

No matter how well you eat, take a multivitamin daily.
It may just save your life, says biochemist Bruce Ames.

The Ames Prescription



BY PETER JARET



Well into his 70s, at a time when most of us would be content to settle in an easy chair and watch the world go by, biochemist Bruce Ames, Ph.D., shows no signs of slowing down. On the contrary. When he's not dashing around the world to speak at scientific conferences, he's scurrying between an office piled high with teetering stacks of research journals and the bustling research laboratory he directs at Children's Hospital of Oakland Research Institute in Oakland, Calif. He's a tall, slender, bespectacled man with the rumpled look of an Oxford don. Don't let his age and appearance fool you, though. Ames has the drive and energy of a man half his years—and one possessed by a burning mission to boot.

Among fellow scientists, Ames is best known for developing a laboratory procedure called the Ames test, which is widely used to identify potentially cancer-causing substances. Over the years he's helped to detect carcinogenic compounds in a number of commonly used products—from hair dyes to

flame-retardants used in children's clothes—that were then removed by manufacturers. He's also managed to ignite plenty of controversy by insisting that some widely feared substances, including pesticide residues on fruits and vegetables, aren't as hazardous as many people think.

Now he's stirring up controversy again with a surprising new warning. The most serious cancer risk many of us face may not have anything to do with chemical exposures. The real danger, says Ames, is vitamin and mineral deficiencies.

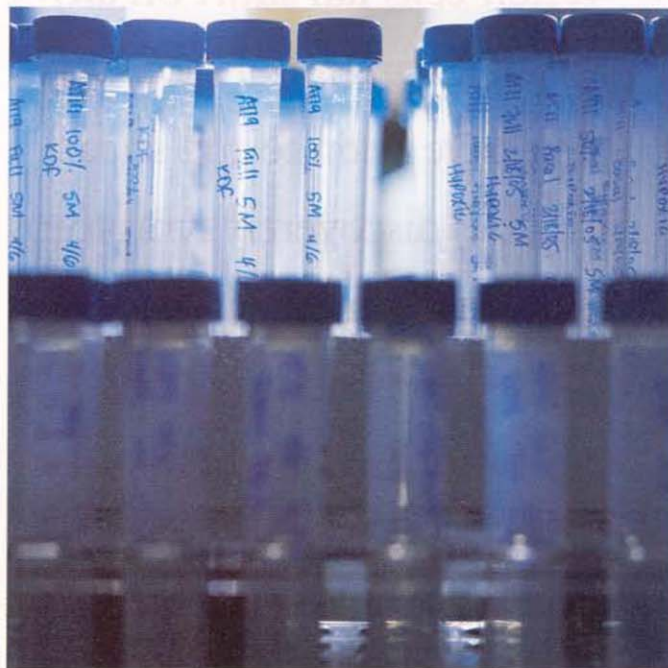
In his lab, he and his colleagues have been systematically depriving human cells of one essential nutrient after another and then looking to see what happens. What they've observed isn't pretty. When cells fall short on any one of a handful of nutrients that have been tested so far, Ames has discovered symptoms of severe genetic damage—the kinds of mutations in DNA that are believed to lead to cancer. Nutrient deficiencies also appear to disrupt the function of mitochondria—the tiny organs that provide cells with fuel. The result: premature aging of cells.



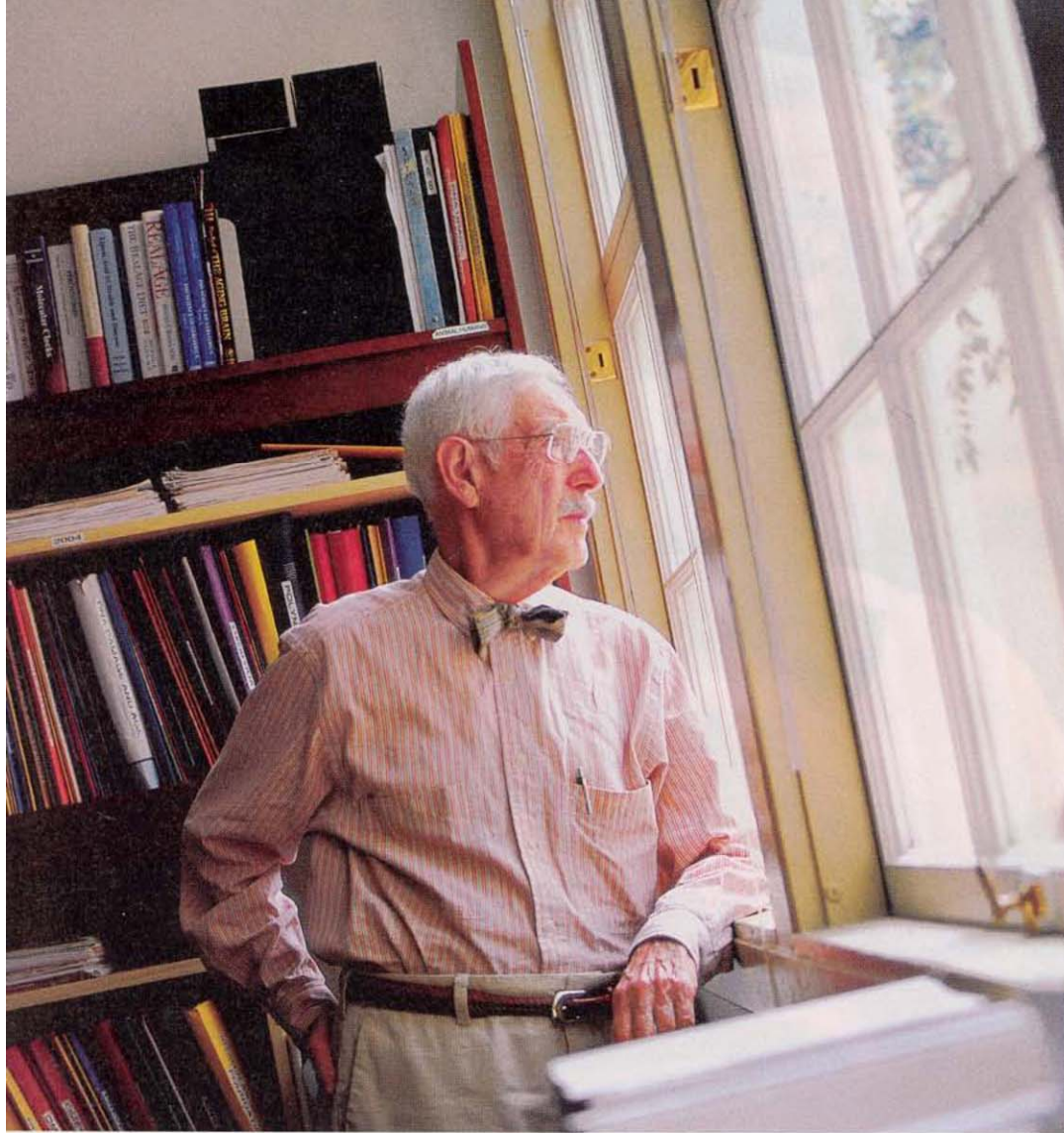
Biochemist Bruce Ames, Ph.D., is stirring up controversy with a new warning that vitamin and mineral deficiencies may well lead to cancer.

“We’ve known for a long time that there are about 40 vitamins and minerals that are essential to human health,” says Ames. “Our research simply demonstrates how crucial they really are.”

His findings come at a critically important time. New surveys show that many Americans are woefully deficient in a number of key nutrients—including several that have shown up in Ames’s studies. For example, more than half of Americans don’t get enough calcium, vitamin E, fiber and potassium, according to a report released in August 2004 by the U.S. Department of Agriculture’s Dietary Guidelines Scientific Advisory Committee. A majority of adults also are deficient in vitamins A and C and magnesium. All you have to do is look at the nation’s expanding waistlines to know it’s not because we don’t get enough to eat. The real culprit is the poor nutritional quality of what we eat—foods overloaded with calories and short on nutrition. At the same time that we’re overfed,



Steve Skoll (top and bottom)



Ames in his office at Children's Hospital of Oakland Research Institute.

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If Ames is right, that combination of factors could be proving more dangerous than anyone imagined.

Ames's scientific approach is remarkably simple. For years, biologists have possessed the ability to keep human cells alive in lab dishes by immersing them in a broth that contains all the nutrients they need. Ames and his colleagues simply remove a single nutrient—iron, zinc or vitamin B6, for instance—and then observe how the cell is affected.

Among the first cellular components they examined were mitochondria, which, as previously stated, function like tiny batteries in cells, converting fats and carbohydrates into energy. The conversion process requires mitochondria to take electrons from oxygen molecules and shuttle them around to create chains of other molecules.

Normally, the process is highly efficient; only a few oxygen electrons are lost, spinning off to become what are called free radicals.

But when levels of some key nutrients fall short, something goes badly wrong. "Suddenly the mitochondria begin pouring oxygen radicals into the cells, almost as if something had ruptured inside," says Ames.

In retrospect, that shouldn't seem surprising. Mitochondria need a variety of nutrients—zinc and iron among them—to create the enzymes that are used in the energy conversion process. When they don't get enough, the process goes haywire. And as mitochondria begin to malfunction, more and more oxidants are allowed to escape into the cell.

One consequence is likely to be premature aging. "Mitochondrial decay is one of the hallmarks of aging," says Ames. "And one of the chief causes of premature aging may be nutrient deficiencies." The most vulnerable cells are likely to be those that require the most energy—specifically brain cells, which are among the most energy hungry cells in the body. Ames suspects that mitochondrial damage may be an important factor in memory loss and other cognitive problems associated with old age.

Bits and pieces of accumulating evidence bolster his suspicions. Both zinc and iron deficiencies are known to cause neurological problems in children, for example. Studies conducted around the world have shown that giving at-risk kids supplements of these minerals allows their brains to develop normally. Adequate levels of both minerals, as well as antioxidant vitamins, may also help protect older brains. In 2004, researchers from The Johns Hopkins University in Baltimore, Md., found that older people who reported taking vitamins E and C were significantly less likely to develop Alzheimer's disease than those who didn't.

When mitochondria fall short on essential nutrients and start leaking those oxidative radicals, they may also increase the danger of other chronic diseases. Heart specialists now believe that oxidation is part of the process that damages cholesterol on artery walls, turning it into dangerous plaques that trigger heart attacks.

Again, there's provocative evidence that keeping vitamin and mineral levels high may offer significant protection. One of the newest risk factors for heart disease is a substance called C-reactive protein, which rises when artery walls have become inflamed. At the Cooper Institute in Dallas, Texas, researchers enlisted 87 volunteers in their 50s, took blood

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samples, and then gave them daily multivitamins. At the end of six months, blood tests showed a significant drop in levels of C-reactive protein.

Furthermore, a 2003 study by Harvard University scientists in Boston offered direct evidence that boosting vitamin levels may lower heart disease risk. The scientists found that among more than 83,000 women who are being followed in the Nurse's Health Study, those who reported taking extra vitamin C were 30 percent less likely than those who didn't to have coronary heart disease.

What worries Ames more than anything else, however, is the extensive chromosomal damage he has seen in cells deprived of essential vitamins and minerals—“damage that rivals and even exceeds the effect of radiation,” he says. Some of that DNA-bashing is likely to be caused by the surge in oxidative

Choosing a Multivitamin

At a cost of just a few cents a day, a good basic multivitamin/mineral pill is one of the cheapest forms of health insurance around. “I tell all my patients to eat a healthy diet,” says James Dillard, M.D., clinical director of Columbia University's Rosenthal Center for Complementary and Alternative Medicine in New York City. “And I tell them to take a multivitamin.”

Which one? With dozens of brands on the market, shopping for a multi can be daunting. Here's what you need to know:

>>>> Choose carefully pills with added herbs or other nutrients, Dillard says. They typically don't include enough to offer therapeutic doses. Stick with a basic multivitamin/mineral formula.

>>>> Choose a pill that contains 100 percent of the daily value of vitamins D, B1 (thiamin), B2 (riboflavin), B3 (niacin), B6, B12 and folic acid.

>>>> Choose a pill that contains 100 percent of the recommended value of copper, zinc, iodine, selenium and chromium.

>>>> Avoid pills with megadoses of anything—unless your physician or nutritionist has prescribed it.

>>>> Choose a pill that's right for you. Pre-menopausal women need iron. Men and post-menopausal women don't—and too much iron can increase the risk of cardiovascular problems.

>>>> Check for an expiration date—your guarantee that the manufacturer cares enough to make sure the product remains active.

>>>> Two organizations certify that a vitamin pill has been produced under good manufacturing standards—ConsumerLab.com and the United States Pharmacopeia (USP). Some products carry their seal. For more information, check out consumerlab.com and usp.com.

>>>> Multivitamins should be stored in a cool, dry place.

>>>> Take the pill with food, which helps the body absorb fat-soluble nutrients. —P.J.

Beyond Vitamins and Minerals

Anti-aging research has begun to focus on mitochondria, the tiny organs within cells that provide fuel. This energy conversion process normally creates small numbers of unstable oxygen molecules, called free radicals; but with age, mitochondria become less efficient, and the levels of free radicals begins to rise, ultimately damaging the cell.

Biochemist Bruce Ames believes he may have found a remedy. Several years ago, he and colleagues at the University of California, Berkeley, began testing a combination of acetyl-L-carnitine (a metabolite used by mitochondria) and lipoic acid, a potent antioxidant, in rats. The combination dramatically rejuvenated the older rats' mitochondria, restoring some key functions to levels seen in rats half their age.

The results were so impressive that the research team created a supplement, called Juvenon, which combines the two natural ingredients used in the rat experiment. Whether it works in people as dramatically as it does in rats remains to be proven. But evidence may be on the way. Ames and his colleagues have agreed to use the proceeds from sales of the supplement to fund a randomly controlled clinical trial of it.

For more information, check out www.juvenon.com.

—P.J.

radicals pouring out of mitochondria. Biologists have long suspected that these unstable molecules, in high enough numbers, can cause breaks in DNA, leading to mutations that may trigger cancer. But nutritional deficiencies also turn out to disable the normal repair system that cells use to identify and delete damaged bits of DNA.

“What we’re seeing is a kind of double whammy,” Ames says. “Cells are more likely to sustain genetic damage, and less able to repair the damage.” The result is a vastly increased risk that cells will undergo the kinds of genetic mutations that can turn them cancerous.

So far, Ames’ team has detected DNA damage associated with deficiencies of vitamin B-12, folic acid, B-6, niacin, vitamin C, vitamin E, iron and zinc. Ongoing research is likely to add to that list.

Ames summarized his findings in 2004 in the *Archives of Biochemistry and Biophysics*. Although his descriptions of biochemical actions and reactions are complex, his conclusion is startlingly simple. Based on what he’s seen in his lab, Ames says, public health officials should be encouraging everyone to take a simple one-a-day type multivitamin.

A multivitamin? That’s hardly a revolutionary idea within the alternative medicine movement, of course, which has championed the use of supplements, including vitamin and mineral formulations, for years. Still, only about one in three adults take a vitamin/mineral supplement on anything like a regular basis,

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recent national surveys show. And many mainstream nutritionists remain reticent to recommend multivitamins. People should be encouraged to eat healthier diets, the thinking goes, not pop pills.

Ames has little patience for that argument. "Of course we should be encouraging people to eat good diets," he says. "But that's no reason not to urge them to take a multivitamin, too."

Indeed, he's launched a one-man crusade to trumpet the message. "Nutritional deficiencies are disproportionately a problem of the poor," says Ames. "That's a national disgrace. The solution is as simple as getting people to take a multivitamin, and that's what we should be doing."

Could a one-a-day supplement help fight cancer—the most audacious of Ames' claims? Several recent studies say the answer could be yes. In the Nurses' Health Study, for example, Harvard researchers looked at vitamin consumption and the risk of colon cancer. They didn't detect much difference between women who took multivitamins containing folic acid and those who didn't in the first 14 years of their ongoing study. But after 15 years, they suddenly saw a huge difference. Multivitamin users had a 75 percent lower risk of developing colon cancer. In a 1999 study, scientists at the Fred

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Hutchinson Cancer Research Center in Seattle reported that high levels of zinc, vitamin C and vitamin E all seemed to protect against prostate cancer. Other studies suggest that keeping folic acid levels high may help lessen the risk of breast cancer.

If you already take a multivitamin, could you do more to make sure you're getting the optimal levels? No one yet knows the optimal amounts of C, E or any other specific nutrients required to keep mitochondria working at peak levels or to head off chromosomal damage. Ongoing studies should help establish those amounts. But there's already

reason to think higher levels may offer important protection. In the Hutchinson prostate cancer study and in Johns Hopkins' research of Alzheimer's disease, people who took extra vitamin C or E gained additional protection. There's also growing evidence that many Americans don't get enough vitamin D, especially in the winter months—and the



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only way to hit the optimum level appears to be a supplement. Along with vitamin D, extra calcium for women over 50 and men over 65 is important for strong bones, of course. And many other vitamins, minerals and herbs are also proving to be beneficial.

The ultimate prescription for optimal health probably should include a handful of supplements, Ames asserts. He and his colleagues have designed their own addition to the line-up—a pill that contains biochemicals that are important for mitochondrial function and could head off premature aging and perhaps prevent disease (see sidebar, page 80).

But with a majority of Americans falling short on at least one or more vitamins and minerals, the most important first step, he points out, is getting people to eat a healthier diet and take a multivitamin. "If we learn about other ways to keep cells healthy and slow the aging process, all the better," Ames says. And with no plans to settle down into that easy chair any time soon, Ames wants to remain young and healthy for as long as he can. **A**

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