variability in size of tumors observed at different times, the speed of their growth, and so forth. The theories to be discussed range from one- and two-step mutation theories, to cumulative processes, to virus carcinogenesis. Since the development of cancer is essentially the process of growth of a population of cells of a particular kind, all theories of carcinogenesis tie in with population dynamics and with problems of epidemiology. Mathematically, all these problems are concerned with stochastic processes of a particular kind.

#### Applications to Physical Sciences

Physical-science applications of statistics and probability to be discussed at the symposium include certain occurrences in cloud chambers, stochastic theory of precipitation, and problems of astronomy. In the latter category, several papers originating in England deal with the chance mechanism of losses of comets. The mechanism contemplated is particularly interesting because it involves not only kinematical considerations, which are comparatively easy to deal with, but also dynamics. Other papers on astronomy deal with the realm of galaxies. Here, one of the problems treated consists in discriminating between two alternative hypotheses regarding the nature of systems of galaxies: double galaxies and clusters. According to one hypothesis these are stable dynamical systems. According to a more recent hypothesis, members of such systems fly apart, possibly as a result of a cataclysmic explosion.

#### Special Events Planned

Special events at the symposium will include a commemorative session for the recently deceased Russian probabilist A. Y. Khinchin, whose works exercised and still exercise a strong influence on research all over the world. The speakers at this session will be J. L. Doob and E. Montroll from this country and B. V. Gnedenko from the U.S.S.R.

Another special session is planned to honor Harold Hotelling, the Nestor of statisticians in the United States. A jubilee volume published by Hotelling's admirers will be presented to him.

In line with the rapidly spreading use of high-speed electronic computers in the course of statistical studies of natural phenomena, arrangements are being made by the International Business Machines Corporation for demonstrations of the effectiveness of two of its machines, the 701 and the 704, on the Berkeley campus of the University of California.

#### Symposium's International Character

The fourth Berkeley symposium will differ from its predecessors in its international character. The first symposium of 1945 was a purely American meeting. At the second symposium, 5 years later, there were eight contributions from abroad. At the third symposium, in 1955, this number grew to 12. Now the program lists 47 papers promised from abroad, 40 percent of the total. The geographical distribution is as follows: 11 papers from England; eight from the U.S.S.R.; four from Sweden; three each from Belgium, France, Hungary, and Poland; two each from Czechoslovakia, Denmark, and Japan; and one each from Australia, Canada, Germany, India, Israel, and Italy.

It is hoped that with this world-wide distribution of invited participants, the symposium will reflect adequately the current status of probability and statistics on this planet. Also, the interchange of ideas on common subjects of study, approached at different points of the globe and inevitably by different methods, holds excellent promise of speedier progress in research. Thus, unless the intricacies of the present political situation interfere, the organizers of the fourth symposium look forward to seeing useful and far-reaching results from this truly international effort at intellectual cooperation.

J. NEYMAN

*Statistical Laboratory,*
*University of California, Berkeley*

## Nubian Archeological Expeditions

Froelich Rainey, director of the University of Pennsylvania Museum, has undertaken a special trip to the United Arab Republic and the Sudan to plan a joint archeological expedition with W. Kelly Simpson of the Peabody Museum at Yale University. The proposed expedition will be made under the auspices of UNESCO's project to preserve the archeological treasurers of Nubia which are threatened with inundation as a result of construction of the High Dam at Aswan.

Accompanying them is Mrs. H. Gates Lloyd, member of the U.S. National Commission for UNESCO and chairman of its special committee which explored the possibilities of U.S. support for the Nubian project. Rainey is a vice-chairman of the newly formed U.S. Committee for the Preservation of the Nubian Monuments. The party plans to visit Aswan and subsequently to ascend the Nile by boat to investigate archeological sites.

The Oriental Institute of the University of Chicago has also announced plans for a program of excavations and documentation in the area. A committee to administer a 5-year project has been formed under the directorship of Keith C. Steele, who is now in Egypt conferring with officials and inspecting sites.

## Additive Report Released by Science Advisory Committee

*The following excerpts (see page 1581) are the major recommendations from a recent report on the use of chemicals and drugs as food additives that was prepared by a special panel of experts convened by the President's Science Advisory Committee. Findings of the study were approved by the President's Special Assistant for Science and Technology, George B. Kistiakowsky.*

. . . Under the Food Additives Amendment of the Federal Food, Drug, and Cosmetic Act, the Secretary of the Department of Health, Education, and Welfare may establish regulations prescribing, with respect to one or more proposed uses of the food additive involved, the conditions under which the additive can be used. The Act provides, however, that no such regulation shall be issued if a fair evaluation of the data before the Secretary fails to establish that the proposed use of the food additive, under the conditions of the use to be specified in the regulations, will be safe. Accordingly, the Food and Drug Administration has an area of administrative discretion in determining the safety of food additives under conditions of proposed use.

This area of administrative discretion has recently been greatly narrowed in those cases where a new food additive is a possible carcinogen. In 1958, Congress enacted the Food Additives Amendment of the Food, Drug, and Cosmetic Act. Section 409 (c) (3) . . . of the Amendment states that "no additive shall be deemed to be safe if it is found to induce cancer when ingested by man or animal, or if it is

found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal." The panel has focused attention on this proviso which, under the language of the Food Additives Amendment, is concerned chiefly with new substances. . . .

The panel subscribes to the intent of the Congress in approving this Section of the Food Additives Amendment to protect the public from increasing cancer risks through the diet. However, there are certain difficulties in its practical application—difficulties which give rise to many uncertainties both on the part of the public and those whose responsibility it is to administer the law.

### Scientific Uses

Several scientific problems raised by Section 409 (c) (3) have been examined in detail by the panel. These are: *Problem of Recognition of a Carcinogenic Food Additive.* . . . It is to be noted that a finding of cancer induction in man or animal must be made as a prerequisite to banning of the additive in question. This recognizes the fact that the present state of scientific knowledge does not permit an *a priori* assumption of the carcinogenicity of a chemical. Since tests on animals or observations on man must be carried out to determine the capacity of an additive to induce cancer, it is pertinent to examine the procedures in current usage to recognize a carcinogen for man and/or animals.

*Recognition in Man.* The recognition of chemically induced cancer in man is based on circumstantial evidence. Although cancer morbidity may be in part related to environmental carcinogens, these have not been specifically identified in most instances because of the numerous, varied, and often unrecognized environmental factors to which man has been exposed. When, however, certain limited populations have had, through their specialized occupation, a concentrated exposure to specific environmental factors, it has been possible in a number of instances to obtain evidence indicative of a causal relationship between the specific environmental factor and the induction of cancer. Examples of this include urinary bladder cancer among workers in the dye industry exposed to 2-naphthylamine, lung cancer among chromate industry employees, and skin cancer among those engaged in the paraffin pressing operation in oil refineries.

The recognition of the relationship between an environmental factor and an increased frequency of a particular type of cancer in these examples rested on a marked difference between exposure of the individuals involved and the general population. Since, by contrast, exposure to food additives is general throughout the population, it is unlikely that carcinogenic properties would be recognized from examination of data obtained on man. From a practical standpoint, therefore, the indication of possible carcinogenicity to man of chemical additives must come from observations on laboratory animals or on persons exposed to unusual amounts of these chemicals during their manufacture or use, or in the treatment of disease.

*Definition of Induced Cancer in Animals.* The recommended procedure for testing the possible carcinogenicity of a chemical additive calls for its incorporation into the diet of several animal species, at several dosage levels, and for the duration of the animal's life span where feasible. Like all biological assay methods, this procedure has more inherent variables than do procedures involving physical and chemical methods. Further, the recognition of a carcinogen by the bioassay technique presents greater difficulties of interpretation than are usually encountered in assaying the effects of other pharmacologically active substances. These difficulties of interpretation are related to the identification of the tumor as a cancer, and to the way in which the experiment is designed. . . .

*Problem of the Relation of Dose to Cancer Production in Man.* Section 409 (c) (3) of the Food Additives Amendment of the Food, Drug, and Cosmetic Act prohibits the approval of a food additive regardless of the amount that is found to be required to increase the incidence of cancer in test animals. A literal interpretation of the Section must lead to the prohibition of such a substance even though present in trace amounts. Since new substances will be evaluated by animal tests, in practice the prohibition is based on the assumption that a substance which increases the incidence of cancer when included in the diet of animals at any dose level may increase the incidence of cancer when included in the diet of man even when present in amounts detectable only by the most sensitive analytical techniques. For a number of carcinogens that have been studied, however, there is evidence for the existence of a level of ingestion at which no carcinogenesis occurs during the life of the animals when tested in limited numbers. Also, dose-response curves for certain potent carcinogens in animals have been worked out from which can be reliably predicted the probability of an individual, in a given sized population, developing a tumor from a given dose of carcinogen. Such curves lead to the conclusion that dietary levels of carcinogenic agents exist at which the probability of cancer induction in animals is near zero.

The conclusion derived from animal studies has relevance to certain common components of the diet of man. In foodstuffs, as they occur in nature, one finds traces of chemicals which in larger amounts are generally accepted as carcinogenic, such as certain inorganic arsenic compounds, radium, and selenium. It can be shown by methods of analysis now available that ordinary table salt derived from rock salt contains trace amounts of radium and that foodstuffs containing iron salts are contaminated by minute quantities of arsenic. Although it cannot be stated absolutely that these traces of carcinogenic materials have never induced cancer in any human, the available evidence has not directed suspicion to these trace amounts as significant to the over-all cancer morbidity.

There is additional evidence which indicates that a dose-response relation for carcinogens exist in man. Thus, the bladder cancer incidence rate in those exposed to 2-naphthylamine . . . was highest among those most intensely exposed among several groups of workers in the dye industry. Another example of the existence of the relation of dose of a carcinogen and duration of exposure to cancer production is creosote, to which there is widespread exposure of workers in several trades. Although it has been demonstrated that creosote can produce skin cancers in mice and men, the frequency with which this has been observed in man is very low and only in those persons exposed to high amounts of the material over prolonged time periods. Finally, there is some indication in the literature that the frequency of cancer induction in man might be decreased by reduction of the amount of exposure to a particular carcinogen. Examples of this are the absence of reports of skin cancer in paraffin pressing operators in oil refineries following the introduction of

hygienic practices, and the reduction of nose cancer in nickel industry workers following the introduction of dust control measures. In these examples, it can reasonably be assumed that there has been a reduction in the exposure to the carcinogen rather than a complete removal of the cancer producing substance.

From the experience obtained in animal experiments and study of humans who have been exposed to carcinogens in the course of their work such as cited above, the panel believes that the probability of cancer induction from a particular carcinogen in minute doses may be eventually assessed by weighing scientific evidence as it becomes available.

#### Conclusions and Recommendations

The rapidly increasing number of new chemicals potentially useful in agriculture and food production demands vigilant and careful scrutiny of the compounds offered in order to safeguard the consumer from those that may present carcinogenic and other toxic hazards.

In applying the provisions of Section 409 (c) (3) the enforcing agency must employ the "rule of reason." . . .

The definition of a carcinogen implicit in the language of Section 409 (c) (3) requires discretion in its interpretation because so many variables enter into a judgment as to whether a particular substance is or is not carcinogenic.

It is to be emphasized that the present difficulty in establishing whether there are permissible levels for certain possibly carcinogenic food additives is accentuated by the limited relevant scientific information available. From the experience obtained in animal experiments and study of humans who have been exposed to carcinogens in the course of their work such as cited above, the panel believes that the probability of cancer induction from a particular carcinogen in minute doses may be eventually assessed by weighing scientific evidence as it becomes available.

The special emphasis placed by the Congress on the protection of the public from the dangers resulting from the addition of possible carcinogens to food calls for prudent administration of Section 409 (c) (3) of the Food Additives Amendment of the Food, Drug, and Cosmetic Act. Since an area of administrative discretion based on the rule of reason is unavoidable if the clause is to be workable, it is essential that this discretion be based on the most informed and expert scientific advice available. Until the causes of carcinogenesis are better understood, each situation must be judged in the light of all applicable evidence. In this way the protection of public health can best be assured.

Accordingly, the following recommendations are made:

. . . That the Secretary of Health, Education, and Welfare appoint a board advisory to him to assist in the evaluation of scientific evidence on the basis of which decisions have to be made prohibiting or permitting the use of certain possibly carcinogenic compounds.

The advisory board should be composed of scientists from the National Cancer Institute, the Food and Drug Administration, the U.S. Department of Agriculture, and the scientists outside the Government from a panel nominated by the National Academy of Sciences.

It would be the function of the board to weigh evidence and to make recommendations to the Secretary of the Department of Health, Education, and Welfare on the basis of available scientific data, both on applications for approval of new food additives and in all cases where the withdrawal of a prior approval or sanction is under consideration. . . .

If existing legislation does not permit the Secretary of Health, Education, and Welfare to exercise discretion consistent with the recommendations of this report, it is recommended that appropriate modifications in the law be sought. . . .

#### Members of the Panel

Detlev W. Bronk, chairman, president, Rockefeller Institute and president, National Academy of Sciences.

Robert F. Loeb, vice chairman, Bard Professor of Medicine, Columbia University—on leave.

Edwin B. Astwood, professor of medicine, Tufts University School of Medicine, New England Center Hospital.

Alfred Gellhorn, director of the Institute of Cancer Research, and professor of medicine, Columbia University.

J. George Harrar, vice president, Rockefeller Foundation.

Harold C. Hodge, professor of pharmacology and toxicology, University of Rochester.

James G. Horsfall, director, Connecticut Agricultural Experiment Station.

C. N. Hugh Long, Sterling professor of physiology, Yale University.

C. Chester Stock, scientific director, Sloan-Kettering Institute for Cancer Research.

---

## Biological Sciences Curriculum Study To Test New Courses

The Biological Sciences Curriculum Study has announced the establishment of centers for testing proposed new courses to improve the quality of biology taught in American high schools. Approximately 15,000 high-school pupils and 100 teachers in 28 school systems will cooperate throughout the 1960–61 school year in testing both the scientific content and the design of instructional materials.

At each center, seven high-school biology teachers and a university biologist, serving an consultant, will take part, according to Arnold B. Grobman, director of the Curriculum Study. The nationwide evaluation program will begin in September.

The Biological Sciences Curriculum Study is an educational program of the American Institute of Biological Sciences. Funds for the study have been provided by the National Science Foundation in grants totaling $738,000.

The Curriculum Study has its headquarters at the University of Colorado. It is an autonomous activity, directed by a steering committee of 26 outstanding biologists and educators, of which H. Bentley Glass, professor of biology at Johns Hopkins University is chairman.

## Elementary School TV Biology

The television series "21-inch Classroom," in cooperation with the Children's Museum of Boston and the Massachusetts Audubon Society, has been presenting a series of 30 half-hour television programs dealing with the principles of biology. Teacher for the series is professor William H. Weston of Harvard University, and the producer is Charles Walcott. The programs have included presentation at the fifth-grade level of some of the major ideas of biology. This has involved the extensive use of live animals and plants, original film, and special art work.

During the current year the series is being used in several thousand New