

FROM

01/21/86 11:52 P. 2

CICC

CHEMICAL INDUSTRY
COUNCIL
OF CALIFORNIA

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Executive Director:
Richard L. Davis

TO: File

FROM: Dick Davis

SUBJECT: Visit with Dr. Bruce Ames

For Your Info.
JACK JONES

DATE: December 22, 1985

FOR YOUR INFORMATION
DICK DAVIS

Copies To

- R. Long
- B. Miller
- J. Martin

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ENVIRONMENTAL QUALITY 2 1986

On Friday morning, December 19, I spent approximately an hour and twenty minutes with Dr. Bruce Ames in his office at UC Berkeley. I had asked him for 15 or 20 minutes to tell him about current UC efforts to deal with scientific illiteracy in the general public. My intention only was to stimulate his interest in participating in the environmental public policy debate.

Dr. Ames is well ahead of us on that issue (see attached letters. He made it quite clear that he is very concerned about present public perceptions. He was most contemptuous of "environmentalism" as it is now practiced.

After taping my card in the middle of a lined yellow sheet, he took scribbled notes as I told him about CEPUP, the Toxic Risk Information Center, the SRP, and the UC Toxic Substances Research and Training Center. As I catalogued various individuals involved in these efforts, he made such comments as, "That's a good person", "I don't know him", "Hmmm".

After my brief discourse about our current efforts at public education, he pulled from his brief case the draft of his current article for Science on relative risk. For more than an hour, he went through the article, step by step, explaining to me how he arrived at his conclusions.

Dr. Ames has established a computerized data base which records details of every rat and mice bioassay he could find. This is a compendium of data nearly an inch thick printed in very fine print. He has established that mice fail to predict rats in 42% of the cases. His comment, "If mice can't predict rats any better than that, how can they predict humans?"

By plotting data on thousands of rats and mice ($x=LD50$; $y=MLD$), he draws the conclusions that acute potency is related to chronic potency. Further plottings demonstrate the dose response curve is not linear but flattens at the low dose.

Through statistical manipulation of potency and exposure data, he establishes a potency score for hundreds of man-made and natural chemicals, then compares those scores showing that natural carcinogens present a vastly greater risk than do man-made chemicals in the

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environment. Some exceptions are the current allowable levels of some occupational exposures standards. In this case I could not quite follow his reasoning since he equates the burden resulting from inhalation directly with the burden from ingestion. I'm not sure that's biologically plausible.

At each point in his discussion, he stressed that all of this is based on rat and mice data, and he is (not) convinced this is really representative of the risks to humans. He kept repeating that he is convinced man-made chemicals in the environment presents no measurable risk to humans.

I asked him for a source which catalogue the man-made chemicals which have been determined to occur naturally, particularly the chlorinated hydrocarbons (my pets). He replied that he knows of no such definitive work but that was something the chemical industry should be promoting. He added, "I do know that thousands of chlorinated hydrocarbons are produced by flora and fauna in the oceans". It is logical, he added, that others are produced in land environments.

I brought up TCE in the American River. His response was that it is probably man-made, but who knows? And who knows where it might have come from, given the laws of thermodynamics. More important (he added) what's the health significance?

I showed him a copy of the latest California Guidelines for Carcinogen Risk Assessment. He said he hadn't read it, but asked me what was my greatest objection to it. When I said that it was too rigid in forcing scientific decisions to comply with political policy. He replied, "Exactly".

At one point he remarked that the chemical industry should be conducting animal bioassays of natural carcinogens. He said such data is badly needed for comparison purposes.

Visiting Dr. Ames in his office and laboratories (where everyone calls him Bruce) is an experience all should have. When I finally pleaded I was taking too much of his time, he gave me a collection of his recent written statements to the press and government, and as we walked to the elevator, assured me that he was very much involved with the public policy issue but -- he accepts no consultancies (very pointed on that).

According to Dr. Ames, his final draft paper is ready to go to his scientific colleagues "around the world" for review, then will be put in final form for Science. This may take up to six months.

It appears to me this paper may well mark a watershed in the "chemophobia" saga. It will be in the chemical industry's best interest to assure wide dissemination once it is published.

URL 04908

FROM

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UNIVERSITY OF CALIFORNIA, BERKELEY

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DEPARTMENT OF BIOCHEMISTRY

BERKELEY, CALIFORNIA 94720

November 11, 1985

Testimony of
Professor Bruce N. Ames, Chairman
Department of Biochemistry
University of California
Berkeley, California 94720

REC'D DEC 17 1985

Professor Ames was formerly on the Board of Directors of the National Cancer Institute (National Cancer Advisory Board). He is a member of the National Academy of Sciences. He was the recipient of the most prestigious award for cancer research, the General Motors Cancer Research Foundation Prize (1983), and of the highest award in environmental achievement, the Tyler Prize (1985). He does no consulting for the chemical, drug, or food industry, or for law firms. .

UPL 04909

The Honorable Art Torres
Chairman, Senate Committee on
Toxics and Public Safety Management
State Capitol, Room 4062
Sacramento, California 95814

Dear Senator Torres:

The carcinogens and toxic chemicals being found in California water supplies are present in extraordinarily tiny amounts and, except in rare cases, are present in trivial amounts relative to the background level of carcinogens in Nature. I am convinced that water pollution is irrelevant to the causes of human cancer.

The main current fallacy consists in thinking that carcinogens are rare and that they are mostly man-made chemicals. My own estimate is that over 99.99% of the carcinogens Californians ingest are natural (e.g., natural toxic chemicals in plants, mold carcinogens) or traditional (e.g., cooking food, smoking cigarettes, alcohol).

Every meal is full of carcinogens and when one compares the level of carcinogens in contaminated water (or pesticide residues in food) to the level of natural carcinogens, it is clear that water pollution represents a trivial risk. Every common drink contains carcinogens. I list a few sources and

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levels of natural carcinogens below, and I compare them to the Silicon Valley's contaminated wells as an example.

a) Coffee contains about 1,000 micrograms of hydrogen peroxide (a known carcinogen) per cup (4,000 ppb; ppb = parts per billion) as well as about 1,000 micrograms (4,000 ppb) of methylglyoxal, which has recently been shown to be a carcinogen. b) Tap water contains the carcinogen chloroform at 83 micrograms per liter (83 ppb U.S. average), which is generated from chlorinating the water. c) Cola contains the carcinogen formaldehyde at 2,800 micrograms per 12 ounces (7,900 ppb). d) Beer contains nitrosamines, formaldehyde (700 ppb), and alcohol (50 million ppb), all known carcinogens. Ethyl alcohol is a known human carcinogen (3% of U.S. cancer) as well as a carcinogen in rats. e) Milk contains a high percentage of fat, and high fat has been implicated in human breast and colon cancer and rodent cancer (though milk is an important source of calcium, which may be important as an anticarcinogen); and f) organic fruit juices may have various amounts of carcinogenic mold toxins. We are just completing a study where we compare risks for humans due to intake of carcinogens. In this study we adjust for the potency of each carcinogen from rodent data. This adjustment is necessary because the potency of carcinogens varies over a million-fold, e.g., aflatoxin, a mold carcinogen, present in small amounts in peanut butter (2 ppb U.S. average) or corn products such as tortillas, is about a million times more potent as a carcinogen than trichloroethylene, which often contaminates well water.

I give some comparisons below.

Contaminated water. The level of carcinogens in contaminated well water (e.g., Silicon Valley or Yoburn) only rarely involves a risk above the risk of ordinary tap water. Of 35 wells shut down in Silicon Valley because of their supposed carcinogenic hazard in an EPA study, only two were of greater risk than ordinary tap water (well water usually lacks the chloroform present in chlorinated tap water), and the most polluted well (2,800 ppb trichloroethylene) is at least 1,000 times less hazardous than an equal volume of cola, beer, or wine. Given that the consumption of tap water is only about 1 or 2 liters per day, it seems unlikely that man-made water pollution is causing more than a minimal hazard. This is in contrast to inhalation, particularly in the workplace, where breathing in 10,000 liters of air containing a carcinogen in a work day can result in appreciable doses and thus could represent a significant hazard.

Pesticide residues. Man-made pesticide residues present in our food amount to about 150 micrograms/day on the average; most of these residues are composed of non-carcinogenic compounds. The most significant man-made pesticide carcinogenic residue in food is likely to be DDE, a metabolite of DDT. The risk of the DDE in the average U.S. daily intake is equivalent to the risk due to chloroform in 1 glass of tap water and, thus, it is insignificant compared to the risk due to the high level of natural carcinogens in our diet. Even an occasional highly DDE- or PCB-contaminated fish (e.g., 100 times the average level) would contribute a risk that is small compared to other very common minor risks such as a glass of beer or a peanut butter sandwich.

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Nature's pesticides. We are ingesting natural pesticides in our diet in amounts at least 10,000 times more than man-made pesticide residues. Natural pesticides are natural toxic chemicals, which are present in all plants, usually making up 3-10% of a plant's weight. They have an enormous variety of chemical structures, though only a few are present in each plant species. Their function is protection against fungi, insects and animal predators. A major aspect of evolution of plants is chemical warfare. There has been relatively little interest in the toxicology or carcinogenicity of these compounds until quite recently, and very few of the large number present in the human diet have been tested in animal cancer bioassays, and only some of these tests are adequate for estimating their potency. Some of those tested are carcinogens. They include astragole (in basil), safrole (in herbs), symphitine (in comfrey tea), psoralens (in parsley and celery), hydrazines (in mushrooms), and allyl isothiocyanate (in mustard). Calculations on the carcinogenic risk of these compounds show that they completely overshadow the traces of man-made pollutants found in the daily diet, e.g., 5 basil leaves are 100 times more hazardous than the worst well in Silicon Valley (at least 5 basil leaves would be ingested in a portion of "pasta al pesto"). Thousands more of Nature's pesticides are present in the human diet and because many mutagens are being discovered among them, many are potential carcinogens.

Skepticism about extrapolating risks from rodents. All risk calculations based on rat and mouse cancer tests, both from natural and man-made carcinogens, are hypothetical: thus, they should be taken with a great dose of skepticism, unlike known human carcinogens such as radioactive radon gas coming out of the ground into California houses or smoking (400,000 real deaths per year in the U.S.). There are many new reasons for skepticism of low-dose extrapolation of risk to humans from rodent data, and for suspicions about linear dose-response extrapolations, which I won't discuss here. I will just mention one qualitative point. Of the carcinogens tested in both rats and mice in our database on potency, 42% of the chemicals were positive in the mouse and negative in the rat, or vice versa. Thus, even two closely related short-lived creatures, the rat and the mouse, don't predict very well for each other whether a substance is a carcinogen.

We might possibly eliminate every trace of man-made carcinogen from our water supply, but it will cost an enormous amount of California's wealth (wealth is related to health) and be irrelevant to causes of human cancer and also might cause new risks to arise that are worse and distract health workers from real, more important risks. Thus, one can either chase after parts per billion of every man-made carcinogen that turns up or have some sensible regulation about pollution. As one of the world's most eminent epidemiologists has said:

"But if no explicit use is to be made of the degree of activity of each chemical, then instead of effective reduction of the total of all human cancer the chief result may be complete paralysis (either of the regulators or of the 'regulatees')." [R. Peto, Epidemiological reservations about risk assessment, in Assessment of Risk from Low-Level

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Exposure to Radiation and Chemicals, A. D. Woodhead, C. J. Shellabarger, V. Pond, and A. Hollander, eds. (Plenum Press, New York, 1985), pp. 3-16.]

Yours truly,

Bruce N. Ames

Bruce N. Ames
Professor and Chairman

BNA/ask

Enclosure:
Cal Monthly article

cc: Assemblyman Bill Jones

[I am sending a copy to Assemblyman Bill Jones because he sent me a copy of his bill. Unfortunately, I cannot appear to testify concerning it, but I support the idea of reasonable standards.]

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FROM

01/21/85 12:03 P. 1

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UNIVERSITY OF CALIFORNIA, BERKELEY

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DEPARTMENT OF BIOCHEMISTRY

BERKELEY, CALIFORNIA 94720

June 3, 1985

Honorable James Scheuer, Claudine Schneider and Don Ritter:
Committee on Science and Technology
2321 Rayburn HOB
Washington, D.C. 20515

Dear Representatives,

Your recent EPA authorization bill has taken an important step by directing EPA to continue its work in Indoor Air Quality. If EPA (and other concerned agencies) will put a reasonable emphasis on radon alone, we can save several thousand lung cancer deaths each year. This number is comparable with one estimate (see below) of the total number of lives EPA could possibly save with its entire \$1.2 billion budget (budget not including the Super-fund).

However EPA should update its priorities even further, via a study which should include CIAQ (Committee on Indoor Air Quality--the interagency group which coordinates work on indoor air). EPA envisions its role is to protect us from artificial pollutants, particularly those which are being inflicted upon us unfairly. We argue that the US public is much more in need of protection from natural and traditional pollution and toxins.

The major known pollution-related deaths in the US are from cigarettes, followed by indoor radon. The annual death rates are roughly:

Cigarette smoking (cancer, heart disease, etc.)	350,000
Cancer due to man-made pollution	8,000
(This is 2% of 420,000 total cancers: Estimate by Doll & Peto (very uncertain numbers)).	
Indoor radon	10,000
Passive (non-participant) smoking (very uncertain number)	1,000-10,000

The annual deaths above are measured in units of thousands. By contrast, EPA spends most of its marginal dollars on risks which involve 1-10 hypothetical deaths, or perhaps no premature deaths at all.

We next discuss separately 1) air pollution and 2) toxins in food and water.

1) One of EPA's major mandates is air pollution. The major source of polluted air inhaled by humans is cigarette smoke which for smokers causes 350,000 premature deaths per year. Other sources of air pollution are quite minor by comparison. For example, it takes a year of breathing Los Angeles air to

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inhale the same amount of pollution (burnt material) as smoking 2 packs of cigarettes. We also ingest more burnt material in a day from cooking our food (which produces many known carcinogens) than we get in one year of breathing Los Angeles air. Indoor air is more polluted on average than outdoor air and we spend more than 75% of our time indoors.

Recently it has been realized that a major source of carcinogens in indoor air has been unrecognized. Radon, a natural volatile source of radioactivity, is known to be a human carcinogen (hundreds of dead uranium miners attest to this) and is present in millions of American homes at exposure levels greater than those presently experienced by uranium miners, and corresponding to a lifetime risk of 2-3% for each occupant. Radon in US homes is likely to be causing 10,000 lung cancers each year. (This is an EPA estimate and is a much more precise number than the usual hypothetical extrapolation from rats.) The radon comes from the soil, in a very non-uniform distribution, and can also come from well water. It appears that 20-30% of these 10,000 lung cancers come from 2-3% of US homes (the million homes mentioned above). In half a million of these homes, each occupant runs a risk of lung cancer from radon as great as if he/she smoked 2 packs of cigarettes per week. It is inexpensive to locate many or even most of these homes, and their occupants can be warned. Many homeowners can modify their homes fairly simply to minimize radon concentration. In addition, length of exposure is a critical variable: for smokers, 1 pack a day for 40 years is much worse than 2 packs a day for 20 years. This accentuates the concern about radon, to which people are exposed from the time of birth. In addition radon and smoking are suspected to be synergistic so that the risk for a smoker could be very much higher than for a non-smoker.

Finally there are risks and discomfort from other outdoor pollutants -- such as combustion products and organic chemicals -- which often occur indoors at levels substantially higher than outdoors, but whose risks cannot yet be reliably quantified.

Given these facts, what is the government doing? Its response to 350,000 cigarette-caused deaths (2 packs a day for 40+ years causes an average life shortening of 9 years) is to subsidize tobacco farmers, allow seductive advertising of cigarettes, and reduce the tax on cigarettes. Of its \$1.2 billion annual budget, EPA spends 230 million on outdoor air pollution and only 2 million on indoor air pollution or radon. The radon case is particularly noteworthy because it could be solved relatively easily.

2) A second major mandate of EPA is pesticide and toxic chemical residues in food and water. In fact almost all carcinogens and toxic chemicals we are ingesting are natural, not man-made. (See attachments). Natural carcinogens tend to be ignored by government regulators. For example, there are over 500 micrograms of methylglyoxal, a mutagen and a carcinogen produced by roasting coffee, in a single cup of coffee. The total amount of pesticide residues we

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eat in a day on average is 60 micrograms, and most of these are not carcinogens. A national turmoil was caused by residues of EDB, a carcinogen in rats and mice and an essential fumigant for grain and fruit. EDB has now been banned by EPA, although we do not have satisfactory alternative fumigants. The risk created by EDB, however, is trivial relative to that due to natural toxic chemicals in edible plants or natural pollutants such as mold toxins (see attached two articles). For example, the risk (to rats) from the average amount of EDB residue we eat in a day from grain is about 100x times less than the risk from the average peanut butter sandwich. Peanut butter is contaminated with the mold toxin, aflatoxin (an unusually potent natural carcinogen) at 2 ppb (U.S. average) and FDA allows 10x this level in feed. The EDB risk is equal to the risk from an average glass of water (water chlorination produces the carcinogen chloroform: 84 micrograms/liter U.S. average). All of these above risks, even that from peanut butter are likely to be trivial for human cancer. Even the most highly contaminated well waters reported appear to have trivial amounts of carcinogens when compared to the background of natural carcinogens we are ingesting. For example, drinking 10 quarts of the most highly contaminated well water in Silicon Valley (reported in the newspaper as 1100 ppa trichloroethylene) would have a risk (to rats) equivalent to that of 1 peanut butter sandwich (with US average aflatoxin contamination).

UHL 04915

When EPA told the public that EDB residues will cause 3 cases of cancer in 1000 people, it was extrapolating from rats to people, which is unjustifiable scientifically (it is really based on the idea of prudence as we don't know how to do a quantitative extrapolation between species); furthermore, it was a worst-case estimate at every possible assumption. If FDA did the same calculation for a peanut butter sandwich the results would suggest that peanut butter is accounting for a good part of the cancer in the country (which no one believes is true). Perhaps the various government agencies could agree on a scale of risk. One can question the usefulness of these worst-case, very hypothetical calculations which scare the public and don't put risks in perspective. It also seems important to calculate the amount of money spent eliminating risks in order to have some comparability between different regulatory agencies, and some competition between these agencies and the scientific community for "risk funds". This might give each regulatory agency some incentive to maximize cost effectiveness and to address the more important risks. It is taking years from the first knowledge of the radon hazard to get anyone to pay attention to it. What seems to be called for at this stage of the knowledge in the field is to try and sort the important risks out from the very many trivial risks and to concentrate on very large known risks such as cigarettes, and some smaller risks such as radon, certain occupational risks, and any others which surface, rather than to chase after every trace of carcinogen at great cost and little effect.

What to do? The real problem lies not only with EPA, but also with the Congress, which needs to reconsider and update the way it funds and organizes

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all the agencies that are protecting our health. Agency budgets should be related to their potential contribution to our well-being. OTA has underway a study of Technology and the American Economic Transition, which partly addresses these issues, and Dr. Henry Kelly, the study director, can offer some relevant comments. This globally important issue deserves Congressional hearings, and probably a study by the National Academy and/or OTA.

But your Committee, which is responsible for EPA, and has interests in indoor air quality, should not wait for lengthy studies, when major improvements are easy. As we stated at the beginning of this letter, EPA and CIAQ could convene a study to reprioritize funding within the related agencies so that each dollar spent has a fair chance of contributing equally to improving our health and well-being.

This study should also consider the role of extramural funding. NIH does internal research and also sponsors external research, complete with unsolicited proposals, thus helping to keep NIH on its toes. We wonder if the same competition and evaluation is as widespread in EPA and related agencies.

If we can provide any more information, please let us know.

Bruce N. Ames
Bruce N. Ames
Professor of Biochemistry
(415) 642-5165

Art Rosenfeld
Arthur N. Rosenfeld
Professor of Physics
(415) 642-7031

Attachments:

California Q&A (Questions and Answers: Ames), California Monthly, May 1985;
Ames' Carcinogen paper, Science 221, 1256 (22 September '83);
Resumes.

cc: Senators Frank R. Lautenberg, NJ
Robert T. Stafford, VT
George T. Mitchell, ME

URL 04916