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FOOD AND CANCER

The Suspicious Chemicals in Your Marketbasket

Through the earliest ages of history, man struggled for survival against smaller living things—the pests that ate his crops and the germs that diseased his body. Defeating them, he still had to battle the slow attrition of age and its degenerative effects. Now while holding off age with one hand, he faces yet a new and far more subtle foe: the chemicals he has injected into his own environment. Some of these are known to start cancer. How many of them do we eat with our daily meals?

Cancer specialists from all over the world gathered in Rome in August, 1956, to argue that question in a Symposium organized by the International Union Against Cancer. After five days they voted unanimously to recommend precautionary action. Believing that the survival of democracy depends on the willingness of the ordinary citizen to work with the scientists in harnessing science to enrich—rather than to enslave—the human individual, SR/RESEARCH *here presents for its readers a consideration of cancer's possible origins in food, and a program for action which seems practical and sensible to the Chief of the Environmental Section, National Cancer Institute, U. S. Department of Health, Education, and Welfare.*

BY JOHN LEAR

This material was prepared by Saturday Review's Research Section: Science & Humanity.

Of all man's enemies, cancer is the best disguised. So well does it cover its tracks that most people think of it as one disease. Actually, it is a huge family of afflictions with a conspicuous characteristic in common: cells growing wild.

Few, if any, qualified investigators of cancer's ravages expect a quest for a cure that will lead them to a single agent. Instead, the conviction is spreading that just as each of the infectious diseases has had to be fought with particular antitoxins, vaccines, and drugs, so each of the different types of cancer will have to be vanquished separately by means directed specifically at its individual causes. Antibiotics may be effective against one cancer, chemicals against another, radioactive isotopes against a third, and a fourth may be treated with something like a vitamin for lack of which the body initiates an alternate growth pattern that goes berserk.

"We are not yet sure what type of weapon will be most effective," Dr. R. Keith Cannan, chairman of the Division of Medical Sciences of the National Academy of Sciences, reported recently after a decade spent in allocating $25,000,000 for cancer research—$3,000,000 in this year 1956 alone. "The war on cancer is still a war of maneuver. We are not yet in position for the grand assault. . . . The biologist, in ever closer cooperation with the biochemist . . . must cover the whole field of cellular interactions and of the influences of genes, viruses, and hormones on growth development and susceptibility to malignant change.

"At the clinical level the trend in therapy is strongly toward the development of chemotherapeutic agents for the control of diffuse and inaccessible tumors. At the same

time interest is growing in the prevention of cancer by an intensive screening of man's chemical environment in the search for extrinsic carcinogenic agents."

Concern about cancers that originate in man's environment—the effects of cigarette smoke and motor-exhaust fumes are but two examples—is not merely contemporary with the chemotherapeutic attack against malignancy. The one is a natural result of the other. In hunting chemicals that could kill cancer, medical researchers have discovered chemicals which, if they do not actually cause cancer, do provoke the wild cellular growth to proliferation.

There is no evidence that any fruit, vegetable, or meat in the natural state contains carcinogens (cancer "starters"). But these suspicious chemicals can and do get into food in scores of different ways, from deliberately introduced colorings to accidental residues of poisons used by farmers to kill worms and bugs.

Only last year the United States Food and Drug Administration cut the number of food dyes that are legal in this country from eighteen to fifteen; the three thus banned had been proved capable of inflicting harm on humans under certain circumstances. Today the American housewife buys nothing through her normal markets that is known to cause cancer in man. But it cannot be said that her kitchen is free of artificially added substances either similar or identical with chemicals known to cause cancers in rabbits, rats, mice, or dogs.

In itself, this last fact would not necessarily be ominous. The weird metabolic pathways through which the wild growths of cancers proceed differ from one animal to another, from animals to man, and even from one type of man to another. A cancer-provoking agent which kicks up trouble in the liver of one individual may do its damage at a quite different site in a different victim.

The immediate reason for caution in human use of any chemical suspected of even remote relationship with cancer is the pattern of malignant growth in the human digestive tract (see sketch, page 59). The points that cancers most frequently attack are the "narrows" through which our food passes—a clear suggestion that prolonged contact between food chemicals and the intestinal lining could be a primary cancer mechanism. Although this is only a theoretical consideration now, it would seem to be strengthened by the established fact that body tissues "remember" even brief encounters with cancer "starters" and accumulate the ill effects over long periods of time before a wild growth actually appears.

As far back as 1950 J. R. Heller, Jr., Director of the National Cancer Institute, wrote in the *Archives of Industrial Hygiene:*

"Considering that danger from the chemical cancerigens lies in the slow, almost unnoticeable harm that comes from contact with them, it might be wise from a preventive point of view to consider all chemical agents which have elicited cancer in animals as having the potential properties for producing cancer in the human organism."

Four years later, the Committee on Cancer Prevention of the Commission on Cancer Control, International Union Against Cancer (organized in 1933 by cancer specialists of thirty-three nations), passed the following resolution at Sao Paulo, Brazil:

"In the case of agents whose carcinogenicity for man is not known but which elicit cancer in experiments conducted upon animals—although it is recognized that the development of cancer in response to such materials may be conditioned by the type of exposure, notably the species of animals or the route of administration—it is not prudent to regard such agents as harmless for man."

Dyes were the only food hazards discussed at that time, and no definite conclusions were reached about them. This state of affairs did not satisfy the stern conscience of Dr. Hermann Druckrey, Professor of Pharmacology at Freiburg, Germany, and he proposed a worldwide symposium on the potential dangers. While preparations were going forward for this meeting, enforcement of the Pure Food regulations in this country started to tighten. The Supreme Court had found that existing laws gave Federal inspectors no right to enter food processing factories. In his first message to Congress, President Eisenhower proposed new legislation to fill the gap, and it was passed. A second law put new controls on pesticide residues. General expansion of Food and Drug investigations was guaranteed by approval of a new headquarters building, including up-to-date laboratories capable of dealing efficiently with the problem of chemical additives. Eleven different bills were introduced for still further reforms, but the confusions they stirred up in Congressional hearings stalled them all. During the hiatus that followed, the world Symposium was held in Rome from August 10 to 15, 1956, and was attended by fifty-two scientists from twenty-one lands. There was so much talk about that the usual Italian siesta had to be abandoned in order to complete the agenda. At the end, unanimous approval was voted for a flat prohibition against any intentional additive to food or drink which is not specifically authorized by law.

There are hundreds of additives and contaminants in the foods we eat today. Which ones are safe and should be legalized? Which ought to be banned? Participants in the Symposium wrote no list, but did agree upon guiding principles. In their final report, approved unanimously, the cancer experts insisted that first of all their work should be directed toward assuring the primacy of that forgotten individual

THE CONSUMER: NO. 1 MAN

INTRODUCTION

The participants unanimously recognize the urgent necessity for international collaboration for the protection of mankind against exogenous carcinogenic factors (cancer "starters" originating outside the human body), and notably against carcinogenic substances that may be present in food.

This collaboration should tend to encourage, help, coordinate, and if possible support research so as to achieve practical results in the shortest possible time. Thus, the necessary scientific basis could be established for industries to plan their production and for governments of different countries to legislate for the

effective protection of the health of consumers.

General Principles

Members of the Symposium adopted the following basic principles by unanimous vote:

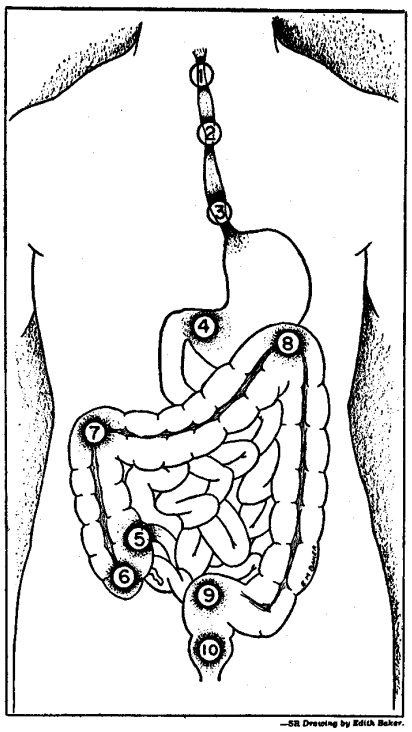
1. Substances intentionally added to foods.
   a) Food and drink should not contain intentional additives unless authorized by legislation.
   b) The best safeguard is provided by the introduction of lists of substances which can be authorized from the point of view of toxicity and carcinogenicity. These list should be continuously reviewed in the light of new knowledge and experience. Revisions should be possible *with a minimum of delay.*
2. An additive should be permitted only if it fulfills these requirements:
   a) It should conform to agreed official specifications.
   b) It should be shown by adequate scientific evidence to be innocuous to the consumer.
   c) Its use should meet a recognized need and be in the interest of the consumer.
3. In introducing permitted additives:
   a) The amount used should be as small as possible for the purpose.
   b) The consumer should not be misled as to the quality of food.
4. Substances unintentionally present in foods:
   Food and drink should not contain unintentional contaminants in amounts that constitute a risk to the consumer.

Biological Experimental Methods

As far as toxicological methods are concerned, covering foreign substances voluntarily or involuntarily added to food, with particular reference to their potential carcinogenic activity (a "potential carcinogen" in this Report refers to any substance which has been convincingly demonstrated to be carcinogenic to animals, and though not yet shown to act as such in man, must be suspected of having a similar effect in man. It should be distinguished from "a substance suspected of carcinogenic action" where the tests are deemed to have been inadequate), the symposium has unanimously recognized that the way in which experiments are carried out depends in large measure on the nature of the substances, conditions, and modes of use, and that it is only possible to formulate some general rules. Experimental conditions and their evaluation should be left of course to the expert responsible for the experiments themselves. (Nevertheless, the Symposium agreed that presentation of experimental results should precisely identify the chemicals tested, their degree of purity, their companions in compounds or solutions, other ingredients in the diet, age and sex and strain and species of the experimental animals, length of treatment, times of appearance and nature of tumors, and the comparative health of control animals which are not fed the suspected chemicals.)

Considering that through the world the use of food additives and the presence of contaminants in food constitute a potential danger including carcinogenic risks for mankind and that the magnitude of the problems is such that it is impossible for any one body or country to undertake all experimental work necessary for the establishment of adequate safeguards, the Symposium has become convinced that a vigorous and effective campaign against the growing potential cancer hazards from food additives and contaminants demands the cooperation and coordination of all research efforts and facilities suitable for such work in different countries and the organization of an overall and closely integrated investigative plan.

The Symposium considers it advisable that the qualified experts should exchange through an international organization, such as the Committee of Causative Factors of Cancer of the International Union Against Cancer, all relevant information concerning their methods of experimentation and the results obtained, whether positive or negative. The Symposium recommends that each of the investigators do his best to make available, if



—SR Drawing by Edith Baker.

THE INTESTINAL BATTLEFIELD: There is strong medical support for the belief that many cancers might be prevented by eliminating "starter" chemicals from food. Malignant growths of the human digestive tract tend to appear in the "narrows" of that tract, where food slows down its passage and rubs against the intestinal linings most forcefully. These "narrows" are the shaded spots in the above sketch, marked with numbers: 1. the larynx; 2. the tracheal bifurcation; 3. the entrance to the cardiac stomach; 4. the pre-pyloric stomach; 5. the ileo-cecal valve; 6. the cecum; 7. the right colonic flexure; 8. the left colonic flexure; 9. the sigmoid colon; and 10. the rectum. Occurrence of cancers at these points is significant when one notes how relatively long are the cancer-free portions of the intestine.

needed to other workers equipment, substances, and animal strains required for carrying out the experiments.

The following two points have been approved unanimously:

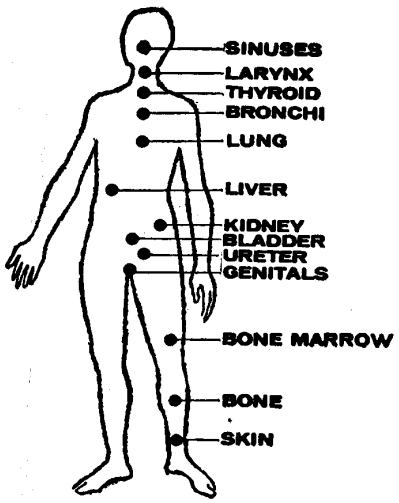
1) Food additives should be permitted only if, after long-term administration to at least two species of animals (one preferably a non-rodent), orally and parenterally (by injection), in amounts which must be considerably higher than would be present in food, so as to give adequate margin of safety, and after observation of the animals over their lifetime, and through at least two generations in at least one suitable species, they have no toxic effect. 2) Any substance which causes cancer in man or which, when tested under these conditions, is shown conclusively to be a carcinogen at any dosage level, for any species of animal, following administration by any route, should not be considered innocuous for human consumption.

The Symposium considers that attention should be given to the possible action of substances which, though not carcinogenic themselves, favor carcinogenesis.

Analytical Methods

(This section of the report is a recitation of technical details about purity of chemicals and standardization of animal experiments. Its purpose is to set standards that would make international exchange of information and cooperation in enforcement practical. Greatest attention is directed to dyes used in coloring food, and there is one finding of significant interest to the ordinary citizen. Not a single dye is listed as having been "adequately studied" to "satisfy the agreed criteria of safety." But among the chemicals "considered unsuitable or potentially dangerous which should not be added to food or drink for man or animals" there are nine shades of red, seven shades of orange, three yellows, three greens, three blues, a violet, three browns, and a black.

(After deliberating about food additives other than dyes, the Symposium reaches the conclusion that, because of "the limited amount of information available," it is "impossible to deal at this moment with all the different groups of food additives." Hence the report limits itself to preservatives, antioxidants, and some general remarks about emulsifying agents. Here again the language is technical. But in essence the Symposium report calls for "urgent retesting on an extensive scale" of these preservative chemicals: ethyl and butyl esters of p-hydroxy-benzoic acid, sulfurous acid and related compounds, formic acid. Preservatives condemned as "carcinogenic and . . . (to) be avoided for human use" are thiourea, thioacetamide, and 8-hydroxyquinoline. Among the antioxidants, thiodipropionic acid is tagged for "urgent retesting" and hydroquinone is on the prescribed list. "Extensive investigations of emulsifying agents" is deemed "of the utmost importance," "urgent testing" is urged for sorbitan fatty acid esters and polyoxythylen sorbitan fatty acid esters, and a flat ban is recommended on "highly oxydised and highly viscous polymerized oils.")



Cancer from chemicals added to food is not a bizarre concept. Cancer "starters" invade us at many points from the environment of our everyday life.

Food Contaminants

The Symposium limits itself to the formulation of general observations:

1. It recommends that attention should be given by public-health authorities to pesticides containing arsenic, since cancers of the skin have been observed following the consumption of foods contaminated with arsenical pesticide residues.

   Furthermore it is felt that more information is needed as to the safe use of chlorinated hydrocarbons as insecticides and miticides. It is recommended that investigations should be conducted on the potential dangers of long-term ingestion of pesticide residues in foodstuffs since exposures to chlorinated hydrocarbons are sustained from various sources in addition to contact with chlorinated hydrocarbon pesticides in food.

   Though no carcinogenic effects have been demonstrated in man so far, similar to those found in experimental animals, the problem requires careful study. Attention should not only be paid in such investigations to the pesticide itself, but also to the vehicle which carries the active ingredients, because the vehicle may be carcinogenic.
2. It notes that an improper use of estrogens (hormones) as fattening agents deserves critical consideration, because of a potential cancer hazard of human beings resulting from an excessive and long-term contact with such agents.
3. Extensive experimental studies are indicated concerning the late effects of antisprouting agents because little information is available on a possible carcinogenic action of these chemicals influencing cellular mitotic (division and reproduction) activity.
4. Since various petroleum constituents, including certain mineral oils and paraffin, have produced cancer in man and experimental animals, the presence of such chemicals in foods appears to be objectionable, particularly when such materials are subject to high temperatures.
5. The recent observation of cocarcinogenic and promoting effects exerted by several detergents calls for caution in the use of such chemicals in foodstuffs.
6. It is felt that the possible production of carcinogenic substances by non-ionizing or ionizing radiations in foodstuffs should be considered as potentially dangerous. Similar considerations should be applied to the presence of radioactive substances in foodstuffs originating from environmental radioactive contamination.

It follows from the existing experimental evidence on the carcinogenic action of certain food contaminants

a) that wherever possible, the further use of such chemicals should be discontinued and, when this is found to be impossible, that such chemicals in foodstuffs be kept at a minimum;

b) that the observance of such minimum levels be rigidly enforced;

c) that efforts be made to find non-carcinogenic substitutes for those chemicals entering

foodstuffs as contaminants which have proved to be carcinogenic in animals and/or man.

GENERAL CONCLUSION

The Symposium recommends that, as a basis for active cancer prevention, the proper authorities of various countries promulgate and enact adequate rules and regulations prohibiting the addition to food of substances having potential carcinogenicity.

The Rome Symposium had no enforcement power. It could only suggest cooperation to achieve its ends. So far as the United States was concerned, responsibility passed to the Food Protection Board of the National Research Council (which has been considering a memo on the subject for a year but has not yet acted), the Food and Drug Administration, and the National Institutes of Health, whose environmental cancer chief, Dr. W. C. Hueper, read the following paper at Rome.

A PRACTICAL APPROACH

This is a condensation by John Lear, Science Editor of The Saturday Review, of a paper read in Rome by Dr. W. C. Hueper, Chief of the Environmental Cancer Section, National Cancer Institute, U. S. Department of Health, Education and Welfare.

A rapidly growing number and variety of non-nutritive substances have been introduced during recent decades into foodstuffs intended for general human consumption through the use of modern methods of food production and processing. Some of these chemicals are intentionally added to foods for various reasons, while others are employed for different purposes in the production of foodstuffs and remain unintentionally in them as residues. A disturbing aspect of this development is that there exists no mandatory provision for assuring, *a priori*, that biologic properties of each of these additives and contaminants, particularly long-term or delayed effects, have adequately been studied. The circumstances suggest the virtual certainty that many have not.

It is especially important in this respect that observations made during recent years in men and experimental animals have demonstrated a not inconsiderable number of chemicals similar to, or identical with, those introduced into foodstuffs which possess carcinogenic (cancer-provoking) properties. The actual or possible existence of cancer hazards related to carcinogens in foodstuffs therefore poses a serious public-health problem. The daily and life-long exposure to such agents would represent one of the most important of the various potential sources of contact with environmental carcinogens for the population at large.

The main groups of food additives and contaminants . . . include . . . natural and synthetic dyes, antioxidants of fats and lipoids and vegetable matter, thickeners, sweeteners, flavoring agents, surfactants (detergents, foaming agents), humectants (smoke agents), preservatives and chemical sterilizing agents, water conditioners (iodine, fluorides), antifoaming agents, salt substitutes, shortenings, softeners, bleaches, modifiers and improvers (meat tenderizers, etc.), oil and fat substitutes, organic solvents, emulsifiers and solidifiers, pesticide residues, antisprouting and antimaturition agents of fruits and vegetables, insect repellents, hormonal fattening agents, antibiotics (fed to food animals and added to foodstuffs), enzymes, antienzymatics, pan-glazes (silicones), pan-greases (mineral oils), water pollutants, chemical sterilizing agents, wrapping and coating materials (paraffin, waxes, resins, plastics), soot adherent to smoked foodstuff and roasted and toasted products, household detergents and their coloring agents, non-ionizing radiation (ultraviolet) products, ionizing radiation (radioactive) products, and radioactive substances taken up by plants and food animals from air, soil, or water contaminated by radioactive fall-out.

The bulk of the still rather restricted pertinent information on potential cancer hazards from these additives and contaminants is of relatively recent date. Knowledge of such observations is often limited to parties mainly interested in scientific aspects of carcinogenesis and is sometimes not fully appreciated by those parties concerned with the practical aspects of potential human cancer hazards inferable from these experimental findings.

There is no necessary relation between toxicity (poisoning now effectively prevented by food and drug laws) and carcinogenicity of chemical agents. As a rule, the minimal carcinogenic dose is distinctly lower than the minimal chronic toxic dose. It is for this reason that not infrequently carcinogenic reactions may develop upon exposure to carcinogenic chemicals without a preceding or simultaneous appearance of any toxic symptoms.

In a graduated scale of the relative significance of potential environmental carcinogenic agents from a public health viewpoint, the highest priority for carcinogenic screening should be extended to those agents with which large parts of the general population have frequent and prolonged contact, whose possible carcinogenic effects on man can least readily be ascertained, and which for this reason are most difficult to control by preventive methods. Chemicals included in this group are those which enter the general human environment of every home in the form of consumer goods, or as environmental contaminants. Agents of this type are the large group of chemical additives and contaminants of foodstuffs in addition to many environmental poisons, pollutants of water, air, and soil, household drugs, sanitary supplies, cleaning agents, polishes, paints, and cosmetics.

If one adopts the principle that the protection of the health of the general public deserves foremost attention, the following considerations may profitably be used as guide lines in arriving at intelligent and rational decisions.

1. Carcinogens vary greatly in their relative potency. Coal tars of different derivations, for instance, vary greatly in their relative carcinogenic potency in man and experimental animals. Coal tars are in turn usually more potent than wood tars or vegetable tars or tars obtained in the fractionation of petroleum.

2. Dose observations made in experimental animals are not directly applicable to man. There exists marked differences in potency of a particular chemical for various species.

3. Repeated exposures to carcinogens produce a cumulative carcinogenic effect in the exposed tissues. Cells once exposed to a carcinogen seem to retain the entire or a considerable portion of the initial effect exerted by individual exposures, even if these by themselves may be insufficient for eliciting a neoplastic (ma-

lignant) response. Subeffectively exposed cells can be challenged into carcinogenic activity either by additional subminimal carcinogenic exposures or by contact with specific promoting chemicals.

4. Actual exposure to a dietary carcinogen does not always stop with the cessation of environmental contact. Some chemicals are not metabolically destroyed or excreted but are retained in active form in certain tissues from which they may gradually be mobilized long after the environmental exposure has ceased.

5. Exposure to a dietary carcinogen may be complicated by occupational, medicinal, cosmetic, sanitary, or environmental contact with the same chemical or some other chemical.

6. It is perhaps possible to enforce to a reasonable degree laws concerning the maximal content and adequate purity of food additives and contaminants in foodstuffs merchandized by relatively large trade organizations dealing in large quantities in nationwide and interstate commerce and using standardized and well controlled methods of processing, handling, and shipping. Considerable difficulties in this respect may be encountered, on the other hand, regarding the proper supervision of foodstuffs produced and sold on a local level. The mere passage of laws establishing standards in such matters without providing adequate means to enforce them might produce in the population a deceptive impression of safety. The most effective method of control of health hazards of this type doubtless is found under such circumstances in a complete elimination of the dangerous agents from the human environment wherever such a procedure is possible.

7. Since many foodstuffs containing artificial food additives and contaminants are not adequately labeled as to the amount and type of chemicals added to the natural food products, the general consumer is relatively rarely able to make any intelligent selection between different products of the same type, particularly between "natural" foodstuffs and "artificially modified and contaminated" ones. Indeed, in many instances, he may have little choice in such matters, because all or nearly all foodstuffs of certain types which he is able to purchase are of the contaminated or modified variety. The consumer under such circumstances is a member of a "captive" population which may be subjected to potential, long delayed health hazards which he has neither consented to nor is able to avoid. For these reasons the general public is entitled to expect that all chemical additives and contaminants are subjected to comprehensive and thorough studies for toxic, carcinogenic, and cocarcinogenic properties before they are used or introduced in human foodstuffs.

It is unlikely from an application of our present knowledge of environmental carcinogens that many of the presently used additives and contaminants of foodstuffs introduce any carcinogenic hazard into the general food supply and, therefore, deserve any immediate attention. The large number of additives as well as the complexity and costliness of the biologic testing for carcinogenic properties of any one of them, moreover, precludes for merely practical reasons any large-scale attack of the problem on the entire front at the present time. It is quite obvious that under the existing conditions a step-by-step procedure will have to be adopted and that investigative efforts would best be expended for the time being on those circumscribed groups of chemicals which from the already available information have furnished carcinogenic or cocarcinogenic agents, *i.e.*, synthetic dyes, chlorinated pesticides, animal and plant hormones, and detergents.

Among the various formerly and presently used synthetic food dyes, carcinogenic properties were discovered during recent years in a surprisingly large number when tested in rats and mice. Rodent cancers have also been produced by chemical compounds of the same stilbene family which has recently been introduced as coloring matter in many household detergents used for the cleaning of kitchen utensils, dishes, and cooking equipment of homes and commercial eating places.

Potential carcinogenic contaminants also may be introduced into foodstuffs if vegetables, fruits, fish, oysters, and livestock are grown on soil or in water polluted with known carcinogens, such as radioactive matter, arsenicals, selenium and polycyclic hydrocarbons contained in ship fuel oils. Consideration, moreover, must be given to the possibility that carcinogenic chemicals may be formed from noncarcinogenic ones under the influence of heat. Possible examples are (1) charred or tarry carbonaceous matter formed when bread or biscuits are excessively toasted or meats are grilled or roasted or (2) hydrocarbon constituents of mineral oils freed by cracking of the oil when it is used as a fat substitute and subjected to heat during grilling or baking.

There exists also the possibility that original noncarcinogenic additives and contaminants may interreact with each other or with food constituents and form new compounds possessing carcinogenic properties in the foodstuffs. They may be produced under the influence of processing procedures or during the preparation of food in the kitchen. Plastics used as wrapping material, sausage skins and coating material of fruits, cheese, meat, butter, and can linings may carry a similar hazard.

Mention may finally be made of several experimental observations indicating that a dietary intake of certain species of alkaloids which contaminate foodstuffs (chilies, alkaloids of senecio plants, crude ergot) may result in the development of liver tumors when given to rats.

The use of various types of radiating energy in the processing of foodstuffs also deserves consideration from a carcinogenic viewpoint, since these agents (ultraviolet radiation, ionizing radiation) produce in the constituents of food, such as sterols and nucleoproteins, definite chemical changes. No reliable information exists and no adequate experimental studies have been made for establishing the noncarcinogenic nature of the radiation products, although both types of radiation are eminently carcinogenic when acting on living tissues of both man and various species of animals.

The great majority of the different cancerous reactions mentioned here were produced either by the administration of excessively high doses or followed upon their introduction through routes distinct from those encountered under ordinary alimentation. The cancers developed in animals differed in various metabolic respects from man. But the mere fact of the existence of such responses presents a definite warning deserving serious attention if possible endemic and epidemic cancerous manifestations among exposed population groups are to be avoided.

—W. C. HUEPER.