get sick.

> **Almost 15 percent of foods that hit U.S. dinner tables come from outside the country. Imported food products do not receive the same degree of scrutiny as U.S. foods.**

Part of the problem is the lack of resources we ourselves direct to food from abroad: The FDA has a minuscule team of some 1,500 inspectors devoted to food imports, a workforce too small to screen more than a tiny fraction of the food that arrives at U.S. ports each year for microbial pathogens or other disease-causing contaminants.

"We have been a domestic agency operating in a globalized world," says Charlotte Christin, a senior policy adviser at the FDA. But things are set to change.

The change-agent, optimists say, is the Food Safety Modernization Act of 2011. Regarded as the biggest update to the FDA since the agency's founding, the act is intended to turn the agency from what it has traditionally been — a watchdog with exclusively domestic fangs — into what the public expects it to be: a proactive international tiger that vets all foods (as well as medicines) entering the U.S.

But it may not be good enough. A lack of funding and resources can still render the FDA somewhat helpless to work across borders to implement food safety plans as stringent as the ones we apply to domestic food products. "Ultimately, we're going to have to collaborate with other countries to help them change their food safety culture," says the University of Georgia's Doyle, especially where food is produced under less than satisfactory sanitary practices.

—VERONIQUE GREENWOOD

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