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CANCER AND ENVIRONMENT

Scientific and technological progress have exposed man to new physical and chemical agents. Some are believed associated with the rise of cancer as a cause of death

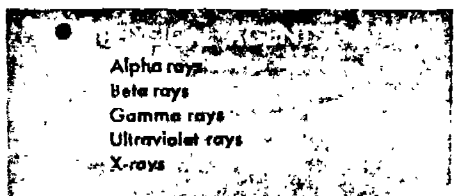
by Groff Conklin

THE industrial era in its full expansion is barely two generations old, yet during that short period literally thousands of entirely new chemical and ph[...] constituents have been added to th[...]n environment. Few of these con[...]its have been exhaustively analyzed for their long-range toxic effects on man. They are now being studied, however, as possible contributors to the rise of cancer.

The growth in the relative importance of cancer as a cause of death is one of the outstanding medical facts of the past 30 years. The disease has moved from eighth to second place in the U. S. since 1900, and today only heart ailments surpass it. The reasons customarily given for this rise—improved diagnosis and the aging of the population—do not entirely explain it. They provide no satisfactory answer to the fact that approximately seven and a half per cent of the known cancer deaths in 1944 occurred in age groups under 40. There is evidence, moreover, that the disease is not an inevitable consequence of bodily degeneration due to age, although the changes of senescence under certain conditions may be contributing factors. It seems certain that there is a net increase in true cancer deaths, if only because fewer people die from other diseases than in the past.

An explanation of this increase and of the causes of the disease is therefore being sought in our environment, so much m[...]mplex than it was in 1900. The [...]tion is focused on carcinogenic agents, as the substances that produce cancer are called, and on the general question of the extent to which the increase in cancer may be caused by agents in the environment that have hitherto been considered comparatively harmless.

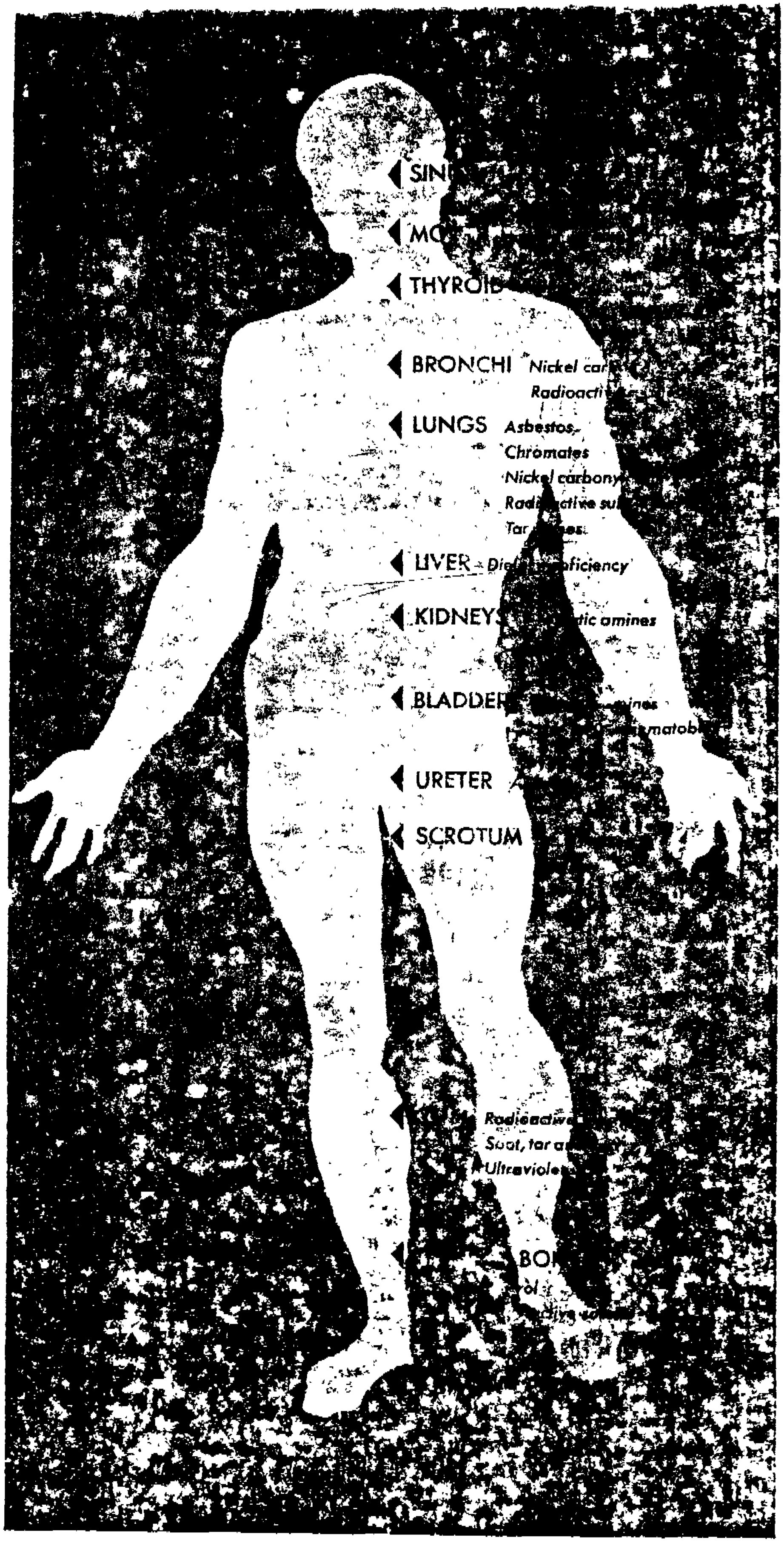
It has been established that certain agents to which people are exposed in industrial occupations cause cancer if the exposure to them is sufficiently intense and prolonged. As an example, over 75 per cent of the miners in the Schneeberg cobalt-uranium mines of Germany die of lung cancer; more than 50 per cent of those in the Joachimsthal uranium mines across the border in Czechoslovakia die of the same cause. In the 18th century it was learned that among chimney sweeps exposed to intense concentrations of soot, deaths from cancer were between three and four times as high as those in the general population. It is known also that certain common substances in concentrated doses can produce cancer; for example, mouth cancers are uncommonly frequent in a tribe in India which smokes cigars with the lighted end in the mouth. This causes them to suffer frequent burns and to receive a concentrated dosage of tobacco tars.



CARCINOGENS known to be present in human environment are classified. Less certain agents are in italics.

Although these are special cases of intense exposure, they naturally suggest speculation as to whether the average human being's relatively mild but long-continued exposure to new substances in a contaminated atmosphere, in processed foods, in cosmetics and in other elements of our environment may be a contributory cause of cancer. We have as yet no conclusive evidence for or against this possibility. We have no accurate estimate of how many of the artificial substances common to our industrial civilization may be carcinogenic under special circumstances, nor how many seemingly harmless substances, interacting with others that appear to be equally innocuous, may produce carcinogenic results.

There are, of course, many theories about cancer's causes: chronic internal irritations in the body, changes in cell



ORIGINAL SITES of malignant growths due to carcinogens in the environment are scattered among almost all the organs of the body. Some agents, such as the aromatic amine dye intermediates, regularly affect the same organs even though they may use any one of many routes for attack.

metabolism, tissue degeneration, viruses and so on. Most of these theories, however, describe mechanisms rather than first causes. Indeed, with two or three exceptions all of them seem to require the presence of a triggering agent.

Possibly the most fruitful current theory is the one that attributes cancer to mutations in body cells. Cancer-causing mutations, it has been demonstrated by experiments, may be produced by ultraviolet radiation, X-rays, radioactive substances and a number of chemicals. While more than 99 per cent of all cancers are still of unknown origin, nearly all of those for which a proved cause has been found arise as the result of external agents. These seem to mutate the cells into a state which is, or can become, cancerous.

The methods by which these external agents act upon the body vary considerably, depending on the substance involved. Some carcinogens may cause cancer directly. Examples of these are tar, the mineral oils and certain dye intermediates known as aromatic amines. Tars generally affect the skin. Mineral oils may cause cancer of the lungs through inhalation. The aromatic amines, strangely, concentrate on the bladder, no matter what their route of attack. Whether they enter the body through the respiratory system, the mouth or the skin, they gravitate to the genito-urinary system and there build up a concentration that eventually causes cancer.

Other agents seem to cause cancer by altering organs so that the organ itself produces a carcinogen, resulting in a cancer. The mechanism of this transformation is little understood. It is known that some radiations and certain metallic compounds including the chromates, the arsenicals, nickel carbonyl and possibly asbestos, cause cancer in this relatively roundabout way.

RADIOACTIVE materials are less specialized in their effects: they can produce a wide variety of cancers. They may cause skin cancer by direct attack on the skin, and lung cancer in people who inhale radioactive dust. When exposure is intensive and prolonged, as in the case of the women who worked in the radium watch and clock dial industry some 25 years ago, they produce bone cancer. And a slight but very prolonged exposure to penetrating radiation can result in leukemia, a cancer of the blood cells. The latter kind of cancer is often found among radiologists whose whole professional lives have been spent in theoretically safe and well-protected dealings with X-rays or radioactive materials.

Most subtle of all carcinogens are those believed to cause general metabolic disturbances that produce cancers in a roundabout way. Thus the liver may produce carcinogens that can cause it or some other tissue to turn malignant. Among the agents thought to have this effect are the

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azo dyes and certain chlorinated aliphatic hydrocarbons. But the mechanism involved is so obscure that the carcinogenicity of these substances has not been completely proved.

One aspect of such indirect causation, however, is susceptible of proof. Among some Negro tribes working in the gold mines of Africa, an excessive incidence of cancer of the bladder has been traced to deficiencies in the workers' diet. It was found that most of the Negroes had lived for years on a vitamin-deficient diet of pap and sour milk. Only recently South African research workers have succeeded in producing cancer of the liver in rats fed just this diet.

In view of the relative novelty of the concept of environmental cancer, and of the small amount of well-organized research in this field, it is not surprising that most of the known carcinogenic agents have been found in industry. Here workers suffer exposures many times more concentrated than the average citizen encounters in a non-industrial environment. Fully 90 per cent of the known carcinogenic agents are industrial, and a similar proportion of cancers of known cause arises from carcinogens of industrial importance. These known agents are listed in the chart on page 11.

The difficulties in the large-scale study of carcinogenic agents are formidable. The modern environment is so ramified that efforts to evaluate it in terms of long-range carcinogenicity may appear nearly hopeless. Nevertheless, the techniques already developed in the study of occupational carcinogens may be of some value in analyzing the environment as a whole, even though more refined methods may have to be developed if such a program is to be successful.

The two principal methods now used to uncover the more obvious occupational cancer hazards are animal experimentation and statistical analysis. Cancers have been produced in experimental animals by most of the known physical and chemical carcinogens. Hundreds of other substances have been and are being tested. Some that have been shown to be carcinogenic in animals have not as yet been proved dangerous to man, or else they do not form a part of his normal environment. Among these substances are urethan, ergot, selenium, and diethylene glycol.

One aspect of the work on animals that is important in considering human cancer is the phenomenon known as "species specificity." Many carcinogens that cause cancer in some animal species have thus far proved harmless to others. For example, certain tars, when correctly applied, produce skin cancer in mice, rats, rabbits and dogs, but not in monkeys. Rats and mice get skin cancer from ultraviolet rays, but rabbits do not. The probability is that specialized metabolism is at the bottom of this species specificity for cancer. If such metabolic differences were completely understood, human beings might be endowed with resistance to certain types of cancer by modifying the individual's metabolic processes. Such ideas are still beyond the realm of practical application in man. In experimental animals, however, cancer susceptibility or resistance to certain external carcinogens, such as several of the azo dyes, may be created at will by the omission or addition of certain vitamins in the diet.

Without animal experimentation, scientific proof of the carcinogenicity of various substances and radiations would be nearly impossible. On the other hand, laboratory experiments alone cannot prove definitely that such agents are dangerous to man. Other methods must be used, and the principal instruments so far available have been statistical studies and medical records.

In large, unselected population groups, variations in the incidence of one kind of cancer are usually not sufficiently marked to be significant. That is why environmental carcinogens are usually difficult to detect. Up to half a century ago, indeed, evidence of specific extrinsic causations of cancer was discovered largely by clinical observation. Physicians practicing in urban or manufacturing areas began to notice a remarkably high incidence of certain types of cancer among workers in individual trades. Such was the case in the diagnosis of cancer of the scrotum in chimney sweeps. Discoveries by direct observation continue to be made, as in the case of radium and X-ray cancers that occurred with alarming frequency among people working with these agents in the not so distant past.

But observation has its limitations. Unless very careful medical records are kept, or unless workers remain in a carcinogenic job for many years, the fact that the job is carcinogenic may escape notice. Characteristic of environmental cancers is the long period between the beginning of exposure to the carcinogen and the actual appearance of a tumor. A worker who leaves a dangerous job before the cancer appears may later develop a malignant tumor without realizing its origin.

The process of tracing cancers to their source through medical records and health statistics has become a work of skilled deduction. When a given community is found, on careful examination of its illness and mortality statistics, to have an unusual number of cases of cancer in certain sites, the biometrician at once suspects the presence of an active environmental carcinogen. The chances today are very great that it will be traced to one or more factories in the area, since so few non-industrial carcinogens have been found. Conversely, if it is known that certain plants are producing or using known carcinogens, the statistician searches for evidence of an abnormal incidence of cancer among men who are employed in these plants.

Obviously such investigations present difficult problems and demand a high order of judgment. It has often been said that statistics can be used to prove both sides of a question. Environmental carcinogenesis is no exception.

An example in American experience is a study which was made some time ago of the incidence of lung cancer among 40,000 workers in an industry suspected of producing a carcinogenic agent. It was known from studies in other countries that lung cancers were exceptionally frequent in this industry, and there was no evidence that the American manufacturing methods differed in any major respect from those abroad. Yet this study reported no lung cancers at all! In any group of 40,000 adult males several cases of lung cancer are bound to occur, merely on the basis of the incidence of the malignancy in the population as a whole. The results of the study surely suggest a lack of thoroughness in the collection and evaluation of data.

A clear example of the intelligent use of statistics as a tool in uncovering environmental carcinogens is the way in which cancers of the bladder were identified as an occupational hazard in plants using the aromatic amine dye intermediates mentioned earlier. The following composite description, based on a number of European and American investigations of this problem, illustrates the method:

The people in a certain industrial region have a frequency of bladder cancer that is a slight fraction higher than normal. The variation is well within the range of random probability, but the fact that several cases of this not too common malignancy have been found in a single community leads to a further study of the region. It is found that the incidence of bladder cancer jumps from .02 per cent in the province as a whole to .1 per cent in the particular community under study, an increase of 400 per cent. On further investigation it is learned that among the workers in a particular dye plant in the town, 5 per cent are suffering from or have died from bladder cancer—nearly a 5,000 per cent increase. Following this clue, every operation in the plant is studied, and one particular job is found in which over 90 per cent of the workers have bladder cancer or have died from it. Obviously the focal point of the disease has been established.

It is from just such relatively slight statistical anomalies that much of the original evidence of carcinogenesis in industry arises. Of course, as more carcinogens become known and are added to the list, the statistical techniques change. With the cooperation of the industries involved, medical and public health experts go directly into the plants and study the operations and the workers. Often, however, public medical and death records offer the

...reliable source of information. Many industries actually do not know of the existence of carcinogenic hazards in their factories. The study is so new that only plants in which the incidence of specific cancers is notoriously high are aware of the problem. A few industries do know of the existence of carcinogens in their [illegible]s. and probably some of them have [illegible]oped their own methods of coping with them.

The reluctance of industrial managements to publicize the existence of a carcinogenic hazard is understandable, for it could easily become difficult for plants so labeled to recruit workers, or even to sell their commodities. To make factories employing carcinogenic materials safe to work in, furthermore, sometimes requires extensive and costly alterations. If one firm makes such alterations and others do not, the competitive position of its product is endangered.

Generally speaking, however, employers are no more responsible for the lack of information about industrial cancer than are the many thousands of physicians who have cancer patients in industrial areas or who actually are associated with factories. It is an unquestionable fact that an appreciable number of occupational cancers slip through the hands of doctors unidentified. This is due in a great degree to a general ignorance of the occupational aspects of cancer. Physicians have never been adequately informed of the basic symptomatic and sociological factors involved in identifying occupational carcinogens.

THE medical profession should be better educated about the need for exhaustive case histories which carry the individual's job record in detail back as far as 25 years, about the urgency of checking medical suspicions of industrial cancer hazards against careful epidemiological studies of all the workers in a plant, and about the paramount importance of impressing plant management with the seriousness of the problem.

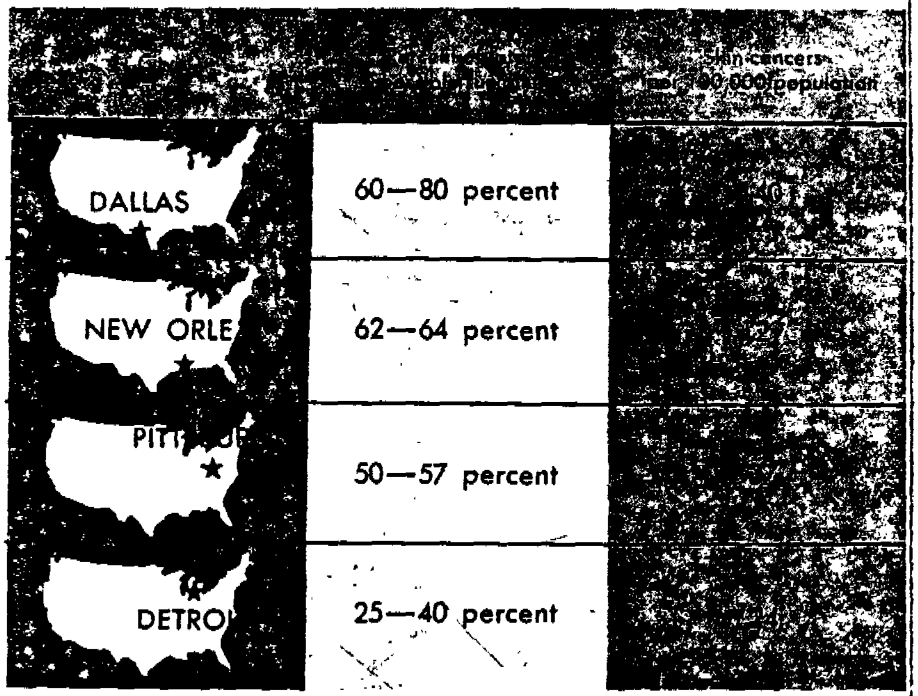
The standard protective and hygienic measures currently used in industry to combat industrial poisons and other health hazards are not always adequate for the control of occupational cancer. The following case history is a compelling illustration: Some 30 years ago workers in one of the newer metal industries began to develop lung cancers. At that time the cancers were found to remain latent from 10 to 15 years. The incidence was unusually high in certain operations where the carcinogenic substance was present in particularly high concentration as an airborne dust. An effort was made to safeguard these operations. Up-to-date equipment for removing dust and fumes was installed, and a standard industrial hygiene program was inaugurated, including protective clothing. But the outcome was exactly the opposite of what had been expected. The incidence of lung cancer did not diminish; in fact soon afterward cancers began to appear among workers who had been exposed for less than six years, a much shorter period than had been previously observed. What had happened was that at the time when the protective measures were adopted the factory had also begun to use a more finely ground material to improve production. The finer dust, though present in a much lower concentration than the original material, penetrated farther within the bronchi of the lungs. Thus despite the installation of the latest in protective devices and procedures, the cancer hazard was actually increased.

IT is obvious, therefore, that the control of occupational carcinogenesis—and even to a great extent of cancers stemming from more indefinite environmental agents, if and when they are discovered—is a public health problem of considerable magnitude. This is made even more apparent by the scope of a control program that has been proposed by Dr. Wilhelm C. Hueper, head of the new Environmental Cancer Section of the National Cancer Institute. Dr. Hueper, one of the world's leading experts on occupational cancer, has studied the problem in the U. S. and elsewhere for many years. Several of the elements of his program have already been put into effect in European countries. The program proposes that carcinogenic agents be eliminated from industrial, military and civilian use as far as is possible and practical; that manufacturing processes which must use such materials be enclosed; that the community be protected by the prevention of the discharge of carcinogenic wastes; that factories be licensed and inspected; that workers be provided with protective clothing, equipment and medical supervision, including frequent and thorough physical examinations.

The Environmental Cancer Section of the Institute, which is a part of the U. S. Public Health Service, is preparing an immediate, comprehensive campaign of education and information, the purpose of which is to bring physicians to a realization of the existence of the problem. Plans are also under way to make exhaustive surveys of major industrial areas in the nation. These studies are essential preliminaries to the institution of the controls that Dr. Hueper has suggested.

Many of the control recommendations admittedly are far-reaching in their implications. Years of work will be required to put them into practice with maximal effectiveness. This is particularly true of the recommendations for social controls. On the technical side, some of the elements can be instituted at once and without great expense, if management and labor can be persuaded to agree to them.

For example, effective medical and sanitary supervision of exposed workers can be undertaken immediately. This supervision should include X-ray examinations at frequent intervals; careful clinical study of suspicious lesions; preparation of exhaustive and detailed job analyses and case histories; regular quarterly or semi-annual physical examinations of all workers who might possibly suffer exposure to



CARCINOGEN IN NATURE is sunlight. Such natural carcinogens, however, are few. An abnormally high concentration of arsenic in drinking water has been shown to cause cancer of the skin and internal organs. Infections of certain parasites have also been found to lead to malignant growths.

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the carcinogenic agents; a constant review of dangerous plant operations to enforce constant good housekeeping and to check on the level of carcinogenic dusts, fumes, and mists.

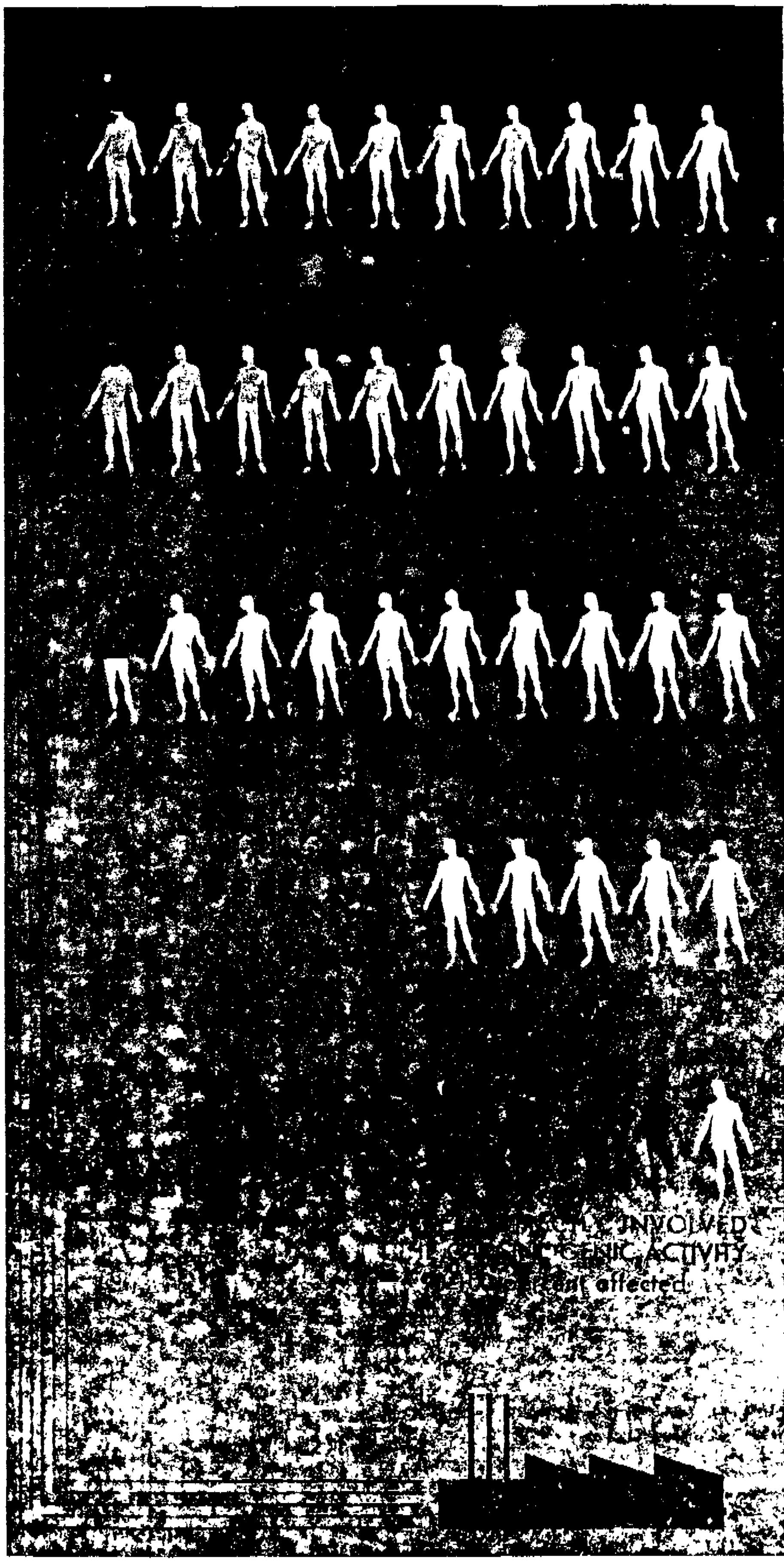
Protective measures for the workmen themselves are also simple and relatively inexpensive, although the enforcement of their use is sometimes made difficult by the discomfort they cause. They include the regular wearing of respirators and sealed clothing whenever exposure to a carcinogenic hazard is likely, daily showers for all persons working in or near the hazardous operations, use of separate lockers for street and work clothes, and adoption of work techniques that will minimize the dangers of exposure.

Other, and more important, technical measures are likely to involve heavy expenditures for management. In some instances, entire factories would have to be rebuilt. Others would require costly waste-control equipment, such as electronic dust precipitators, and extensive remodeling to enclose carcinogenic operations and keep the workers from any contact with dangerous agents. Few plants could afford the necessary changes unless all other plants in the same industry were required to make the same improvements at the same time.

In some instances, such changes might possibly be undertaken as a result of an industry-wide agreement. In others, legislative and administrative enforcement might be essential. Such action would include factory licensing and inspection by government, improved compensation laws recognizing occupationally acquired cancers as compensable, and revision of the health codes to make occupational cancers notifiable just as are many other diseases. These measures would require coordinated and carefully planned action on the part of management, labor, the medical profession, state public health and labor departments, and state and Federal legislatures. A precedent for such a program has already been set by the successful control of communicable diseases through public health laws and through the organized cooperation in their enforcement of both private and public agencies.

How effective these controls would be in diminishing the hazards of still undiscovered environmental carcinogens is a question that only time can answer. Meanwhile, the known causes of occupational cancers would be placed under technical and social restraint, and patterns would be established for the future control of new carcinogens as they are found in our environment.

Groff Conklin is a science writer and a former consultant with the National Cancer Institute.



EXTREME CASE of environmental cancer is represented by record of aromatic amine plant in Germany. Of workers directly in contact with chemical, 90 to 100 per cent developed cancer of the bladder. Running from top to bottom is illustration of statistical analysis used to locate such hazards.