

Of Mice and Men

Bruce Ames interviewed by [Virginia Postrel](#)

In the 1970s, Bruce Ames was a hero to environmentalists--the inventor of the Ames Test, which allows scientists to test chemicals to see whether they cause mutations in bacteria and perhaps cancer in humans. His research and testimony led to bans on such synthetic chemicals as Tris, the flame-retardant used in children's pajamas. A world renowned cancer researcher with a calm, reasoned manner, Ames was an ideal witness in the case against man-made chemicals. As science writer John Tierney aptly described him in *Hippocrates*, "He has a quiet, kindly tone of authority as he patiently explains why things are the way they are....He sounds so sensible. which is one reason he made such a good witness for the environmentalists in the 1970s."

But it's a scientist's imperative to change his mind when the data change-- and recent data have made Ames deeply suspicious of high dosage chemical testing and especially of the notion that man-made chemicals are uniquely dangerous. We are, he has discovered, surrounded by mutagens--not only synthetic chemicals but also natural ones--and blindly banning suspicious modern substances can do more harm than good.

Today, Ames, a professor of biochemistry and molecular biology at the University of California at Berkeley, stands on the other side of the chemical-ban debate. In 1990, he spoke out against California's Proposition 128, which would have banned many pesticides, and he has been highly critical of the ban on Alar. The best way to prevent cancer, Ames now believes, is to "eat your veggies." Any government action that makes fruits and vegetables more expensive ultimately causes cancer. In recent years, Ames has added a dollop of the economist's sense of trade-offs to the cancer researcher's zeal for prevention.

Ames discussed cancer research and environmental politics with Editor Virginia Postrel at his Office in Berkeley.

Reason: You've become well known for saying that we shouldn't worry so much about man-made chemicals causing cancer, that natural carcinogens are far more common and we shouldn't worry about them either. Why is that?

Ames: It isn't that we shouldn't worry about man-made chemicals. In certain occupations, people can be exposed to very high levels. But pollution is pretty much irrelevant to cancer--the kind of pollution that we're getting with water pollution, or with pesticide residue, is in such tiny amounts.

People got off on the wrong track about man-made chemicals. They said, Look, we know workers can get cancer from high doses of beta naphthalene or vinyl

chloride. We shouldn't have the workers be guinea pigs--we should test these things in rats. And that was reasonable. So they started testing the industrial chemicals in rats.

Reason: And they picked these chemicals because they were known to be associated in high doses with cancer?

Ames: Originally the driving force was high-dose occupational exposure. but soon it came out to be testing every synthetic chemical and half of them came out positive in rat tests. I think we're drawing the wrong conclusions from high-dose rat tests. They are testing enormously high doses--the maximum tolerated dose in the rats or the mice, which means you find the level that causes overt toxic effects and back off just a little bit and feed the animal that amount every day for a lifetime. That sends toxicologists up the wall because that's a very high dose, and they are afraid that will do something that isn't relevant to low doses.

But the control. which people should have thought of but they didn't, is what about all the chemicals in the natural world? People got in their head, well, if it's man-made somehow it's potentially dangerous, but if it's natural, it isn't. That doesn't really fit with anything we know about toxicology. When we understand how animals are resistant to chemicals, the mechanisms are all independent of whether it's natural or synthetic. And in fact, when you look at natural chemicals, half of those tested came out positive.

Of course. almost all the world is natural chemicals, so it really makes you rethink everything. A cup of coffee is filled with chemicals. They've identified a thousand chemicals in a cup of coffee. But we only found 22 that have been tested in animal cancer tests out of this thousand. And of those, 17 are carcinogens. There are 10 milligrams of known carcinogens in a cup of coffee and that's more carcinogens than you're likely to get from pesticide residues for a year!

Reason: Why not conclude that you shouldn't drink coffee'

Ames: But half of all the things tested are coming out positive. The point isn't to worry so much about cups of coffee, but to rethink what we're doing with animal cancer testing We're eating natural pesticides, which are natural chemicals that plants use to try to kill off insects that try to eat them. And we eat roughly 1,500 milligrams of them per day. We eat 0.09 milligrams of synthetic pesticide residues. So we're talking about incredibly tiny amounts of synthetic pesticides, and yet the same percentage of natural chemicals come out positive.

So then the question is, What's wrong with high-dose animal cancer tests? I've been arguing in the literature that cell division is a risk factor for cancer, as is mutation. A mutagen damages your DNA, and everybody agrees that that's a risk factor for cancer, and cancer can occur with accumulated mutations. But when the cell divides, DNA damage is converted to mutations. So what we 'v been arguing is that raising either increases your risk of cancer--either the rate of cell division or the rate of mutagenesis. So when you test these enormous doses of a chemical, cell division can be caused in various ways. It's like a chronic wounding experiment. When you wound tissue. you get a lot of cell proliferation, because you get signals for the cells to come in and heal the wound and start dividing. So I think that a sizable percentage of the chemicals are only going to be a risk factor in high doses--like saccharin.

Reason: Because they have this wounding effect?

Ames: Yes, at these enormous doses. Saccharin is a carcinogen at high doses, and

everything we know about the theory says there's no risk at all at low doses. I think that some sizable percentage of all the chemicals we're calling carcinogens are going to be like that.

Now if something's a mutagen, it can both damage the DNA and kill cells. If you get to high enough doses where it's killing cells as well as damaging the DNA, then you're getting an extra multiplier. For a mutagen there might be a small risk at any level. But in most cases you also get this big multiplier that's only a high-dose effect. So all this says is that the risk numbers people are throwing around are going to just be wrong. And the further you get from the dose you gave the rat, the less you want to worry about it.

Reason: People do want to know what causes cancer.

Ames: That's what I'm very much interested in. Cancer is primarily a degenerative disease of old age. It goes up very sharply with age. Rats live about two to three years and by the end of their lifetime, 30 percent of them have cancer. At 1 year old, very few have cancer. Mice have a slightly shorter lifespan, and the curve is shifted to the left. And people show a similar relation, except we live to 80 years. This suggests that cancer is a degenerative disease of old age, in the same way as heart disease and cataracts and all the other things you'll find out about soon enough as you get older. It doesn't mean that external factors can't influence it--we know cholesterol influences heart disease, and smoking is 10 years off your life, so if everybody stopped smoking the curve would move out. But underlying it all, the reason there is more cancer is more people are going up that curve. More people are living longer and longer every year, and as we're living longer we see an increase in cancer.

Reason: The incidence of childhood leukemia would seem to go against the idea that cancer is an aging disease. **Ames:** There is some risk of cancer at any age. But what people have recently turned up is that male smokers are more likely to have kids with childhood leukemia. So smoking has genetic effects. With cancer you need a number of hits--a number of different mutations-- and if you have one genetically, from a father who smokes, then the other one can occur soon afterwards and show up as childhood cancer.

Reason: Male smokers but not female smokers?

Ames: Studies show that smoking by either parent increases the child's risk of cancer.

Reason: Lately breast cancer has started to get a lot of attention in the media.

Ames: OK, now with breast cancer, the two best people right now are down in Los Angeles, and they think they are solving it--Brian Henderson and Malcolm Pike at USC, two of the world's leading epidemiologists. They've been studying breast cancer for a long time. It seems to be mainly hormones. It was known for a long time that women who have lots of children have very low rates of breast cancer, and nuns have very high rates of breast cancer. It has to do again with cell division. Every time a woman has her cycle, she has cell division in the breast, so that seems to be a critical risk factor. Childbirth interrupts that.

We know how to prevent breast cancer: You live like a Chinese peasant who lived 100 years ago. You work in the fields, on a meager diet, so you have your first period at age 17 and then you start having a child every year. It's a good recipe for not getting breast cancer but not very practical. The question is, Can one intervene with hormones? What Henderson and Pike say is that it's known that if you take out a woman's ovaries, it stops ovulation, but that is another solution that is not

but a hormone status, it stops ovulation, but that is another solution that is not very practical. But certain birth control pills do something similar. So Henderson and Pike are coming up with a complex of hormones that they think would make a good oral contraceptive and also cut the risk of breast cancer dramatically. They're trying to test it out and get it through the FDA. If they're right, it's going to be terrific. If they're not right, somebody else will figure it out in five years.

I think people are going to figure out the causes of cancer and heart disease and aging. It's coming very fast, and it's due to science and technology and a healthy economy. Basic science is the child of a healthy economy. The reason you have all these scientists in the United States is because we can afford to spend money on basic research.

Reason: How accepted are your views among cancer researchers?

Ames: Well, we've had a controversy going back and forth in Science recently, and I got fan letters from all sorts of people that I really respect in the world, saying, Keep on, you're on the right track, we agree with you. And there are people who disagree. But I do think I'm winning the scientific wars.

Let's go back to what's really causing cancer. If you ask the epidemiologists, after years and years of studies, they say eating more fruits and vegetables lowers the cancer rate.

Reason: Regardless of what kind of cancer?

Ames: Many kinds of cancer. And eating more meat and saturated fats seems to raise the rate of some cancers. There's evidence for this, and I'm more and more convinced. But then the question is, What are the dietary factors? And more and more, it looks like folic acid is very important, which is one of the vitamins you get from fruits and vegetables, as well as antioxidants.

We're doing experiments with mice. You make them slightly folic-acid deficient, and it breaks their chromosomes. There's a little evidence that the same thing might be true in people, and there's some epidemiological evidence that women who don't eat their fruits and veggies have more kids with birth defects.

Reason: Why does folic acid appear to be the crucial thing?

Ames: Because folic acid is involved in making the purines and pyrimidines that go into DNA. And if you're deficient, what happens is deoxyuridine gets into the DNA. The body's balanced between damage and defense. If you leave out one of the vitamins or micronutrients, then you're in trouble. Maybe more micronutrients will turn out to be very important, but right now it seems the antioxidants such as vitamin C are important and folic acid's important.

Reason: What do you mean by antioxidants?

Ames: Among the vitamins you need are a set of antioxidants--vitamin C and vitamin E and beta carotene. We've shown that there is a horrendous amount of oxidative damage to DNA just from living--from normal metabolism.

Just living is like getting irradiated. Radiation is an oxidizing agent. You're adding four electrons to oxygen to make water, you add them one at a time, you make superoxide and hydrogen peroxide and hydroxyl radicals, which are the substances you get from radiation. If the DNA gets damage, then repair enzymes, which are always cruising along the DNA looking for trouble, take out the damaged product--this oxidized base--and they repair it. Well, the oxidized base goes into the urine, and we've learned how to fish all these things out of urine and ask how

much damage a human gets per day or how much damage a rat gets per day. The higher your metabolic rate, the more damage, so a mouse is battering up its DNA at a higher rate than the rat, the rat higher than the monkey, the monkey higher than a human--which fits with lifespan and the cancer rate. So we're all excited about oxidative damage and aging and all these degenerative diseases associated with aging.

The epidemiologists are finding that antioxidants are some of the ingredients in fruits and vegetables. If people don't eat their veggies then they are in trouble. My main interest now is to find what's the optimum level of all these things. Maybe the optimum level is much more than the RDA. We don't know that but right now people aren't even getting the RDA, the Recommended Daily Allowance.

Reason: Can people take vitamin pills?

Ames: Well, the nutrition people don't like that. They say you should be told to eat balanced diets. Two fruits and three vegetables per day at least. On the other hand, only 10 percent of the population are eating two fruits and three vegetables a day. So I'm coming to the conclusion that people should be taking one-a-day pills. Certainly pregnant women and poorly nourished people and anybody of childbearing age and older people.

Reason: Activists are very suspicious of you.

Ames: All I can say is I've done good science. In part, I think my talent in this area is I've always been a bit of a generalist and being a generalist is hard, because there's so much specialized knowledge. To be a successful generalist one has to know the best people in each field so that you can call them up on the phone and ask them questions and get feedback on ideas.

I've gotten very suspicious of a lot of the activists because I just feel that they are not good problem solvers. If you push in the wrong direction, then you're counterproductive. If we are spending \$125 billion a year on EPA regulation, and it's not effective, that kills people, because it diverts resources from important things and it takes money that could be used for starting new companies and generating wealth and generating money for science.

I'm not saying you shouldn't have rules. You don't want every chemical company dumping its garbage out the back door. But what we're telling companies is, Well, air is free and water is free, but be good guys, don't pollute. That isn't how capitalism works. You want to have an incentive in there, so what we should be doing is charging people to pollute. Any time anybody wants to pollute--whether you drive your car or put a log in your fireplace--you should have to pay for pollution cost. Then there are incentives to figure out how to make cars that put out less pollution.

Reason: Within the academic research community, how do people look at people who have gotten involved in public policy debates?

Ames: Most scientists tend to steer away from that. You get promoted and you get recognized by your peers, you get to go to international conferences and all that. by doing good science. And if you make a mistake, then everybody jumps on you. There's no incentive for scientists to be getting involved in policy, though people do it when they feel a responsibility.

Reason: Are there incentives not to do it?

Ames: Yes, I would say probably so. If I spent 5 percent of my time talking to you

or talking to Omni or other people, then it's time I'm not spending working on what causes aging and maybe I'm better off being in a lab trying to do that.

Reason: Do you see yourself at this point as something of a popularizer as well as a researcher?

Ames: Yes. a little bit. I feel it's partly my duty. I'd really like to prevent cancer. The best way to go about it is prevention rather than trying to find a cure for cancer, because that's so elusive. though we need to work on that. too...

Reason: You mean on treating it?

Ames: Yes. I'm much more interested in preventing cancer. Then we have to get out to the public what's important. If you tell them about trivia all the time, they get completely confused, and it's counterproductive. I just think all this business of organic food is nonsense basically. We should be eating more fruits and vegetables, so the main way to do that is to make them cheaper. Anything that makes fruits and vegetables more expensive may increase cancer.

Reason: Do you think there might be legitimate concern for worker exposure?

Ames: Worker exposure is very different. I think you want strict rules, because there people can get very high doses. We were having some guy paint our house. He was up on a ladder with a spray can, spraying the house. I said. "Hey, you have to wear a mask. You just can't be in a cloud of that. Don't you know you shouldn't be breathing all that stuff?"

"Oh, I can't wear a mask. I need to stop every once in a while and smoke." So he stopped and took out a cigarette and smoked. So partly it's hard to convince people. It's a macho thing or whatever. But we do need rules, and people whose occupations expose them to high doses of chemicals need to follow the rules.

Reason: Aside from the specific scientific issues where your research has a direct bearing on policy, how would you describe your own political views?

Ames: Well, I guess I feel I'm neither a leftist nor a conservative. It's probably more libertarian. Again. I'm not a fanatic. I feel we should give people the maximum choice possible and let them pay for their mistakes. I think if the government starts trying to insulate everybody from their mistakes, from the consequences of their acts, we're in trouble, because that's a constant feedback in people's lives. If somebody doesn't save his money, should you really then have to provide for him, when the person who saves is skimping now and thinking long term? Of course, with kids, you educate them. But we have to treat adults as adults.

Reason: Do you favor any kinds of regulations to restrict smoking?

Ames: Smoking is 10 years off your life. If somebody voluntarily takes 10 years off his life, fine. But the rest of us shouldn't have to pay for it. Now second-hand smoke I don't think is a big deal in terms of causing cancer. But a lot of people just don't like second-hand smoke around them. I don't either.

It seems to me it's reasonable that, if someone is polluting the air, then he should do it in his own little cubbyhole or some part of the restaurant that doesn't get to the rest of us. But on the other hand, I walk to work, but I don't think everybody who drives to work should be prohibited from using his car because he's polluting the air. Life is full of trade-offs.

Reason: Do you consider yourself a very political person?

Ames: Well. I like to read economics and think about these things. I'm trying to be a wise man in my old age, which is hard because everything is so specialized, so again maybe it's part of being a generalist.

Reason: Are there particular books or thinkers...

Ames: I was influenced by reading [economist F.A.] Hayek and people like that and thinking the way economists think about trade-offs and optimizing. There is an optimum level of pollution, but most environmentalists throw up their hands. They want no pollution. Having dealt with EPA and FDA and these government bureaucracies, I'm fairly disillusioned. When we developed our test system for detecting mutagens, I thought industry would fight it and the government would have everybody using it. It was just the reverse, because industry has an interest in not making mutagens and carcinogens. It's bad for the business. And government bureaucracies are hard to turn around on anything.

Reason: You accept no money from industry.

Ames: No. If I give a talk at Du Pont. I have them send the honorarium to charity.

Reason: So the research money comes from the government?

Ames: My research money all comes from the government. It's fiercely competitive.

Reason: Over time, the government, especially the federal government, has acquired a near monopoly on the funding of scientific research...

Ames: As a sort of crypto-libertarian, I worry about that. And in a way, scientists have a self-interest in jacking up the government funding of science. But I think the people get their money's worth from it--the U.S. has the strongest science in the world, and all kinds of industries come out of research, so it's good for the economy, it's good for human knowledge, it's good for our health. I once had dinner with Milton Friedman, and he started off the conversation saying that he thought they should abolish the EPA, the FDA, and government funding of science. The first two I could have at least considered, but the government funding of science didn't fly. Probably what Friedman would say is if you didn't have government funding of science, industries would think much longer term and they'd fund basic research, because it would be in their interest to do it in a technological society. But there are some things that are very long-term, and in a way having government funding is good. As long as it's competitive.

And so far it's been fiercely competitive. You have committees of your peers judging all these things. They don't always make the decisions that I think that they should make, but at least it's a reasonable system where merit wins out. Now you could politicize that and start getting one representative from each state or whatever. But then it becomes less a meritocracy, and if there's too much of that the system's going to go down.

Reason: You seem extremely optimistic both about scientific research and about understanding cancer.

Ames: I'm incredibly optimistic because science is growing so fast. There are millions of scientists in the world, and every new rich country needs them and trains them. And everybody's communicating. Life expectancy gets longer every year, and it's going to get even longer, and it's due to modern science and technology. All these romantics are trying to paint science and technology as the thing that's dooming the world--I just don't believe that either. Everything I know

says the opposite.

Reason: Do you think that science is threatened by those kinds of ideas?

Ames: Oh yes. In some fundamental way, a lot of environmental extremists are anti-science, anti-technology. They want to go back to some imagined, idyllic world that never existed.

Reason: Does the general public's lack of understanding of science bother you?

Ames: Sure, but nowadays people are sitting in front of the TV, and they get what they get on the TV, which isn't very much science.

Reason: How much is it just a function of specialization that people don't know science?

Ames: You can't know everything, but you can read about some of it, and science is so much fun. You'd think people in the modern world would want to know how the cell works, what DNA is doing and all of these things. It just seems so exciting.

Reason: You've written a piece for the Social Policy Research Center about science as a spontaneous order. What do you mean by that?

Ames: It's not being planned from on top. Everybody has his enthusiasm. If I decide I want to go off on this tangent and that tangent, I can do it. Scientists are always thinking of a way to get new knowledge cheaper or faster or whatever, and so it tends to come up from the bottom. It's not some bigwig saying, I thought it all out--you do this, you do that.

Reason: How does government being a big source of funding affect that?

Ames: Well, the government does say, We're giving money for heart disease, we're giving money for cancer. So in that sense it's from the top down. But they've always been relatively good about saying, Well, since cancer is so complicated, anything that helps the understanding of general knowledge of how cells work we'll call cancer research. So it wasn't directed, which is a good thing, because all the advances come from people following their individual enthusiasms.

Reason: What would be an advance that no one would have planned?

Ames: Well, I was working in bacteria and got interested in mutations and mutagens and thought I'd set up this test system in bacteria. And then I thought that carcinogens might be working as mutagens, so that turned out to be an advance in cancer research. But I couldn't get funded from National Cancer Institute because people in the National Cancer Institute in those days weren't interested in mutagens or they weren't thinking along that line.

Reason: So you got funding from...?

Ames: Eventually from the Atomic Energy Commission.

Reason: So the fact that it's chopped up into all these different places is a positive?

Ames: The more sources of funding, the more different people with different views, the better it is. Because it's not directed from on top.

Reason: What about the criticism that a lot of scientific research is just waste?

Ames: A lot of scientific research is unimaginative. But that's part of the nature of it. It's hard to know beforehand. If you could weed out all the research that would

never lead anywhere, then we would know everything before we started. It's a discovery process and you don't know where everything is going to go. People who are doing the research always think, Ah, that's an important experiment.

Reason: Do you ever worry that your critics are right and you're wrong and you account for cancer deaths by making these arguments?

Ames: All the time. I mean a good scientist is always thinking, where could I have gone wrong? So I'm always kicking all my assumptions and one of the reasons why I'm successful is I'm always challenging assumptions. If there's a paradigm around and somehow too many uncomfortable facts start coming up, then you say, Ah, how do I knock it down? What's better? So one's always doing that. But I'm as sure of these ideas as anything I've ever done in science.

Reason: Thank you.