

Bruce Ames in the lab at Children's Hospital Oakland Research Institute, where he's been researching the link between micronutrients and obesity.

The Hunt to Fix Hidden Hunger

Biochemist Bruce Ames thinks a simple multivitamin may fight obesity

The biochemist who invented one of the first tests for carcinogens, the same man who made a career of decrying organic agriculture and infuriating environmentalists with his full-throated defense of pesticides, has just devoured a massive pile of glistening, organically farmed arugula. He nibbles a piece of warm bread as he waits for the second course: steaming polpettini, tiny fried meatballs. “Ooh, that looks good,” Bruce Ames says, as he prepares to tuck in.

Ames, who is tall and small-framed with an academic moustache, thick, round glasses and a penchant for bow ties, has long been a regular at Oliveto in North Oakland. Between bites, he recalls his decades-long love affair with the laboratory, a liaison that continues to cultivate controversy in this, his 78th year.

Since 1950, Ames, who was born and raised in Manhattan, has worked in biochemistry and molecular biology, first at the California Institute of Technology and the National Institutes of Health in Maryland, then in Francis Crick’s Cambridge, England, laboratory, and since 1968 at UC Berkeley. Today he’s a senior scientist at Children’s Hospital Oakland Research Institute (CHORI), where he manages a group of 20 researchers. Thirty years ago, he developed the Ames Test, still one of the key diagnostic tools for detecting cancer-causing substances. He became a fixture in *Science* magazine with a review in 1983 on dietary carcinogens that appeared behind a cover reading: “Eat. Die.” The article explained that most fruits and vegetables contain natural mutagens and carcinogens, and seemed to suggest that produce

consumption could lead to cancer.

Four years later, Ames published a study in the same journal, calling environmentalists to task for their criticism of agricultural pesticides. He argued that exposure to synthetic mutagens and carcinogens comprises only 0.10 percent of all chemical exposure, making pesticides a “distraction” from real cancer research. (Today, Ames explains that the original *Science* article was intended to undermine pesticide claims rather than highlight vegetables as a health threat, though the editor’s note that precedes the article indicates otherwise.) To date, Ames has written more than 150 papers on the pesticide “scam,” leading some to characterize him as a shill for the chemical industry. Despite their disagreements with the social and policy implications Ames draws from his experiments, many of his critics concede he’s an exceptional researcher. No one was surprised when, in 1998, President Clinton awarded him the National Medal of Science for his “creativity, resolve, and a restless spirit of innovation to ensure continued U.S. leadership across the frontiers of scientific knowledge.”

Years ago, Ames invested in the business venture of one of his postdoctoral students. When the firm was sold, Ames found himself supremely wealthy — he’ll narrow it down to “less than half” of the \$100 million the company sold for — but even the dual siren calls of leisure time and luxury couldn’t separate him from his work. “I’m not a Ferrari type and I don’t have anything better to do,” he says.

Six days a week Ames can be found in his paper-filled office, catching up on the latest journal articles, overseeing his gaggle of scientists and conjuring ex-

periments to slow the body's response to time and gravity. With his wife, Giovanna Ferro-Luzzi (a retired professor of biochemistry), Ames splits his year between the Bay Area, an apartment in Rome and a villa in Tuscany. He says he doesn't treat the trips as just vacation and glances up from his laptop only occasionally to take in the view. A cousin recalls a family cruise when Ames' relatives informed him that he would be required to join them in practicing free throws on a basketball court. Between shots, Ames stood in line shuffling scientific papers; he looked up only when it was his turn to throw the ball.

For years, Ames kept his microscope focused narrowly on cancer and aging. Today, he's increasingly concerned with the cellular consequences of a diet short on vitamins and minerals. The required intake of these micronutrients varies according to gender, age, geography and body type, and Ames believes the people now in greatest need of micronutrients are the poor, elderly and obese.

Like Ames, epidemiologists are increasingly studying the phenomenon of "hidden hunger," which occurs when people eat a low-cost diet that's filling, but provides few micronutrients. In less developed countries, this type of malnutrition often stems from only eating a single type of grain. Here, it can evolve from a diet of unhealthy processed foods, which are often the cheapest calories available. People who eat little fresh produce, Ames says, are "starving for vitamins and minerals. They're not starving for calories, but you need more than calories."

A variation on the phenomenon of hidden hunger that occurs in the visibly obese is undernutrition, overweight, and Ames predicts it will result in health problems beyond those already associated with obesity. The lack of micronutrients, says Ames, can upset functions throughout the body. "I think it is likely," he wrote last year, "that when one input in the metabolic network is inadequate, repercussions will be felt on a large number of systems and lead to degenerative disease."

Besides diabetes and heart disease, Ames predicts we're likely to see decreases in brain function and accelerated aging among the overweight and obese. And more cancer, too. "The relationship between diet and cancer has, historically, been thought of in terms of exposure to potential carcinogens, such as alcohol," he wrote in 2002. "Dietary deficiencies, however, might be a much more important factor in cancer risk."

To some, Ames might seem an unlikely critic of a diet based on processed foods. One could be forgiven for wondering whether his new work isn't leading him to turn his back on the industrial food system he's spent most of his career defending. But it seems he looks at diet and poverty through an unusual lens, one that filters out many external factors, such as the influence of a multibillion dollar food marketing industry and the many impover-

ished American neighborhoods where fruit and vegetable are rare.

"Nobody should be getting fat. If they're fat, it means they're probably eating a lousy diet and they ought to shape up," Ames announces over lunch, with an exasperation that reaffirms his libertarian soft spot for personal responsibility. Instead of promoting traditional nutrition education or farmers' markets as a way to minimize micronutrient deficiencies, Ames has concocted a new idea, one with origins in the laboratory. He calls it the "metabolic tune-up." In layman's terms, it's a bottle of pills.

It's a simplistic solution to the multifaceted problem of modern-day obesity, one that avoids the logistical and political difficulties of more established responses. It's faster and cheaper than improving access to produce or removing soda vending machines from schools. And perhaps one reason Ames isn't interested in revolutionizing the 21st century food supply is that, at least a part of him, thinks that in the process of looking for a cure for micronutrient deficiencies among the obese, he may have stumbled upon a cure for obesity itself.

Four Tons of Spinach

The types of deficiencies Ames now studies fall somewhere between the complete absence of a micronutrient and the optimal intake levels, the RDA. "There are degrees of deficiency," explains Fernando Viteri, an M.D. and scientist who has worked with Ames. "You may have a mild deficiency, you may have a moderate deficiency, you may have a severe deficiency. We know a lot about severe deficiency, we know some about moderate deficiency, we know little about mild deficiency."

Ames's fallback example is that of folate, a type of vitamin B that helps form red blood cells, if only because his mentor in graduate school discovered the substance after isolating it from four tons of spinach. A severe folate deficiency can lead to a type of anemia. In 1997, Ames co-authored a study that showed how, over time, a milder deficiency in folate leads to breaks in chromosomes, as massive amounts of uracil, a component of RNA, become incorporated into DNA. The effects of the damaged chromosomes on the human body are the equivalent of "stepping in front of an X-ray machine," says Ames, who traces a direct link from the deficiencies and chromosome breaks to colon cancer and cervical lesions. What's more, this work indicated to Ames that half of the nation's poor might suffer from broken chromosomes.

Recently, Ames overheard a colleague mention 60 cases of rickets at nearby Children's Hospital Oakland. The disease, which is caused by vitamin D or calcium deficiency and had essentially been eliminated in the United States, is still common in countries with an unpredictable food supply. How, Ames wondered, could ailments such as rickets,

which have historically been associated with malnutrition occur in a population that grows increasingly plump?

Could it be, he asked, that a society gorging on empty calories is simultaneously starving itself of the vitamins and minerals needed to keep its internal gears churning? Or that children who once played outdoors in the sunshine required to make vitamin D in the skin now stay indoors, hypnotized into inactivity by their TV screens? For years obesity was a sign of wealth; people with limited cash went hungry. But as cheap, highly processed foods have taken root in our supermarkets, narrowing the shelf space for fruits and vegetables, obesity is more frequently associated with poverty.

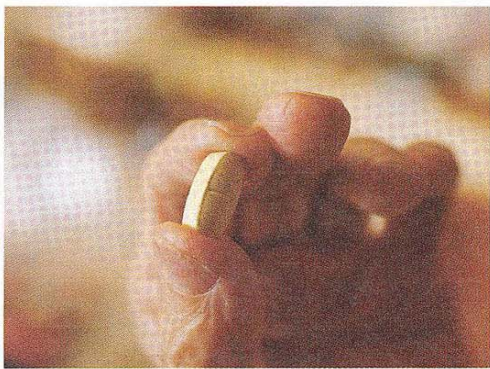
Ames continues to assemble evidence that a dearth of micronutrients can damage DNA. "We've been taking human cells in tissue culture, and they go through a certain number of generations and then they senesce," he explains, adding that when the cells are deficient in a certain micronutrient, they senesce, or age, prematurely. "We still have to prove it in people and at what level, but so far for every vitamin and mineral deficiency we've looked at they senesce early and we see a lot of DNA damage."

A properly functioning body requires healthy mitochondria, the "power plants" of nearly every human cell. Vitamins and minerals fuel the mitochondria, which in turn burn fats, carbohydrates, and protein in food to form energy for the rest of the body. With age, mitochondria degrade and lose efficiency. Oxygen radicals, atoms with unpaired electrons that are also called "free radicals," result from that inefficiency and bind with other molecules to interfere with normal cell operations.

Inadequate micronutrient intake, Ames believes, affects the mitochondria in much the same way as aging. He has proved in tissue cultures that micronutrient deficiencies can degrade DNA, leading to the production of mutated chromosomes that can cause cancer. Over the short term, nature appears to be kind to the mildly micronutrient deficient human body. But chromosome disintegration will result in dire long-term health consequences, Ames says. In the absence of enough nutrients, he postures, "What nature would want is for the animal to survive, but anything long term will be ruthlessly dispensed with. So it's a triage system. And I think DNA damage is long term. It shows up as cancer 30 years later."

The Metabolic Tune-Up

"This is not established, it's a hypothesis, but it's a very interesting hypothesis," says Walter Willett, Harvard epidemiology and nutrition professor, who is best known for his ongoing health surveys of thousands of health professionals. "Like much of what Dr. Ames has raised over the years, this is



If supplements provide the absent micronutrients, Ames wonders, would the body finally tell the brain it's full?

somewhat beyond conventional thinking.” In his own studies and in surveying the research of others, Willett says he has found convincing evidence of increased rates among the obese of endometrial, kidney, colon and esophageal cancers, as well as leukemias and lymphomas. There’s also, he says, “quite good suggestion” of decreases in brain function and advanced aging among the obese, the people in whom micronutrient deficiencies are likely to be the most pronounced.

To prove his hypothesis, Ames has initiated a blood sample study of 20 obese Oakland teenagers. It’s in the study’s second stage that the metabolic tune-up comes in. At its essence, the metabolic tune-up is a multivitamin and mineral supplement that provides the nutrients absent in a diet of processed foods. “Of all the aspects of a bad diet,” Ames says, “I’ve taken out the part that we can do something about cheaply, and that’s the micronutrients. It’s vitamins and minerals because they don’t cost anything. I just went to Costco and bought a year’s supply for 11 bucks.” (Despite his new interest in malnutrition, Ames is well-versed in the supplement market. In 1997, he invented an anti-aging supplement, which sells online. He says he put his stock in the company, Juvenon, in a foundation, and adds that he doesn’t plan to sell additional supplements.)

Once people receive the nutrients they’re lacking, Ames predicts they’ll improve their cellular health and probably eat less. “Mechanisms are not well understood,” Ames has written, “but we are pursuing the possibility that a shortage of . . . micronutrients inhibit[s] satiety leading to a continued cycle of over-eating.” The basis of his suspicions rest partly in the still-confidential results of an obesity study conducted by another member of the Ames lab.

Though he’s spare on details, Ames believes his colleague’s study convincingly connects obesity to an inflammation of the gut brought on by poor nutrition. “Maybe if you’re short of micronutrients, you’re hungry all of the time,” Ames says. “That could be plausible, that if you don’t have enough iron, you eat to try to find the missing iron.” If sup-

plements provide the absent micronutrients, Ames wonders, would the body finally tell the brain it’s full?

Though it has worked in certain contexts, some question whether supplementation is the proper response to micronutrient deficiencies in a food-rich environment. Ed Blonz, the Bay Area nutritionist behind the “Ask Dr. Blonz” Web site, argues that the body can’t interpret vitamins and minerals in pill form as effectively as micronutrients absorbed directly from fruits and vegetables. “The problem with reductionist approaches to micronutrition and macronutrition,” Blonz says, “is you’re not presenting it in the way it’s present in food. Stick with food,” he continues, “food seems to have it down.”

Scientists who have worked with Ames also raise concerns. Fernando Viteri, the CHORI scientist and professor emeritus of nutrition at UC Berkeley, points out that the combination of foods eaten at a meal can determine how well micronutrients are absorbed. Glancing down at his cup of coffee during a recent interview, Viteri pointed out that had he used the coffee to wash down a multivitamin and mineral pill at breakfast, the polyphenols in the coffee would have blocked his intake of iron and other micronutrients.

“The composition of the diet is important,” Viteri explains. It’s not enough to manufacture pills. “You have to work with a community. You have to work with the people and so it isn’t just the fact that there are these pills or bars or whatever. Will people take them? Will they know what they’re for? What are their attitudes toward them?” To effectively target micronutrient deficiencies, Viteri says, you need to consider culture, not just the inner workings of individual cells.

Deconstructing Dinner

If you want to see Ames grow impatient, try asking him to contemplate food policy or the roots of poverty in America. He dances nimbly around the topics, insisting that they’re not his area of expertise while making vague references to individual choice and an unwillingness of people to take an interest in what’s good for them. “More than 20

years of effort to improve the American diet has not been particularly successful with less-educated people,” he pronounces.

Joan Gussow, professor emeritus of nutrition education at Columbia University, first learned of Ames’s new work on a recent trip to California for a meeting of the Roots of Change Fund, a foundation whose anti-Amesian mission is to transform the state’s food system. She offered a critique on a ride across the Bay Bridge. “This is the standard line that scientists have used about fortification for the past 35 years, ‘Well, it would be good if people ate a good diet, but since they’re not going to anyway, we had better fortify. We better give them nutrients.’ That’s what they’ve always said, but nutrition education hasn’t failed. It hasn’t even been tried.”

She continued. “We have an incredibly unhealthy population and we have the richest population in the world. There’s something wrong. There’s something wrong with how we’re being sold food, there’s something wrong with how food is being produced, there’s something wrong with selling children on the worst kind of food there is. All these things are really questionable and we have to do something about that.”

Ames disagrees. “It’s a matter that people have to take charge in their own lives in eating a good diet.”

The effects of hidden hunger could have an impact beyond the United States as the American diet continues its circumnavigation of the planet. Six years ago, the research group Worldwatch Institute challenged conventional health assumptions with its report that, “For the first time in human history, the number of overweight people rivals the number of underweight people.” This year, the United Nations Food and Agriculture Organization detailed the emergence of a “double burden of malnutrition” in such countries as China, India, and South Africa, where public health officials are now battling obesity along with starvation.

Of course, a micronutrient pill wouldn’t address inequitable access to fresh foods or add an extra hour to the day in which to prepare healthy meals. And indeed, those factors are a bit too broad to solve with a microscope. “I’m just trying to understand the science,” Ames says. “If you can solve poverty that’s terrific, but I don’t think people know how to do it. I mean, you throw money at it, you often get just the opposite of what you’re trying to accomplish.”

Then again, he’s open to being proven wrong. “It’s up to us to show that our solution is more cost-effective than the next guy’s solution,” Ames says, “and which one is going to win out, I don’t know. So let people try. Let 100 flowers grow and we’ll see which one blooms.” ♦

Leah Messinger is a freelance writer who lives in Northern California. She can be reached at leah_messinger@hotmail.com.