

F. A. S. PUBLIC INTEREST REPORT

Formerly the FAS Newsletter

THIS ISSUE:

CANCER & THE ENVIRONMENT

Vol. 29, No. 5

May, 1976

CANCER: ATTENTION IS TURNING TO PREVENTION

Fashions change in the world of cancer theoreticians. In the forties, there was intense interest in radiation as a cancer-inducing mechanism (carcinogen). Later, in the fifties and sixties, viruses became the prime suspect. Now chemical carcinogens are emerging as the focus of attention. What lessons should the public draw?

The perspective that we live in a sea of dangerous radiation has saved many lives. Radiation can indeed cause cancers, and dangerous mutations as well. No one doubts the desirability of the caution this view impelled in the use of radiation.

The analogous view that we live in a sea of cancer-inducing viruses has thus far been disappointingly unproductive of public health implications. Decades of intense research, and many hundreds of millions of dollars, have left viral researchers backpeddling. While viruses have been shown to cause an array of cancers in small mammals, none has yet been unequivocally shown to cause cancer in man. Theories that viruses carry into man's chromosomes a cancer-causing gene (oncogene) are being shaded into theories that these genes were left there by viruses much earlier. It becomes increasingly difficult to determine how some variants of such theories could even be tested, much less to deduce from them some method of protecting the public. The underlying hope of viral cancer specialists had been, of course, to pro-

duce a vaccine against the virus; this hope is presently in retreat.

Fortunately, the third view that we live in a sea of potentially carcinogenic chemicals has — as did the view concerning radiation — some useful implications for public health. Chemicals can and should be tested for their carcinogenicity and, to the extent that circumstances permit, man should avoid contact with those that cause significant numbers of cancer. This means a strong toxic substances bill requiring pre-market testing of the thousands of new compounds that pour onto the market each year. And this, in turn, requires the validation and adoption of testing methods that can inexpensively, quickly, and reliably screen these chemicals. Fortunately, there is timely hope that the Ames test — which correlates carcinogenicity in mammals with mutagenicity of the bacterium *Salmonella Typhimurium* — will provide such a screen. Nothing could be more important at present than to validate this test. (See page 6.)

We do not wish to overstate the promise of the environmental chemical approach to cancer if only because cancer is a graveyard of such hopes. It is true that, increasingly, many observers now consider cancer to be 70%-90% environmentally induced. Epidemiologists observe that a reduction of the U.S. cancer rate for each cancer to the lowest rate observed

—Continued on page 2

CANCER: RUNNING THE GAUNTLET FOR TWENTY-FIVE YEARS

... In recent years, it has become clear that only by preventing disease from occurring, rather than treating it late, can we hope to achieve any major improvement in the nation's health. [Heart disease, cancer and stroke] are caused by factors (e.g. the environment and individual behaviour) that are not susceptible to direct medical solution."

—HEW Forward Plan for Health, 1977-1981

So far we have been lucky. The perennial rise of 1% in cancer mortality for the last forty years can be attributed to earlier dramatic increases in smoking with a subsequent rise in lung cancer. Thus the only important carcinogen to which we are known to be societally addicted is cigarettes. But since cancer mortality reflects the environment of twenty or thirty years ago, we have only just begun to experience the results of the post-World War II surge in chemical production. Is the asbestos in the brake-linings of the post-war flood of automobiles contributing synergistically to the lung cancer caused by smoking — as it does so dramatically in the lungs of smoking asbestos laborers? No one knows. And

among the hundreds of thousands of new compounds produced in this post-war period, there is room for a great many surprises; virtually none have been tested for their cancer-causing qualities.

If a toxic substances bill passes this year, then — if we survive without disaster to the year 2000 — we will finally be able to (excuse the pun) breathe more freely. It will have been a miracle not to have run across one, much less several, widespread and highly carcinogenic substances in the constant chemical reshaping of our environment over the last thirty years.

Without this bill, the Government approach to cancer prevention can only be described as chaotic and laggard. HEW's NIOSH (National Institute for Occupational Safety and Health) has a list of 1500 substances for which the literature demonstrates some carcinogenic activity. NIOSH has been in existence for many years in one form or another but has drafted its "criteria documents" for only two dozen of these substances, of which most resulted from the requirements of a single suit brought

—Continued on page 3

Continued from page 1

in the world would provide a 90% decrease. But much of that gross potential saving is due to difficult-to-change dietary, cultural, or social habits rather than only to industrial effluents.

On the other hand, we do know from the chemical exposures of industrial workers that high dosages of many chemicals can, do, and are causing human cancers. A major new attack on these occupational cancers is a moral imperative. And since most of what is known about cancer-causing agents in man has been learned from often unsystematic research on occupational diseases, this attack will provide theoretical insights.

Quite apart from whether existing chemicals can be pinpointed as significant avoidable sources of cancer, screening of chemicals will eventually avoid a troubling "doomsday" scenario. In principle it is only too possible to imagine the cancer rate suddenly rising 2%, 3%, or 4% a year — rather than the 1% now being experienced. At these rates, cancer would quickly become far more serious even than it is today. Suddenly, it might be belatedly realized that one or more of many chemicals introduced into the environment decades ago was highly carcinogenic and was, after a twenty or thirty year lag, beginning to show its effects. With the present inability to cure substantial numbers of cancers, Americans would be defenseless — with alarm bells ringing much too late. It is obviously insupportable to continue to run these risks. Industrial and societal addiction to highly carcinogenic chemicals must be avoided at all costs.

The importance of this avoidance could not be more clearly indicated than by the seemingly irreversible addiction we call cigarette smoking. A third of all male cancer deaths are linked to cigarette smoking. Smokers are losing, on an average, several years of life. And yet they continue and, indeed, the ranks of smokers grow. The frustration of cancer researchers in finding how cancer works is matched only by their frustration, in this case, in getting society to act when a real and virulent cause has indeed been found.

The time has come for a new attack upon smoking. Perhaps it could be composed of standard mechanisms such as much higher taxes on cigarettes, prohibitions on machine vending, publicity campaigns (which might be focused on life-shortening statistics), etc. Despite our experience with prohibition, perhaps new ideas should be explored such as prohibiting sales to any "new" smokers while providing ration books permitting a last generation of existing smokers to maintain their addiction. The ever higher — and ever more shared — costs of health provide a justification for laws discriminating against smoking. And the evidence that smoking may cause birth defects provides another stimulus to action.

All in all, the notion that cancer is a preventable disease has more promise than the notion that science may provide a "cure". Far more likely than not, the cure is not around the corner. And as likely as not,

it will not be cheap. In any case, the history of medical science teaches us that the largest number of lives has been saved by preventive medicine and public health measures, not by curing the already ill. And history also reveals what we see again today: traditional attitudes among the doctors and biomedical researchers that are overly oriented toward curative research.

In the present era, these are the simple observations which law-makers and agency administrators should take to heart. As for the public, it must somehow adopt the solution that is presently available for a third of cancer cases; with the help of Government it must persuade itself to stop smoking.

—Reviewed and Approved by the
FAS National Council

FAS

Chairman: PHILIP MORRISON

Vice Chairman: JEROME D. FRANK

Secretary: HERBERT SCOVILLE, JR.

Treasurer: HERBERT F. YORK

Director: JEREMY J. STONE

The Federation of American Scientists is a unique, non-profit, civic organization, licensed to lobby in the public interest, and composed of 7,000 natural and social scientists and engineers who are concerned with problems of science and society. Democratically organized with an elected National Council of 26 members, FAS was first organized in 1946 as the Federation of Atomic Scientists and has functioned as a conscience of the scientific community for more than a quarter century.

SPONSORS (partial list)

- | | |
|-----------------------------------|------------------------------------|
| *Christian B. Anfinsen (Biochem.) | *Polycarp Kusch (Physics) |
| *Kenneth J. Arrow (Economics) | *Willis E. Lamb, Jr. (Physics) |
| *Julius Axelrod (Biochemistry) | *Wassily W. Leontief (Economics) |
| *David Baltimore (Microbiology) | *Fritz Lipmann (Biochemistry) |
| *Leona Baumgartner (Pub. Health) | *S. E. Luria (Biology) |
| *Paul Beeson (Medicine) | *Roy Menninger (Psychiatry) |
| *Hans A. Bethe (Physics) | *Robert Merton (Sociology) |
| *Konrad Bloch (Chemistry) | *Matthew S. Meselson (Biology) |
| *Norman E. Borlaug (Wheat) | *Neal E. Miller (Psychology) |
| *Anne Pitts Carter (Economics) | *Hans J. Morgenthau (Pol. Science) |
| *Owen Chamberlain (Physics) | *Marston Morse (Mathematics) |
| *Abram Chayes (Law) | *Robert S. Mulliken (Chemistry) |
| *Leon N. Cooper (Physics) | *Franklin A. Neva (Medicine) |
| *Carl F. Cori (Biochemistry) | *Marshall Nirenberg (Biochem.) |
| *Paul B. Corneley (Medicine) | *Severo Ochoa (Biochemistry) |
| *André Cournand (Medicine) | *Charles E. Osgood (Psychology) |
| *Max Delbruck (Biology) | *Linus Pauling (Chemistry) |
| *Renato Dulbecco (Microbiology) | *George Polya (Mathematics) |
| *John T. Edsall (Biology) | *Oscar Rice (Physical Chemistry) |
| *Paul R. Ehrlich (Biology) | *David Riesman, Jr. (Sociology) |
| *John F. Enders (Biochemistry) | *J. Robert Schrieffer (Physics) |
| *Adrian Fisher (Law) | *Julian Schwinger (Physics) |
| *Jerome D. Frank (Psychology) | *Alice Kimball Smith (History) |
| *John Kenneth Galbraith (Econ.) | *Cyril S. Smith (Metallurgy) |
| *Richard L. Garwin (Physics) | *Robert M. Solow (Economics) |
| *Edward L. Ginzton (Engineering) | *William H. Stein (Chemistry) |
| *Donald A. Glaser (Physics-Biol.) | *Albert Szent-Györgyi (Biochem.) |
| *H. K. Hartline (Physiology) | *Howard M. Temin (Microbiology) |
| *Walter W. Heller (Economics) | *James Tobin (Economics) |
| *Alfred D. Hershey (Biology) | *Charles H. Townes (Physics) |
| *Hudson Hoagland (Biology) | *Harold C. Urey (Chemistry) |
| *Robert W. Holley (Biochemistry) | *George Wald (Biology) |
| *Marc Kac (Mathematics) | *Myron E. Wegman (Medicine) |
| *Henry S. Kaplan (Medicine) | *Victor F. Weisskopf (Physics) |
| *Carl Kaysen (Economics) | *Jerome B. Wiesner (Engineering) |
| *H. Gobind Khorana (Biochemistry) | *Robert R. Wilson (Physics) |
| *George B. Kistiakowsky (Chem.) | *C. S. Wu (Physics) |
| *Arthur Kornberg (Biochemistry) | *Alfred Yankauer (Medicine) |
| | *Herbert F. York (Physics) |

NATIONAL COUNCIL MEMBERS (elected)

- | | |
|-----------------------------------|-----------------------------------|
| Ruth S. Adams (Science Policy) | Franklin A. Long (Chemistry) |
| David Baltimore (Microbiology) | Francis E. Low (Physics) |
| Nina Byers (Physics) | Victor Rabinowitch (World Devel.) |
| Rose E. Frisch (Human Biology) | George W. Rathjens (Pol. Science) |
| Arthur W. Galston (Biology) | Marc J. Roberts (Economics) |
| Morton H. Halperin (Pol. Science) | Leonard Rodberg (Pol. Science) |
| Garrett Hardin (Human Ecology) | Joseph L. Sax (Environment) |
| Denis Hayes (Environ. Policy) | George A. Silver (Medicine) |
| William A. Higinbotham (Physics) | Jeremy J. Stone (Mathematics) |
| John P. Holdren (Energy Policy) | Vigdor Teplitz (Physics) |
| Daniel Koshland, Jr. (Biochem.) | Frank Von Hippel (Physics) |
| Raphael Littauer (Physics) | Myron E. Wegman (Medicine) |

*Nobel Laureates

The FAS Public Interest Report is published monthly except July and August at 307 Mass. Ave., NE, Washington, D.C. 20002. Annual subscription \$20/year. Second class postage paid at Washington, D.C.

Continued from page 1

against them. NIOSH's excuse is a \$40,000,000 budget and the duty to worry about every conceivable occupational health hazard including how far apart should be the rungs of ladders.

The Environmental Protection Agency (EPA), created in 1970, has promulgated regulations or bans on five substances thought to be carcinogenic; it awaits the toxic substances bill to take charge of a struggle involving at least 17 Government agencies.

The National Cancer Institute (NCI), which spends \$750,000,000 of the National Institutes of Health's \$2,200,000,000, is only just emerging from a binge of viral research. Beginning in the late fifties, this reached a point where, in fiscal 1966, more grants were given in "viral carcinogenesis" than in all other categories of cancer research together, including: chemical, endocrine-related, radiation, and environmental carcinogenesis epidemiology.

In the mid-sixties, the inspiring hope was that cancer might be caused by viruses in a fashion analogous to that by which viruses cause other infectious diseases and, hence, that vaccination against the virus might be no less effective than it had been in preventing so many other illnesses. This hope has been succeeded by the more complicated, and even hard to define, notion that cancer is critically involved with viral material which was incorporated within the cell's genetic material generations before. Unfortunately, even were this viral approach to be vindicated in time, it is unlikely to lend itself to a cure by vaccination; we have no experience with vaccinating ourselves against something we already have but only against *foreign* viral material. If there is hope here, it is much further off than had been anticipated ten years ago; the easy viral hypotheses have been played out.

From Optimism To Environmental Protection

In the mid-sixties, the National Cancer Institute's ally, the American Cancer Society, was optimistic about curative research in general. Its movement from touting an imminent cure to working to protect the environment is a most significant indication of the tidal shift in thinking in the cancer community. In 1967, an ACS pamphlet on "New Directions" had this as its virtually concluding paragraph:

The practical and theoretical advances in chemotherapy, the promising leads in virology and immunology, the advances being made toward an understanding of the fundamental biochemical characteristics of cancer — all are indicators of the progress which is being made. Which of these — or any other — avenues will lead ultimately to the control of cancer, it is impossible to predict. In several areas there is, among the leading investigators, a sense of urgent concentration which seems to convey the unspoken message: "This could be the beginning of the end."

The total absence of any reference to the environment or preventive measures and the almost ludicrous effort to manufacture optimism have been supplanted by this more recent American Cancer Society pronouncement:

"Known causes of cancer in the environment, such as cigarettes and certain industrial chemicals should be dealt with more effectively in the regulatory and political arena, and top priority should be given to research aimed at finding other causes of environmental cancer."

How hard is the National Cancer Institute working to

CLASSIC CASE IN CANCER EPIDEMIOLOGY

Particularly relevant to the question would be data on the health of cyclamate workers. By anecdotal report, cyclamate airborne levels were high in parts of the production cycle. Study of individuals who worked under these conditions should provide direct evidence about the risks from this useful compound. The situation is the classic one in cancer epidemiology. Here we have a substantial theoretical risk of cancer for almost the entire U.S. population, compounds of substantial utility are involved, and although hundreds of man hours are spent on debating the philosophy of risk, no one will take the responsibility to seek out the facts about chemical-human interaction that would help us judge whether or not there is susceptibility.

—Persons at High Risk of Cancer; edited by Joseph F. Fraumeni, Jr. pg. 207 (John W. Berg)

carry out this new charge by the involved public? Its Division of Cancer Cause and Prevention is still divided into three sections: Viral Oncology, Carcinogenesis, and Field Studies and Statistics. Organizationally speaking, this gives viruses as much status as all other cancer-inducing themes put together. Happily, viral research no longer spends almost *twice as much* as the other two divisions combined — as it did in the late sixties. Now it only spends *as much and more* than the other two combined! (1975 figures were \$58 million for the viral cancer program; \$36 million for carcinogenesis and \$12 million for field studies and statistics). These are bizarre disproportions.

NCI authorities are conceding that the vast majority of cancers are associated with chemical, physical, social, dietary, and cultural factors. And it is these factors which, in any case, one could immediately attempt to influence with a view to prevention. Nevertheless, research on viral causes get the bulk of the funding.

Funding of Environmental Carcinogenesis: 10% -16%

In May, 1975, a member of the National Cancer Advisory Board (Dr. Philippe Shubik) estimated that only 10% of the entire NCI budget was allocated toward environmental carcinogenesis. (He was advised by the Director of the Division of Cause and Prevention that the official figure now stood at 16% primarily because various basic studies throughout the Institute were now so allocated). It is at least symptomatic of these disproportionate tendencies to viral research that the Director of the National Cancer Institute spent his entire professional career in the NIH viral cancer research program.

The related strains within the Cancer Institute were evident as this May Report was going to press. A late interview with the chief of Carcinogenesis within the Division of Cancer Cause and Prevention revealed his impending resignation. Dr. Umberto Saffioti's section had received very large increases for contracts but no corresponding increase in personnel to administer the programs. From 1972 to 1976, personnel in his Carcinogenesis Program had been essentially stable but the budget for contracts had doubled and the number of contracts gone up by about a third.

Dr. Saffioti felt that Carcinogenesis (which in NCI

—Continued on page 4

EXPLOITING THE HUMAN EXPERIMENT THE NATIONAL DEATH INDEX

As yet there is no national index showing what state holds the record for a specific individual who may have died in a given year. The effort of following up by inquiry in each of 50 separate states, on the chance that each may be the right one, draws unnecessarily on scarce resources, both among epidemiologists and among state offices handling vital records. As one of a variety of improved tools for epidemiology, a national death index is badly needed.

—Chemical & Health: Report of President's Science Advisory Committee, September, 1973

Continued from page 3

terminology refers to the environmental and chemical carcinogenesis program) now was a program of "major national significance" and deserved divisional status within the Cancer Institute and about a one-third increase in professional job slots. He believed his program needed scientific managers who could interrelate the many different disciplines involved in establishing in detail the emerging view that cancer is a social disease — largely preventable.

Dr. Saffioti called the National Cancer Institute "remarkably passive" in its approach to occupational health. This subject was falling between two stools with NIOSH having insufficient expertise and the Cancer Institute showing little interest.

The smallest division of Cause and Prevention's triumvirate, Field Studies and Statistics, was also feeling badly neglected. It is charged, among other things, with salvaging what can be learned from prevailing patterns of cancer incidence, including especially those patterns induced by industry. This section was receiving only about 10% of the Division's expenditures.

As one result, the National Cancer Institute for the most part simply examines other people's data; its handful of epidemiologists is not funded in such a way as to permit significant studies de novo. It took an historic study involving 1,000,000 persons to confirm the carcinogenic effects of cigarette smoking. NCI has never attempted anything remotely similar to this American Cancer Society study.

ACS Urges More Epidemiology

The American Cancer Society is arguing this year that: "Substances suspected of being carcinogenic to which large number of workers are exposed should be evaluated epidemiologically as well as tested in the laboratory."

But the National Cancer Institute is not prepared to fulfill the charge. It is failing to exploit, and hence wasting, the invaluable data that have arisen from experiments on millions of human beings, experiments performed as a collateral result of industrial exposures. It is bad enough that these cancer experiments have been performed on so many workers. Not to fully study the results borders on the criminal.

America re-examined its role in the Vietnamese War when sons of the middle class began to be drafted. As America learns that it lives, in effect, in a vast chemical factory, an analogous reorientation in approach to the war against cancer is bound to take place. There will be greater empathy with those at high risk in the front

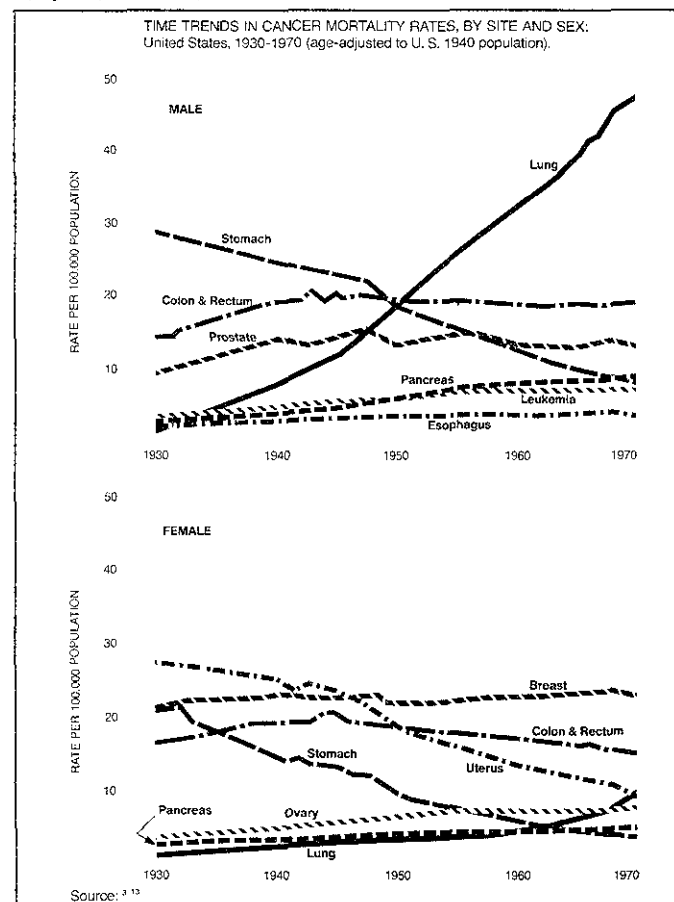
lines; more questioning of the judgment of the experts in charge of the war; less faith in "win-the-war" sloganeering; a truer sense of urgency directed at resolving the immediate problem, and a rise in the attention paid to common sense. As always, last to reflect the changes in attitude will be the funding patterns of the great bureaucracies.

THE SCOPE OF THE PROBLEM

The graphs below show that lung cancer and the smoking which induces virtually all of it make the difference between a seriously rising problem and one that is stable or even slightly improving. If lung cancer is omitted, cancer in men has declined about 10% in the last forty years. And this ignores the extent to which the cause of lung cancer, smoking, has pulled up the curves for such induced cancers as that of the esophagus, or the pancreas, and of leukemia to which smokers are, on the whole, about twice as vulnerable as non-smokers. For women, we see a similar picture — sharp declines in stomach cancer and cancer of the uterus offset somewhat by increases in pancreatic and ovarian cancer and, of course, by a rising curve for lung cancer.

If cancer is considered to have an average incubation period of 20-30 years and to be environmentally induced, then environmental influences and habits of the period from 1900 to World War II were not encouraging cancer — except for smoking. The question at issue, however, is what the impact of the post-war period's tremendous outpouring of new chemicals will be. And this will be discovered in the 1970s, 80s, and 90s.

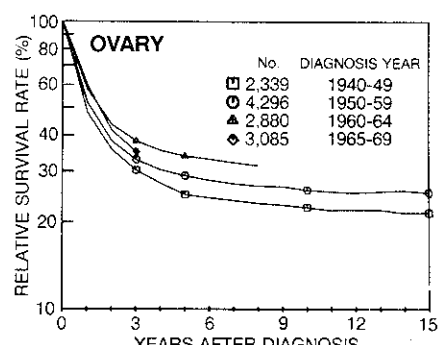
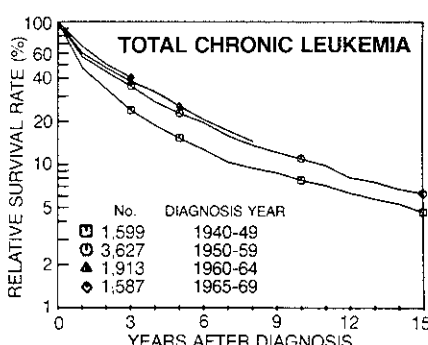
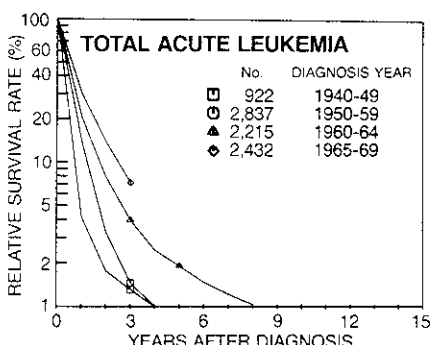
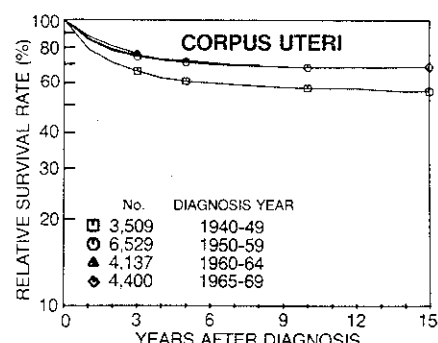
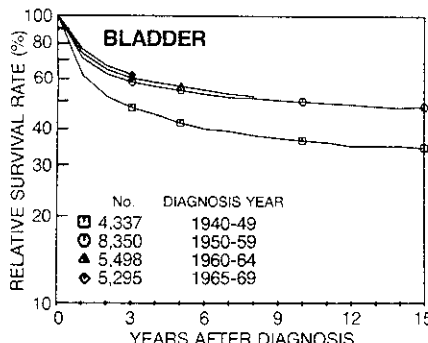
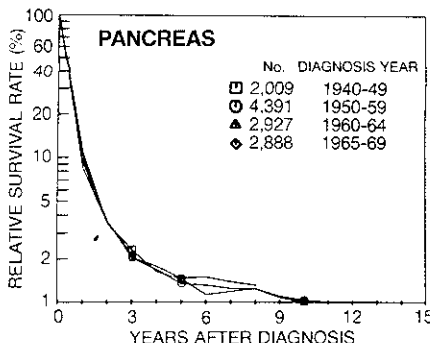
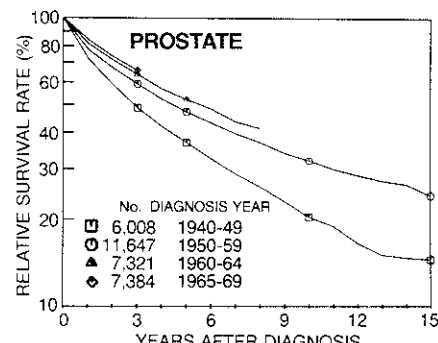
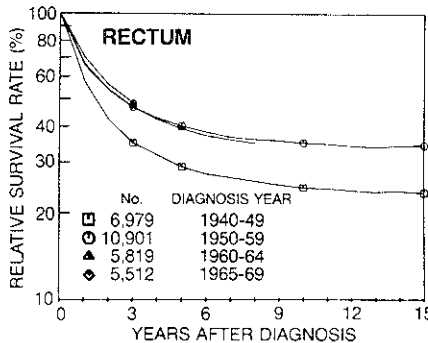
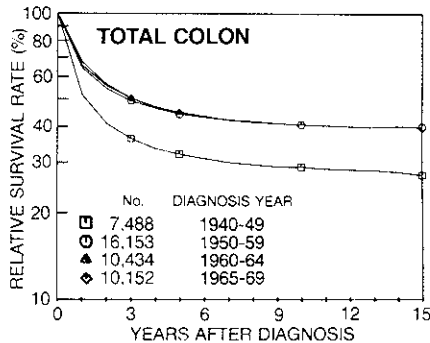
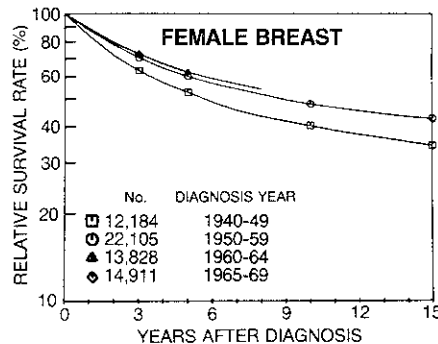
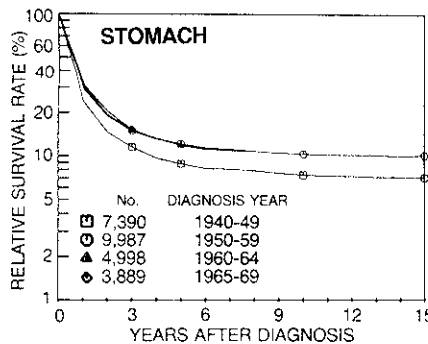
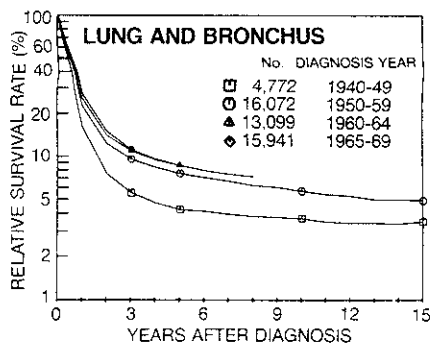
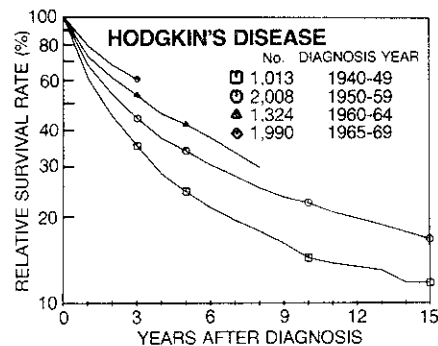
The graphs on the next page make one thing clear. If the cancer rate begins to climb, we cannot now hope to cure the victims.



LITTLE RECENT PROGRESS IN CURES

The lower curve on each of the adjoining graphs reflects the survival for patients diagnosed in the forties. If this curve is ignored, one discovers, in virtually all of these cancers, that there has been essentially no difference in the ability to cure or control cancer diagnosed in the sixties as opposed to those of the fifties. Evidently we learned in the fifties how to keep patients alive longer but — since then — very little indeed. In fact, what minor differences exist may only reflect differences in diagnostic ability: finding cancers earlier, diagnosing some illnesses as cancer which were not (and curing them), etc.

RELATIVE SURVIVAL FOR CANCER OF SELECTED SITES, BY YEAR OF DIAGNOSIS.



THE AMES TEST

The Ames test seeks to identify potential cancer-inducing chemicals by asking whether the substances cause mutations in a single-cell bacterium *Salmonella Typhimurium*. It is the startling result of his investigations that chemicals which cause bacterial mutations seem to have a very high correlation with those known to cause human cancer.

In October, 1975, he reported that, of 174 substances believed on other grounds to be cancer-inducing in man, 156 were revealed by his test to induce mutations in *Salmonella*. Thus 90% of the carcinogens were identified. Of 46 common biochemicals believed not to be carcinogenic, none had been found to cause mutations in *Salmonella*. Thus the test seemed to be screening out the carcinogens.

The test works by placing the chemical at issue on a petri dish amidst one billion *Salmonella* bacteria. The bacteria have previously been treated so that they cannot grow, having lost the ability to produce a critical protein "histidine". If the chemical is a mutagen, some of the bacteria will be mutated back so that they can produce histidine; these will be spotted by the colonies to which they give rise. The others will die. The researcher then simply counts the number of "revertent" colonies as a measure of the mutagenicity of the chemical.

This measure is an important and very desirable feature of the Ames test. It means that the mutagenicity of the chemical can be measured not only qualitatively but also quantitatively over a very broad scale; indeed the virulence of the chemical mutagen can be assigned a potency that varies over a scale of one million. It would be quite impossible to quantify mutagenicity in mammals over such a range; with a few hundred rats, the upper end of such a scale would overkill them all and the lower end show no appreciable effect.

Indeed, this fact is connected with a fundamental inadequacy of animal tests as public health radars for a population as large as our own. When one is concerned with a chemical like saccharin that may reach the entire population, one is seeking to protect 200,000,000 people. If the chemical might induce cancers in only 20,000 persons, this would obviously be quite serious, affecting as it would about half as many persons as died in the Vietnamese war. Yet the rats, mice, or hamsters would have to reveal a result that affected only *one in ten thousand* to alert us to this substantial danger. Thus many tens of thousands of small mammals would be necessary to conduct the experiment and even then the results would not be above statistical question.

Each year, there may be 6,000 new substances with significant human exposure, and the number of suspected carcinogens already has reached 1,500 according to NIOSH. Animal tests far smaller than the one described above cost \$150,000 per chemical tested. Obviously hundreds at most, rather than thousands, of such chemicals can be screened at such cost. By contrast the Ames test requires a few days and costs about \$500 or one three-hundredth as much as a small mammal test. Put another way, for the cost of doing ten full-scale animal tests, 3,000 substances could be screened.

This is not to say that animal tests would not be necessary to verify the results of the Ames test even were it proven to be everything it seems. There is enough

variability in the carcinogenic action of chemicals to leave everyone uneasy about any test, much less any test not done in creatures close to man. Some substances cause cancers, for example, in rats but not in hamsters, and vice versa.

This variation in the vulnerability of different mammals to cancer may be related to their metabolism. Often it is not the chemical itself that induces the cancer but some "metabolite" of it produced by the body's metabolism. And it is possible that the concentration of the chemical, or its metabolite, in various parts of the body depends also on the animal's physiology and hence may vary critically. The Ames test uses liver extract on the petri dish to metabolize the chemical so as to produce, for the bacteria, the kinds of metabolites that might be produced in the mammal. This is obviously only an approximation of a very crude kind to metabolic processes.

It is important to observe that one need not believe that the Ames test unerringly identifies carcinogens to become alarmed if a chemical produces a positive result. The test directly identifies mutagenicity in bacteria. If even this identification can be extrapolated to man, it is sufficient for corrective action. Mutations are generally harmful even if they do not cause cancer. Indeed, some believe that mutations may be at the bottom of heart disease and may be a major contributor to aging. Certainly mutations are the source of that 5% of Americans who suffer genetic defects.

Thus the first and fundamental basis for excitement about the Ames test lies in its capacity as a suitably inexpensive early warning screen not only for carcinogens but for mutagens. Substances which raised a warning flag might later be tested in animal tests or in tissue culture tests (These are tests in which test-tube experiments with human cells look for toxic effects).

However, Dr. Ames notes that there is a "rough correlation between potency, in animals and bacteria" which needs more work. If indeed, it is possible to link the potency of the mutagenic effect of a carcinogen in *Salmonella* with the potency of the same substance in causing cancer in animals, a very startling and useful further result will have been obtained. The screening will be far more precise and the likelihood of successful extrapolation to man enormously strengthened. The billion bacteria on a petri dish not only will have become a useful surrogate for the 200,000,000 humans in America, but,

SOME RESOURCE MATERIAL

Persons at High Risk of Cancer: An Approach to Cancer Etiology and Control; edited by Joseph F. Fraumeni, Jr. Academic Press, 1975. An excellent, readable, and unique survey of all that is known about the links between specific agents and cancer, 525 pages.

Cancer Rates and Risks; 100 page paperback put out by HEW containing graphs and survey of the general problem; quite useful. \$1.80 from GPO (Stock number 1742-00086)

Cancer: The Misguided Cell; David M. Prescott, Bobbs-Merrill Company, 1973; a masterly and readable discussion of the biological basis for cancer. Paperback.

The Cancer Problem; John Cairns, *Scientific American*, November, 1975.

Cancer and the Environment: A Scientific Perspective; Samuel S. Epstein, M.D., #25 Facts and Analysis, Occupational Health and Safety, AFL-CIO (IUD).

unlike the 100 or 1,000 or even 10,000 rats, will have provided a statistically relevant measure of the carcinogenicity of the chemical.

Still more startling, it might then be possible to expand upon existing methods to detect carcinogens in urine or other body tissue. One could identify the metabolite carcinogens in the human being by testing what came out of the person against the bacteria. In the long run, one could apply one's knowledge of what carcinogens were surfacing in the population to monitor the population, to identify high risks, and so on. Dr. Irving Selikoff reports that he is now saving urine samples with this in mind but not now testing them on bacteria because it is "too dangerous". By this he meant that one would not know what to tell the workers who scored dangerously high, inasmuch as the test was not yet calibrated.

Whether the Ames test, or improvements of it, could reduce the level of cancer depends upon whether one believes existing and avoidable chemical substances are *causing a substantial part of the cancers*. Even assuming that chemical environmental causes — rather than, for example, virus or radiation — are at the bottom of most cancers, the environmental sources might not be easy to change. We have learned with smoking how the identification of a carcinogen can be ignored. If, for example, diet were an important factor — as it likely is — and if the carcinogenic substances in the diet could be identified, citizens might still fail to change their diet.

On the other hand, at the very least we would be able, with the Ames test, to avoid permitting *new* carcinogenic substances to enter the environment. For example, Dr. Ames reported in March, 1975 that 89% of commercial hair dyes in which hydrogen peroxide is used are mutagenic; indeed half of the 18 compounds used in these hair dyes gave positive indications on his test, and the dyes in question account for a \$250,000,000 market businly dyeing the hair of 20,000,000 persons, or 10% of the population.

Similarly, the Ames test has pinpointed as highly mutagenic the flame retardant material required to be placed in all pajamas for children. The failure of the Products Safety Board to screen the flame retardant for carcinogenicity before requiring that it be placed next to *the skin of large parts of the population* is the kind of incipient disaster that this test could avoid.

AFTER YOU FIND THE CARCINOGENS, WHAT?

Imagine that there were no scientific uncertainties. Imagine that one knew precisely what different exposures to a particular substance would do. There would still remain the question of what to ban or restrict. As detection schemes pinpoint environmental carcinogens with increasing precision, this problem is certain to plague Government administrators and to grow worse.

For example, it used to be possible to detect carcinogens in parts per million — the equivalent of detecting a single person in a city of persons the size of Washington. Now detection is often one part in a billion and sometimes a part in a trillion. What will this mean to rules requiring that there be no presence of carcinogens at all? (The Delaney Clause, asserts, for example, that no substance which causes cancer when fed to animals should be added to foods.)

The Water Pollution Act requires EPA to protect

against *any* adverse effect and, indeed, to "provide for an ample margin of safety" against any toxic pollutant — defined as those that cause any abnormalities in any organism.

The Clean Air Act also supposes that there is no threshold in requiring the Administrator to protect against any adverse effect on human health, again with "an adequate margin of safety."

The pesticides legislation asks EPA to ensure that a pesticide "will perform its intended function without unreasonable adverse effects on the environment" when used in accordance with commonly recognized practice. Here at least there is a charge to balance risks and benefits.

The Safe Drinking Water Act asks EPA with regard to all toxic contaminants to specify the level at which "no known or anticipated adverse effects on the health of persons occur and which allows an adequate margin of safety." If "anticipated" may be interpreted as permitting one the plausible assumption that no threshold exists, then zero would be the level anticipated for no adverse effects, and allowing for an adequate margin of safety would be simply redundant. Of course, zero contaminant level could not be maintained in a world in which parts per billion of contaminants can be detected. Happily for its workability, the act goes on to urge EPA to ". . . protect health to the extent feasible, using . . . means which the Administrator determines are generally available."

Water, air, and essential foods all possess certain characteristics that make them worthy of the highest possible feasible standards: they are essential, the risk associated with consuming them is undertaken involuntarily, there are no alternatives, and the effects of getting cancer from them are essentially irreversible.

Should the same standard apply to luxury foods, if such are found to be carcinogenic? Or should persons be allowed to consume them, with suitable warnings, much as cigarettes are consumed? After we come to concede that we know it, should workers be permitted to work in situations in which their risk of cancer is much higher than the average? Or could the standards for their workplaces leave them no more vulnerable than suburban housewives? What would this cost per life saved, and what would society pay?

There is needed some simple measure of cost and benefit that would make widely different risk situations comparable so as to attempt to maintain, in different areas, roughly similar standards for spending government and industrial funds to save lives. Without such a standard, as economists will sense immediately, cancer-avoiding expenditures cannot be spent efficiently. And, in addition, the public will have the greatest difficulty distinguishing minimal risks from large ones.

One possible approach is to evaluate risks in terms of life-shortening: so many lives likely to be shortened by so many years. The costs of avoiding a year's loss of life can then be compared in one area with another. This has the benefit of being able to encompass not only the risks of getting cancer but the concomitant risks of many other occupationally or environmentally related illnesses. And it provides, at the same time, perhaps the best possible means of driving home, to the individuals at risk, the nature of the risk they are accepting.

THE TOXIC SUBSTANCES ACT

On March 26, the Senate passed S.3149, "The Toxic Substances Control Act." Alternative versions of this legislation are now being considered in the House of Representatives. This may be the year of success; several earlier attempts to pass a bill of this kind have failed.

The bill assigns to those who manufacture and process chemicals the responsibility for developing adequate data concerning their effect of human health. It gives the Environmental Protection Agency (EPA) Administrator the right to require testing on substances that "may prevent an unreasonable risk of injury to health or environment" after considering the burdens of conducting such tests. The data resulting from the test would have to be made known in the Federal Register within 15 days of receipt by EPA, along with information on the intended uses of the chemical. Within 180 days, EPA must either limit the exposure of human beings to the substance or publish in the Federal Register its findings that no unreasonable risk is presented and why.

Any citizen could petition the Administrator to issue a rule or order, and within 90 days, the Administrator must either grant the petition or explain why not in the Federal Register, after which the petitioner could go to court, and might even be provided costs of the suit by the court.

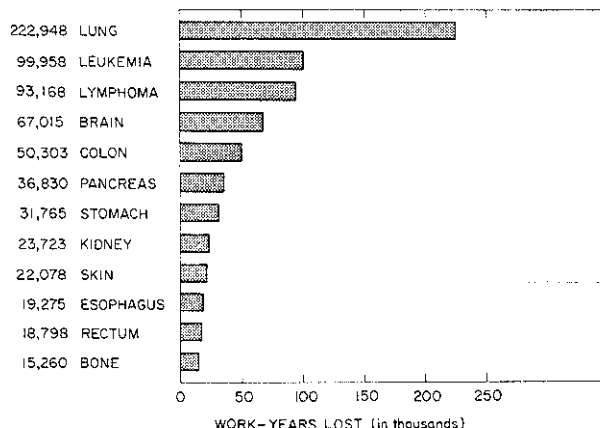
Whistle-blowing employees are protected against being fired for participation in related EPA actions. More generally, employers are discouraged by this act from closing down plants as a result of, or in retaliation for, EPA rulings. This is because any employee who is discharged, or threatened with discharge, because of an EPA rule can demand an EPA investigation to determine whether the rule did indeed require the discharges.

COSTS OF CANCER

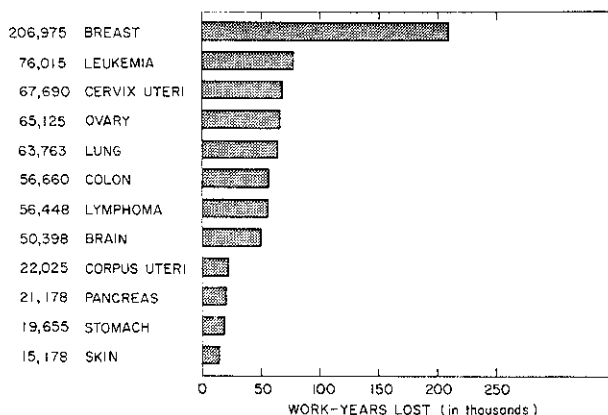
In terms of direct costs, the Social Security Administration reports that cancer was 5% of the nation's \$75 billion health bill in 1972. Measured in terms of total economic costs, it was 9% of a \$188 billion health bill. Measured in terms of deaths, it was still more serious — 17% of all deaths. In sum, because cancer strikes elderly people, it has a much higher impact in terms of deaths than in terms of economic or health costs. Balanced

against this, of course, is the important consideration that death from cancer is often particularly agonizing.

If all cancer were eliminated, the average life expectancy would rise by about two years. As the following figure shows, lung cancer is associated with three times the loss of years of life as the next competitor and about one-third of all years of life lost by males. Breast cancer similarly dominates the loss of years of female life.



TEXT-FIGURE 5.—Work-years lost from the leading types of cancer, 1968: males.



TEXT-FIGURE 6.—Work-years lost from the leading types of cancer, 1968: females.

FAS PUBLIC INTEREST REPORT (202) 546-3300
 307 Mass. Ave., N.E., Washington, D.C. 20002
 May 1976, Vol. 29, No. 5

I wish to renew membership for calendar year 1976.

I wish to join FAS and receive the newsletter as a full member.
 Enclosed is my check for 1976 calendar year dues. (I am not a natural or social scientist, lawyer, doctor or engineer, but wish to become a non-voting associate member.)

\$20 Member \$50 Supporting \$100 Patron \$500 Life \$10 Under \$10,000

Subscription only: I do not wish to become a member but would like a subscription to:
 FAS Public Interest Report — \$20 for calendar year

Enclosed is my tax deductible contribution of _____ to the FAS Fund.

NAME AND TITLE _____
 Please Print

ADDRESS _____

CITY AND STATE _____
 Zip _____

PRIMARY PROFESSIONAL DISCIPLINE: _____

Second Class Postage
Paid at
Washington, D. C.

Return Postage
Guaranteed