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Date February 13, 1980

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Answering letter date

Copy to Messrs. W. B. DeAtley
F. J. Shortsleeve
W. C. Thurber

Subject

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L-2

I believe you will find the attached articles regarding the causes of cancer to be informative. Dr. Demopoulos' article in particular provides an insight that has application to our own personal lives.

Very truly yours,

O. J. Malacarne gt

O. J. Malacarne

OJM:gt

Encl.

AIHC

AMERICAN INDUSTRIAL HEALTH COUNCIL, INC.

1075 CENTRAL PARK AVENUE • SCARSDALE, NEW YORK 10583 • (914) 725-1492

October 26, 1979

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OCT 29 1979

T. W. CARMODY
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TO: ALL AIHC MEMBERS

CANCER CAUSATION

Gentlemen:

At a meeting of the Synthetic Organic Chemical Manufacturers Association earlier this month, Dr. Harry Demopoulos of the New York University Medical Center discussed in some detail a number of important issues relating to cancer causation in the United States.

We believe his talk is especially noteworthy in that it reflects the thinking of much of the independent scientific community with regard to misfocused Federal efforts directed primarily at suspected industrial carcinogens in the workplace and environment.

As Dr. Demopoulos points out in his talk: "University medical scientists...are absolutely enraged at what the Federal government has been doing. The rage stems from the fact that if we are to listen to the Federal government, we will be led down yet another primrose path, blaming industry and air and water pollution for most of the cancer burden, whereas, in fact, the answers to cancer lie elsewhere and have been very well defined through a lot of epidemiological research."

We believe this speech is an important one and should receive the widest possible circulation. Additional copies are available from our office.

Sincerely,

Ronald A. Lang

Ronald A. Lang
Executive Director

Encl.

P.S. Also enclosed for your information is a reprint of a recent article from Science Magazine in which Dr. John Higginson of the International Agency for Research on Cancer also discusses cancer causation.

WASHINGTON OFFICE: 1612 K STREET, N.W., WASHINGTON, D.C. 20006 (202) 659-0060

"ENVIRONMENTALLY INDUCED CANCER...SEPARATING TRUTH FROM MYTH"

A Talk By

Dr. Harry Demopoulos

Associate Professor of Pathology, New York University Medical Center

to the

Synthetic Organic Chemical Manufacturers Association, Inc.

October 4, 1979

Hasbrouck Heights, N.J.

Published by AsbestosClaims.Law
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I appreciate the opportunity to come here and address you. I welcome it very much. It is probably appropriate that this meeting is being held in New Jersey because I think many problems that have beset industry with respect to regulations are founded in some of the misconceived problems that have been painted in New Jersey.

When I came here in 1976, on a leave of absence, the Federal government had just released the National Cancer Institute (N.C.I.) mortality study by county that was conducted by looking at death certificates from 1950 to 1969; several N.C.I. epidemiologists, as well as members of the New Jersey Department of Environmental Protection, and Department of Health, concluded that after adding up the age-corrected, race-and sex-corrected death data, that New Jersey led all the other states in cancer deaths for white males, expressed per 100,000. Now, that was, indeed, a true statement. That was not a lie. The cancer rates in New Jersey were 205 white male cancer deaths per 100,000 versus the U.S. national average of 174 per 100,000. That created a big hullabaloo. It gave this state the label of "Cancer Alley." Some of the people who were in the New Jersey Department of Environmental Protection at that time have subsequently moved to Washington and have continued to amplify this attitude.

I must admit when I came to New Jersey, I shared the view that most New York City dwellers have, that New Jersey is a terrible place, it's horribly polluted. As a matter of fact, on February 16th of this year the New York Times published a map which was sort of the ultimate view that New York City dwellers have. It showed lung cancer rates in various parts of New York City, Staten Island, on the west side of Manhattan, and parts of Brooklyn. The New York City Department of Health blamed polluted air wafting over the river into the city as the cause of these high cancer rates. The report ignored the fact, easily seen on the map, that there vast "skip" areas,and other cancer "hot spots" that were not in the path of such air flows. The New York City Department of Health report ignored rudimentary epidemiologic methods such as correcting all the data for sex and race. Further, no attempt was made to study cigarette consumption patterns.

Ignored in all of these pronouncements and maps at the federal, state and city levels was the old scientific dictum of controls. This is what differentiates science from politics. When you look back at the cancer rates that were published and resulted in New Jersey being labeled "Cancer Alley," nobody mentioned the fact that Rhode Island was number two, with 203 cancer deaths per 100,000. No one mentioned that other heavily industrialized states did not have high cancer rates.

When industry was being blamed in New Jersey, nobody looked at the cancer rates in Pennsylvania and Ohio which are remarkably similar to New Jersey, in terms of the proportion of workers who work in "dangerous" occupations and the number of people who live in communities that are in proximity to major industrial plants that can be viewed by some as polluting. Pennsylvania, Ohio and New Jersey have several things in common. About 40 percent of the workforce is engaged in what you would call heavy, "dirty" industry. Forty percent of the population in those states lives in proximity to so-called "dirty" plants. When you look at the cancer rates, however, Pennsylvania and Ohio have cancer rates that are like the U.S. national average. Yet, only New Jersey had higher cancer rates.

The answer as to what is different about New Jersey is found very simply in the U.S. census. New Jersey has the most urbanized population; 90 percent of the population is urbanized and it also has the most dense urbanization. Only 70 percent of Ohio and Pennsylvania are urbanized. That 20 percent difference explains the difference in the cancer rates among the three states. Before it became politically popular to blame industry, the National Cancer Institute epidemiologists showed unequivocally that urban crowding was a predominant factor in cancer causation. It is clearly a surrogate for something else. New Jersey has a rather small land mass

and over 20 percent of the people are crowded into a rather small area in the northeast part of the state. It is,therefore,like a large city and if you compare it to similar demographic areas, with equivalent land and population density, and look at it in a controlled way, it is shocking to see that many other cities and counties and regions that do not have any industry have higher cancer rates than New Jersey. For example, San Francisco; Washington, D.C.; Nassau County, which is an eastern suburb of New York City; Westchester County; these demographic areas have rates that are equal to or greater than New Jersey's, and those areas are devoid of heavy,polluting industry.

If you look at other questions beyond urbanization and ask what are the surrogate factors, the ecologists would say, well, it's urban air pollution, and it's still ultimately being derived from industry. Well, we tested that hypothesis. The hypothesis was that pollutants in the air and in the water are responsible for increasing the cancer rates by at least 25 to 30 percent. In order to test that hypothesis, we simply looked at the National Cancer Institues's own Third National Cancer Survey which surveyed 20 million people in this country, back in 1969, -70, and -71. Now, that was incidence data and as I said, it covered 20 million people. Our studies incidentally were conducted with the sole support of a grant from the National Cancer Institute when I served as the Director of the Cancer Institute of New Jersey in 1976.

The diagnoses were far more accurate than the death certificates in the N.C.I.'s mortality study because these were surgical pathology specimens. The slides were all read by Board Certified pathologists. In that Third National Cancer Survey, there was a wealth of information and it was not originally designed to answer this hypothesis, but it came out that way. There were seven cities in that survey. Four of them were what we would call"clean" cities; San Francisco, Dallas, Minneapolis and Atlanta. They are urban centers without any kind of heavy industry. In that survey also were Detroit, Pittsburgh and Birmingham, the "Pittsburgh of the South." Those seven cities encompassed 16 million people. We did not massage the data; we simply lifted it out of the tables and put the data next to each other and if the hypothesis was correct that industrial air pollution or urban air pollution were a major factor in cancer causation, we would have expected to have seen that four "clean" cities had lower cancer rates than the three "dirty"cities.

We looked at overall cancer rates for white males as well as for black males, age-corrected, and to our surprise, the three " dirty" cities had an overall 8 percent lower cancer rate than the four"clean" cities. I don't think the 8 percent is statistically significant, however, it invalidates the hypothesis. Furthermore, we looked at specific kinds of cancers that Blott, who is an NCI epidemiologist, and others have said are industry- types of cancers, like lung, larynx, nasopharynx, stomach, lymphomas, leukemias, urinary bladder, liver and skin. These are all supposed to be in industry-associated types of cancers. The Third National Cancer Surve gave us site-specific cancer diagnosis, i.e., by an atomic site. Those supposed industry-associated cancers were not higher or greater in incidence in the three "dirty" cities compared to the four "clean" cities. In Detroit, Pittsburgh and Birmingham,45 percent of the occupational workforce is engaged, and has been engaged for several decades, in industry that most people would say is worrisome. Further, these decades of exposure were without controls. And yet, we did not see greater cancer rates in these cities. A 45 percent workforce engaged in "dirty" industry translates into something like about 22 or 23 percent of the general population, which is a large enough percentage of the population to skew the data up higher if, in fact, these workers were being exposed to significant levels of carcinogenic hazards.

This is the NCI's own data. We didn't manipulate it. And, curiously, in the OSHA hearings and in any discussions that I have ever held with people on the Federal level, nobody ever looks at the Third National Cancer Survey. It's almost

like their unwanted child because if you examine the data, within it is contained certain answers to questions that bedevil society, government, labor and industry. For example, there are questions raised about chronic low-dose exposures. Let's not worry just about the workers, what about the people in the communities? They are exposed to low-dose emissions. What about the question of synergism, which is almost unanswerable in an experimental sense. The answers, again, to those questions, are found in the Third National Cancer Survey and the comparison of the three "dirty" cities with the four "clean" ones. Detroit, Pittsburgh and Birmingham have virtually every kind of pollutant chemical that you can imagine in the air and in the water. If synergism and chronic low-dose exposures were real hazards, and if, in fact, there were no thresholds, we should have seen higher rates in those three "dirty" cities. They have been in "business" for several decades, and the chances existed.

Now, there has to be a reason why we didn't see more of any type of cancer and the reason is as follows: There are thresholds. There is a threshold for virtually every substance that is noxious to mankind. There are thresholds for deadly viruses. There are thresholds for bacteria, fungi, anything that is noxious and harmful to humans generally has a threshold, and this includes carcinogens.

Now, clearly the exposures, although seemingly horrendous in the three "dirty" cities, were well below threshold levels because there was no effect. Recall, the Third National Cancer Survey showed 3% less cancer in the "dirty" cities.

Another thing to keep in mind is there is a real biological reason to explain thresholds. It is not a magical thing. We have DNA repair mechanisms that are very efficient. Furthermore, most carcinogens and many toxic substances act by what we term free radical chemical mechanisms. There are endogenous anti-oxidants that we have evolved with over the eons that protect us against free radical pathology. These anti oxidants can be overwhelmed with excessive doses of a carcinogen, such as occurs in laboratory animals, but human exposures are not at these doses, and we have not been overwhelmed, not even in Detroit, Pittsburgh, or Birmingham. It should be noted that the Third National Cancer Survey was conducted from 1969-1971. The cancers diagnosed at that time were starting to develop during the 1940's and 1950's. In those years, air/water pollutants were not controlled as they are now. We have therefore gone through "worst-case" conditions in our industrialized-urban centers, and nothing happened. Those who beat the drums of doom, as in recent books written by non-scientists, are clearly leading a march down the wrong path in cancer prevention. Abundant controls exist now, and most of them are needed; some are not, however.

Another thing that proves that there are thresholds is the experience with cigarette smoke. Cigarettes of the high-tar variety are perhaps the most carcinogenic substance that mankind deals with in a routine manner on a mass basis. Yet, it has been well proven through smoking dog studies; that thresholds exist; dogs, incidentally, love to smoke. Once they are trained, they jump right into the box and puff like mad. The threshold studies were conducted through smoking dog studies, as well as through careful autopsies on individuals where the smoking history was well recorded, and where the bronchi were serially sectioned and examined. If you smoke 10 to 15 of the 1 mg. tar cigarettes, there are no carcinogenic hazards associated with that. We don't even see the premalignant changes in the epithelium; so that here is the most carcinogenic substance that is massly used and there is, decidedly, a threshold.

Similarly, there are thresholds with alcohol. Alcohol and cigarette smoke are synergistic and together if you smoke the high-tar cigarettes and drink excessive quantities of alcohol, you find that you can account for 35 percent of the cancer

deaths. This type of synergism is rare. Most of the cancers of the mouth, larynx, esophagus and lung are caused by these two factors and they are synergistic. But, again, it has to be with excessive quantities of distilled liquor. It's the alcohol itself, not the congeners or other substances that are found in the drink.

Now, the misconceptions that have been brewing, first in New Jersey, and later in Washington, have aroused not only the ire of you fellows in industry but the ire of University medical scientists who are in the comprehensive and specialized cancer centers such as MIT, Harvard, NYU, Columbia, University of Pennsylvania, McArdle Cancer Center, and others. We are upset at what the Federal government has been doing. Our worry stems from the fact that if society is to listen to the Federal government, it will be led down yet another primrose path, blaming industry, air and water pollution for most of the cancer burden, whereas, in fact, the answers to cancer lie elsewhere and have been very well defined through a great deal of epidemologic research and extensive laboratory research. Whoever attempts to lead the nation towards less cancer had better be correct, because the selection of the wrong path is the equivalent of leading millions of Americans to certain death.

There were two symposia that were held. One on February 28th, March 1st, and March 2nd and another one, June 6th,7th and 8th in New York City. These two symposia were held by the independent university scientists from the comprehensive and specialized cancer centers in this country. The symposia were under the aegis of the New York Academy of Sciences, and the American Health Foundation, with the cooperation of the American Cancer Society, as well as the World Health Organization's International Agency for Research on Cancer.

We came up with the following predominant causes of cancer, and the word,"predominant," is important. An analogous situation is that tuberculosis is predominantly caused by the tubercle bacillus. While there are associated factors in causing tuberculosis, for example, poverty, crowding, and malnutrition, the predominant cause is still the tubercle bacillus,and if you want to eliminate that disease,you control the tubercle bacillus. Similarly, in cancer, there are predominant causes. The University scientists decided to sponsor and attend these two symposia, and to continue putting on such symposia as often as is humanly possible, in order to turn around the propaganda machine that has been launched by the Federal government. This machine is leading the country down the wrong path in cancer prevention and is killing many Americans through misinformation.

The University scientists just went through a 15-year period of going up a blind alley looking for cancer viruses that weren't there. That cost a billion dollars. We cannot afford, not in monetary terms nor in human terms, to spend another ten years and another billion dollars or more chasing the wrong culprit in cancer causation. There will be too many lives lost, especially when we know most of the answers for prevention at the present time. While we are still ignorant about exactly how a normal cell becomes malignant, we do know how to avoid situations that have such a transformation as the end result.

The answers to cancer prevention are as follows. And it's easy to keep the scorecard in mind. There are about 1,000 people a day that die of cancer in this country. 350 of them, or 35 percent, are going to die today from having smoked high-tar cigarettes and having consumed excessive quantities of distilled liquor and they will die from cancer of the mouth, larynx, esophagus and lung.

Another 45 percent are attributable to diet, and this figure was courageously stated by Dr. Arthur Upton,the Director of the National Cancer Institute,on Tuesday,befor a Subcommittee on Nutrition. He has confirmed what the University scientists have been saying for the past few years. No other government scientist has had the integrity to state what Dr. Upton stated; he further and strongly recommended major decreases in fat consumption, with increases in fresh fruit and vegetable

consumption. 45 percent of cancer deaths are related to disordered nutrition. Under the category of disordered nutrition, there are four subcategories: excess calories; excess fat ingestion; obesity, carrying around an extra 30 or 40 pounds; and nutritional deficiencies such as fiber deficiency and Vitamin A deficiency.

Now, with Vitamin A you have to be careful. There is an optimum dose which happens to be the Recommended Daily Allowance. Too much Vitamin A will also cause cancer in addition to being toxic. Too little Vitamin A will also cause cancer.

There is approximately 5 percent of cancers that are occupationally induced due to previous exposures 20,30 and 40 years ago when even the best scientists did not know that many chemicals were capable of causing cancer. Recall that most university scientists and government scientists were engaged in chasing viruses and it's only recently that the blind-alley virus theory was proven invalid.

There is evidence that the 5 percent of cancer deaths that are due to occupational exposures may have plateaued and may be on the way down. If you look at hemangio sarcomas that are caused by vinyl chloride monomer exposure, the latency periods and the ages of the patients are longer and older, respectively. It means they are developing at slower rates. Similarly, we did a study at NYU showing that mesotheliomas, which are caused by asbestos exposures, are at a plateau. We do not see an increasing incidence of mesotheliomas, despite the fact that most of the people that we see at the NYU Cancer Center, where we treat 4,000 new cancer patients a year, are drawn from places like the Veteran's Administration and Bellevue Hospital, and includes a fair number of construction workers, and Brooklyn Navy Shipyard workers. Our Cancer Center is a general one, and does not have a specialized referral component for mesothdiomes, as at Mt. Sinai Hospital; therefore, our rates are indicative of the general rates. We have not been seeing an increasing incidence in mesothelioma over the past 12 to 15 years. It's at a plateau. So that I think if controls are kept over the very dangerous chemicals and physical processes that you use in industry, I think we can continue to see what looks like a decline in occupational cancer, which we think is currently around 5 percent. Sir Richard Doll and others think it's much lower, but I would caution you that you cannot relax. The chemicals that you deal with in ever increasing quantities to meet consumer demands and to try to remain competitive in a ferocious world market are dangerous, and I think there are elements of truth to what the government regulators say; we can see a major explosion in industrially caused cancer if we do not have sensible controls. The question is, how rigid should the controls be? I think that we can be less rigid than what OSHA and EPA have proposed recently since there is clear evidence that there is no need for that kind of rigidity. Occupational carcinogens are under control, and new chemicals are receiving close scrutiny; air and water pollution are blameless in carcinogenesis.

A few other points that I would like to make in closing are that in addition to determining that cigarettes and alcohol, disordered nutrition, and occupational exposures cause 85 percent of the cancer deaths, there is another 3 percent that are caused by exposure to radiation which is largely background, not nuclear plants, but background radiation. We have enough radioactive potassium in our bodies, for example, to cause 4,000 radioactive decays per minute. That adds up.

Another 2 percent of the cancer deaths are caused by preexisting medical disorders, like chronic ulcerative colitis, chronic gastritis and things like that. And about 1 percent are caused by prescription drugs for the treatment of serious medical disorders.

The symposium in June also determined, and this was brought forth by Dr. Cuyler Hammond of the American Cancer Society, that almost zero percent of cancer deaths, it's something like .00001 percent, are caused by air pollution. Water pollution is

in the same category of zero percent. Other studies have shown that nuclear power plant accidents, asbestos in hair dryers, asbestos in school rooms, and saccharin/cyclamates can not cause cancer as presently used. And yet, those things that are listed as being zero percent are uppermost in the public's mind. This is due to the propaganda machines. We are treated to outrageous remarks by individuals like Wolfe from Ralph Nader's group that asbestos is the second leading cause of cancer deaths in males in this country. It's an absolutely unfounded statement that, by no stretch of even Sellikoff's imagination, could that be true. And yet, individuals like this are placed politically on the National Cancer Advisory Board and govern, and help to govern the National Cancer Institute's policy. It is terrifying because our nation can be led down the wrong path in prevention.

So you have an uphill fight in terms of public relations but I think that, if controls are kept, truth and reason are on your side and I think that you can win this battle that you are in. Thank you.

Q: I assume that the reason for the higher cancer rates in the cities is due to the factors you described, more smoking, and so on.

Dr. Demopoulos: And they have far more disordered nutrition. The urban crowding is a surrogate for all of the factors that we know to cause cancer and it is proven too, with animal studies. The reason is ultimately the kinds of stress that you get when you start crowding any living organisms together. This has been well-defined with rat behavioral studies where if you take a room of a given size and keep putting more and more rats in there, even though you provide them with enough food and water, and places to sleep and rest, you will see back biting, tail biting, homosexuality, fighting and all the other things that you see in urban settings. In medical schools, we are taught that certain diseases are urban diseases, i.e., they occur more frequently in urban areas. For example, obesity, hypertension, chronic ulcerative diseases of the GI tract (the gastrointestinal tract), heart disease , suicide, homicide, drug addiction, are all far more common in urban settings. This includes the cities and their surrounding suburbs. Now, I think to that list should be added cancer. And I don't think it's stress per se, but rather it's the way humans choose to relieve their stress, through gorging themselves, drinking themselves into oblivion, and surrounding themselves with smoke, that cause cancer.

Q: I understood that in other parts of the world that different types of cancers occur.

Dr. Demopoulos: Well, there are some interesting reports that have come from China just recently. There are regions of China that have extraordinary rates of esophageal cancer, for example. Even their chickens have esophageal cancer. But, that has been traced to the particular kind of food that these individuals make. They apparently take various kinds of vegetables and peel them and let them sit around for months and months and finally they eat that and their chickens eat the same scraps. There are other situations, where there has been a good deal of epidemiologic research done on the nutritional habits of people in correlating it with diseases, and it keeps coming back to what we eat that causes cancer. And, this is true also for atherosclerosis as well as premature aging. For example, there are tribes in Africa that make a habit of eating raw meat and blood together with milk and this is all they eat. They don't eat any fruits and vegetables. Their life expectancy is about 30 to 35 years of age. They die of heart disease, strokes, hypertension and cancer. And it's the worldwide studies that have been the strongest implicators of diet as a predominant cause of cancer.

Q: In your listing of causes, it seems to me that you came up with about 91 percent. Where is the other 9 percent?

Dr. Demopoulos: God. I think that we are not immortal and we have to accept

certain things. I think it's part of the aging process. Almost every male over the age of 35, at autopsy, has cancer of the prostate gland, if the prostate gland is adequately examined. These cancers are microscopic and produce no symptoms. Similarly, urinary bladder cancer is a cancer of the aged. It keeps climbing as you get into the 80 and 90 year old brackets. I think it's an accompaniment to age and Dr. Handler, the President of the National Academy of Sciences, has offered the hypothesis that oxygen, one of the most toxic gases known is responsible. Oxygen happens to be a diradical. It oxidizes everything, including our lipids and I am sort of surprised, as a free radical pathologist, that we can exist with oxygen. I wouldn't have chosen it. Methane would have been better.

But, Dr. Handler has proposed that simply existing in an aerobic atmosphere is cause enough to give us cancer, and were it not for the major antioxidants that we have, we would have even more diseases. The decline in cancer of the stomach is appropriate to mention at this point in that regard. Cancer of the stomach used to be the commonest cancer killer in this country 40 and 50 years ago. Nowadays, it's a rare disease. In medical centers, we keep these cases extra days as teaching cases because medical students will never see another one like it in their career. The reason for the decline in stomach cancer is the increased consumption of fresh fruits and vegetables and the antioxidants therein. BHT has probably helped. Dr. Arthur Upton concurs in this view, as do many University scientists.

Q: Does a significant segment of the scientific community, people working in cancer causation, feel the same way you do about the problem? From your view, why is it that these scientific arguments about what industry is doing are presented by people like Wolfe, Epstein and Barry Commoner? Why don't we ever hear from those people who have spent their lives actually doing the research?

Dr. Demopoulos: A good reason is that University medical scientists do not have a PR or propaganda machine, nor do they have a policy that they are trying to advocate. It's one of the defects of science in general that unless there is an organized effort to get the truth out of the medical journals wherein it is buried, you are going to have misconceptions, as we have now. I think the reasons for the origins of the misconception lie in the fact that as we prove the lack of validity of the virus hypothesis, there was a void. Everybody asked, well, if it's not viruses, what is it? Unfortunately, the term "environmental cancer" came into being. That was seized as meaning the general community environment rather than the personal environment created by our habits, diet and lifestyle. There was a void, a gap, before the nutritional data was gathered epidemiologically and from animal studies. We now know what the predominant causes of cancer are but, at the time the virus theory was shown to be invalid, the "greenies" and the ecology people came into the picture and stole center stage and they are still at it and they are holding onto it come hell or high water. They seem oblivious to the consequences of leading a march in cancer prevention down the wrong path.

Q: As a taxpayer who was able to pay for tearing the asbestos out of all of the schools and other public buildings, I am gratified that you don't seem to think that's a terribly important factor.

Dr. Demopoulos: I think it's a tragic misconception and it's the height of hypocracy and stupidity to see classrooms being torn apart. This recently happened in New York City where pretty close to half a million dollars were spent redoing the whole school because of the asbestos scare. Somebody had gone in and sampled the air only in the classrooms and found asbestos there. The conclusion was that it was coming from the ceiling. They tore everything down and they went back and they sampled the air again. They found just as much asbestos. Then, and only then, did they go out and do what is called the control. They went to the outside air and sampled it several blocks away and they found even more asbestos in the outside air. The point is, asbestos is a natural product, it's all over the place. We use it

extensively in urban settings, brake linings, construction, everything. The point is that the doses we get in school rooms and office buildings are far below any kind of danger level, yet within these same classrooms we have smoking lounges. As the N.Y.U. study has shown, we are not seeing an epidemic of mesotheliomas.

If you go into the cafeterias and watch what the kids eat, it's garbage, as far as I am concerned. Loaded with fat. No fresh fruits and vegetables, and these are wrong. It's as stupid as when a cigarette company used to advertise high-tar cigarettes as being good for your "T-zone."

Q: Is there any really definitive data on the effect of the so-called social drugs like marijuana?

Dr. Demopoulos: They haven't been used long enough nor in any good epidemiologic studies but just looking at tetrahydrocannabinol, that's a toxic substance. That will damage cell membranes and will damage DNA, so will LSD; so will most of these so-called recreational drugs. I think they are fearsome and they really should be controlled for a variety of reasons, including their carcinogenic and mutagenic potential as well as the fact that they absolutely destroy nerve cells. The reason for producing a "high" is a lot of nerve cells are just getting disconnected. The synapses are missing so that you no longer have the major inhibitions that are inherent in the electrical circuits in the brain that keep us under control. I don't mean moral inhibitions, I mean the ability to be able to focus on one thing at a time, to concentrate. The brain functions by blotting out everything else except what you are supposed to pay attention to. The reason you get a "high" and start seeing visions with LSD and mescaline is that a lot of circuits are disconnected and you can no longer focus on any one thing; virtually every circuit in your brain has been turned on and is short circuiting.

These drugs are very dangerous. Whenever you start damaging cell membranes like that, you damage a lot of cell control mechanisms and open the way to birth defects, cancer and every other chronic disease, including aging.

Q: In our community we have had some questions about asbestos cement water pipes. Is there any problem?

Dr. Demopoulos: I think in specific instances, you would have to sample water like that. You would have to look at it. I don't doubt that in occasional circumstances it is quite possible to carry carcinogenic loads of a chemical substance through the air and through the water, but I think they are unusual; where there are questions, I think you should take a look and see what the concentration is. The dose is all important, for sure. If it's a low dose, I wouldn't worry about it.

Q: There are numerous problems that you have mentioned in your discussion relative to society's view of the cancer situation. Number one, you have the terror factor, the fact that people are more afraid of cancer than they are of heart disease. What, in your opinion, can communities, can we as concerned people, many of us, do to offset that view?

Dr. Demopoulos: Well, I think you have already done one thing as industry groups, and that is, I think, coordinated programs as AIHC has carried out on behalf of industry are very important. You must be unswerving in the pursuit of truth, it's good business.

I was shocked and amazed back in 1976 when I came here to direct the Cancer Institute in New Jersey. The press and the Department of Environmental Protection in Trenton were literally tearing industry apart. I always thought that you fellows were really hot stuff and would have answered back and I was surprised that industry was just laying back being beaten up. There was no response. I

couldn't understand it. I think [illegible]. I think that if you
tap the angry potential that I assure you is [illegible] you talk to serve
university community, you will have a very [illegible] you talk to serve
truth and society. We have had no problems getting [illegible] university scientists
to stand up and be counted and speak the truth even at the risk of angering the
National Cancer Institute from whence their grants [illegible]. [illegible] years judge our
grant applications; think not the politicians and [illegible] not.

Cancer and Environment: An Unpopular View

LARC director says 60 to 90 percent of the anticancer drive has been misdirected; life-style is more important than chemicals

John Higginson, founding director of the World Health Organization's International Agency for Research on Cancer (IARC), is the formulator of a rather complex idea which boils down to something we eat, drink, and breathe. That perception is very broad, but it is a misinterpretation of what he has said over the past 30 years or so. In a long conversation with *Science* recently, Higginson tried to explain his views and how they evolved. He carefully explains the simplicity of too simplistic a view of the cancer problem, which he believes has been the case since 1935.—THOMAS H. MAUGH II

In the 1950's, you compared the incidence of certain types of tumors among blacks in Africa and America and concluded that about two-thirds of all cancers had an environmental cause and were therefore theoretically preventable.

That is a reasonable summary. Once Oettlé and I obtained good statistics from African black populations, we were able to calculate a theoretical concept of what the low incidence of cancer could be, and any increased incidence could then be considered due to an environmental component. Actually, the idea that geographical differences in cancer incidence are due to the environment goes back many years before that. David Livingstone, I think, said cancer is a disease of civilization, and therefore the idea that the differences were environmental has a long history. My contribution, if I may say so, was limited merely to giving a more concrete estimate of the impact of environmental factors, and to show that most cancers were not due to genetic factors and thus that prevention was not impossible. I ought to make that clear because people are giving me credit where it is not due.

But when I used the term environment in those days, I was considering the *total* environment, cultural as well as chemical. By cultural, I meant mode of life. When we ran that study of blacks in 1952, we started looking at their diets, how they lived, the number of children they had, the age of menopause, the age of menarche—all that was included in the term environment. I've checked it in every dictionary and every dictionary gives the same: Environment is what surrounds people and impinges on them. The air you breathe, the culture you live in, the agricultural habits of your community, the social cultural habits, the social pressures, the physical chemicals with which you come in contact, the [illegible], and so forth is the environment. Naturally, such factors presented themselves as an obvious explanation of many human cancers.

During the 1930's, 1940's, and 1950's, industry had shown a great deal of insensitivity to potential dangers in the workshop, and its unwillingness to attack cancer hazards, associated with the changing political climate among scientists and politicians and environmental pressure groups, made it easy to place



the responsibility for all environmental cancers on industry. The environment thus became identified only with industrial chemicals. Even tobacco was neglected. This interaction of scientific and social hypotheses prevented wider recognition of the fact that many cancers could not be explained so simply.

There's one other thing I should say that has led to the association of the term environment with chemical carcinogens. The ecological movement, I suspect, found the extreme view convenient because of the fear of cancer. If they could possibly make people believe that cancer

But you've done a lot more research since the 1950's. Has something come up to change your original hypothesis?

I have found everything to buttress it. I have found nothing to disprove it. Nor do I know any other person who has produced data that are acceptable and published that contradicts it.

Then how do you explain the misinterpretation?

I think this has been due to a combination of reasons. One, many people have failed to distinguish between the environmental origin of cancers with clearly defined etiology—for example, smoking, alcohol, and occupation—and the large group of digestive and endocrine-dependent tumors whose environmental cause can be inferred only circumstantially. The idea of life-style was woolly and ill-defined and not expressible in biochemical terms with the technology available. Most scientists, myself included, don't like something woolly. Two, there was considerable interest in explaining human cancer in terms of virology, so that chemical carcinogenesis became unfashionable. The textbooks of the 1950's thus largely discussed occupational cancers which could be confirmed by nice, distinct, and easy animal models. Rachel Carson's book was a watershed. As suddenly we became aware of the vast quantities of new chemicals, pollutants, pesti-

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ACL Doc 15600 · Page 13 of 15 asbestosclaims.law/library/15600/13

[illegible] her local pattern. And if you take these [illegible], you're dealing with a g[illegible] group of female cancers, breast and cervix, which in the United States and most countries account for 50 percent of female [illegible].

That sounds fine and simple, but running parallel with that is the fact that we've had changes in dietary patterns. . . . The age of menarche in the American female, for example, has dropped extensively. We are having children beginning to have their menarche as early as 10 or 11 in portions of the world, compared to Africa where it is often as late as 16. That difference is probably related to dietary factors. For years we have talked about an improving diet, taller people, better people, but this automatically leads to modifications, for example, of the pituitary axis. These changes themselves, associated with behavior patterns, may tie in together to modify the susceptibility of an individual. Diet is under environmental control, the behavioral pattern is under environmental control, so this is what I mean by environment. But as you see, it's a highly complex system, dealing with humans, and therefore we don't have good models.

Are there any kinds of analogous behaviors in men?

The men are funny, you see. . . . The group of cancers you would attribute to life-style for males [excluding alcohol and tobacco] is much smaller. The major sources are stomach, large intestine, and prostate. Now people have gone around trying to prove that sexual activity is related to prostatic cancer—frustrated sexual relationships, and so forth. But, to date, nobody has come up with a reasonable solution. Now let's take prostate cancer in three groups of males, Japanese, U.S. whites, and U.S. blacks. We'll call the Japanese prostatic cancer incidence one. The incidence in U.S. whites would be about 30 and in U.S. blacks, 60. You look at that and there's no way you can possibly explain that on exposure to air pollution, diffuse dietary pollution, or anything like that. It is just ridiculous to try to do so.

If, however, we look for what we call latent carcinoma, we find that, in the United States, about 10 percent of all men of 75 have a latent cancer sitting in their prostates. And it's almost the same, 10 percent, in Japan and Germany. So [illegible] in the U.S. [illegible] Japanese. [illegible] may be involved [illegible] this, so one [illegible] think of dietary factors. [This is [illegible] by studies of Japanese who have [illegible] to the United States.]

[illegible] the [illegible] thing is to think of the [illegible] of carcinogens. We have [illegible] of evidence that goes back to 1[illegible], and which [illegible] extensively in the Orient, for example, showing that diet has nonspecific factors—the amount of fats, the amount of fiber, and so on. We say lack of fiber is a risk factor for colon cancer. Well how in the world can you say lack of fiber is a carcinogen? It's a ridiculous expression. No one would prefer to use the term carcinogenic risk factor. It is about the only dietary thing there is that has stood up for 30 years. But fats, protein, carbohydrate, vegetable inhibitors may also be important—[illegible] research is going to be in this area. But the problem is, [illegible] to [illegible] answer here, "How should we deal with diet?" and we just don't have the answers. The only thing I can say is reduce calories and fat, and possibly add some fiber, but without making any promises as to what will happen.

We simply don't know enough at the present time in many areas to advise legislation or marked changes of life-style. If you take Copenhagen, for example, we have found that colon cancer is four times more common in Copenhagen than in Finland. Yet both populations drive cars and live exceedingly well. But there are significant dietary differences. So you might say, let's tell the Danes to eat the Finnish type of diet. But then you find that the Finns have the highest rate of heart disease in Europe, and probably in the world, so what they're gaining on the swings they're losing on the roundabouts. One has to be terribly cautious, in my opinion, of making advocation. Now you take urban and rural Denmark. People have said that breast and colon cancer are related to fat intake. Well, when we compare urban Copenhagen and rural Denmark, we find that the incidence of cancer of the breast is higher in the urban area . . . . but they eat much more fat in the rural area, 50 percent more. It's quite contrary to the hypothesis. There is obviously something in the way they live in the rural area compared to the town that hasn't been [illegible] by.

[illegible] of these [illegible] to change their [illegible] your view of cancer [illegible]?

[illegible] I didn't mean to imply that [illegible]. I think it actually offers a [illegible] in practice. It [illegible] impossible to [illegible] of potential [illegible] will be [illegible]. [illegible] necessarily be justified in view of the intense commitments required in terms of national resources, without better supportive data. On the other hand, if cancers of the digestive system or endocrine-dependent systems are eventually related to life-style, it should not automatically be assumed that control of them will be impossible.

Quite obviously, Congress can't legislate an early first pregnancy to protect against breast cancer, but there is a good possibility that we may be able to mimic it with a pill when we know about the biochemical effects. Already there is evidence that contraceptives may reduce [illegible] lesions in the breast. There are also two reports indicating that contraceptives protect against ovarian cancer by inhibiting ovulation. I am optimistic that once we have a better understanding of the mechanisms involved and the relation to behavior and nutritional patterns, not only may it be possible to intervene with some success but also to identify individuals at high risk. Intervention of this type is already being considered and is called chemoprevention, a comparatively new approach to cancer control.

However, the real reason I am optimistic is that in a wider intellectual climate some scientists are no longer thinking in terms of simple carcinogens, mutagens, and initiation, but are developing a new sophisticated approach to study all complex mechanisms involved in multistage carcinogenesis. This is largely thanks to the work of Berenblum, even if in many circles this approach remains unfashionable. Lastly, we do know that there are populations with low frequencies of these cancers; thus, the Japanese have a very low frequency of breast cancer and the Finns have only a quarter of the colon cancer incidence in the United States. Once we can explain these differences at a more fundamental level, I am confident that we will be able to take active measures to reduce this large group of cancers due to life-style in countries of high incidence.

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ACL Doc 15600 · Page 14 of 15
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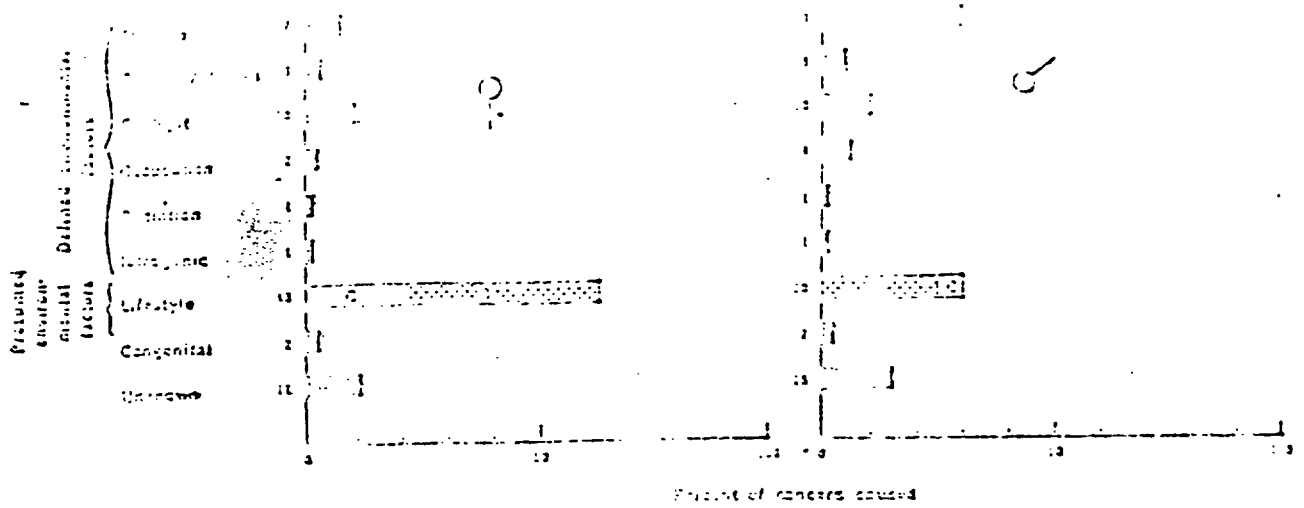


Fig. 1. John Higginson's best estimates for the proportion of cancers ascribable to various causes. The relative importance of diet (D) and behavioral or cultural patterns (C) in lifestyle are only very roughly estimated.

was going to result from pollution, this would enable them to facilitate the clean-up of water, of the air, or whatever it was. Now I'm all for cleaning up the air, and all for cleaning up trout streams, and all for preventing Love Canals, but I don't think we should use the wrong argument for doing it. To make cancer the whipping boy for every environmental evil may prevent effective action when it does matter, as with cigarettes. I think that many people had a gut feeling that pollution ought to cause cancer. You asked me, were people dishonest? I don't think that some people were intentionally dishonest, but rather that they found it hard to accept that general air pollution, smoking factory chimneys, and the like are not the major causes of cancer. I mean, people would love to be able to prove that cancer is due to pollution or the general environment. It would be so easy to be able to say "let us regulate everything to zero exposure and we have no more cancer." The concept is so beautiful that it will overwhelm a mass of facts to the contrary.

You mean there is no relationship whatever between pollution and cancer?

No. The dangers of point-source pollution are well recognized. But you cannot explain much of existing cancer patterns only in terms of simple general pollution by industrial chemicals in low doses. You can't explain why Geneva, a non-industrial city, has more cancer than Birmingham in the polluted central valleys of England. In the United States, reports are coming out that there are few differences in cancer patterns between the so-called dirty and clean cities. In fact, the only thing you can say is that air pollution may, and I emphasize MAY, increase lung cancer in cigarette smokers. These and other epidemiological discrepancies simply cannot be explained by variations in general pollution. Some can, however, be explained by differences in lifestyle. In other words, I believe that overemphasis on chemical carcinogens has diverted our approach to the environment and to cancer for many cancers.

I'm not saying one shouldn't clean up the environment, of course you should, people shouldn't be exposed unnecessarily. (But the simplistic approach] has prevented possible acceptance of the idea that there may be doses of carcinogens which, for practical purposes, are unimportant. If you consider smoking plus asbestos or smoking plus uranium, those combinations lead to more lung cancers everybody knows. But the corollary, then, that small bits of 20 different carcinogens add up to produce a cancer—there are simply no experimental or human data that this is the case. Certainly I used to believe this myself, and I spent many years in the laboratory looking for suitable experimental models to study combinations of chemicals—with little success. Most work has been carried out at relatively high doses and models are more often additive rather than multiplicative. Furthermore, some carcinogens even inhibit the action of others. The existence of nonetfect doses of carcinogens has been very poorly investigated, and there is practically no research on this subject apart from experiments on two-stage carcinogenesis, which is a very different story. And, as Berenblum has pointed out, we are probably being exposed to so many carcinogens all the time that what happens is mostly incomplete at the target-cell level: the cells die and nothing ever happens. Because you and I walk across the street, we are exposed to sunlight, which is a well-recognized carcinogen, but we may only develop one skin cancer in a lifetime, or even none . . . . despite the thousands or millions or billions of cells that have been exposed to sunlight. Only a very rare cell goes on to a cancer. So it may be that zero exposure is out. From an epidemiological viewpoint, I believe that attempts to prevent most tumors through control only of mutagens and carcinogens will prove to be a disappointing approach, as will concentration only on the initiation phase of carcinogenesis. Research should be directed to other possible factors. That's the message which I feel is the adequate summary of the data of the last 30 years.

Beyond smoking and tobacco, what do you consider the most important components of life-style?

Two, diet and behavior.

What types of behavior?

Can I just explain what I mean by behavior in a simple sense. Brian MacMahon and other people showed, for example, that if a woman had her first child at an early age, she protected herself against breast cancer; if she had the child at a later age, there was a much greater chance of cancer. Now we know that pregnancy leads to changes in the body . . . . but we don't know what those are, and hence the biochemical expression of the behavioral pattern is incomplete. On the other hand, the term behavior, as "when I am going to have my first baby," is a technically accurately expressed term which largely depends on the culture in which you live. Another example is the fact that sexual activity from an early age leads to a lot more cancer of the cervix. Why, we don't yet

(Continued on page 1561)

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ACL Doc 15600 · Page 15 of 15
asbestosclaims.law/library/15600/15