

Introduction: National Cancer Institute Pancreatic Carcinogenesis Program¹

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Cancer of the pancreas is a disease that can be expected to claim the lives of over 19,000 Americans this year. Although the incidence of this disease in the male may rank 7th in number of cases per 100,000 population, as a result of a high mortality, pancreatic cancer deaths rank 4th. Until the early years of this decade, this disease received little attention in the study of the mechanisms of carcinogenesis. A number of reasons existed for this neglect: the human disease cannot be diagnosed early enough to develop experimental concepts for analysis; no animal models were in existence with which to perform such studies; and the more responsive organs to existing carcinogens provided ample research opportunities for investigators to study the cellular changes involved in the pathogenesis of cancer in general.

A number of events helped focus the attention of the research community on this problem and ultimately stimulated the investigations presented in the scientific articles that follow. Perhaps the principal event was the observation, summarized in the Third National Cancer Survey (2), that the incidence and mortality of pancreatic cancer in the United States is increasing at an alarming rate. Table 1 shows the changing rate from 1937 to 1969 by race and sex. If these rates continue at their current trend, it can be estimated that the 1969 rate will double by the year 2000. This observation, coupled with the facts that diagnosis is usually late in the course of the disease and therapy has very limited usefulness and that this cancer has one of the lowest 5-year survival rates, comparable to that of acute leukemia in the 1960 to 1964 time period, clearly suggested the need to initiate a comprehensive study of this cancer.

Partly as a result of the observations obtained from the survey, a joint meeting was held by the NCI³ and the American Cancer Society in July 1971. From this grew the commitment to examine experimental pancreatic carcinogenesis with a rational approach establishing reasonable short- and long-term goals.

Another significant event was the report of Druckrey *et al.* (1) in 1971 which showed that guinea pigs could develop pancreatic adenocarcinoma when given methylnitrosourea in the drinking water. Although a low incidence was observed with an exceedingly long latent period, an opportunity was presented that could lead to a suitable animal

model for the study of the carcinogenesis of this disease.

As a result of these factors, the Carcinogenesis Area of the NCI with its staff and advisors developed over a 5-month period a program of coordinated research, articulated in a number of high-priority projects to be initiated as soon as possible. The aims of this program were to reproduce the induction and development of pancreatic carcinoma as observed in human pathology and to develop an integrated study of the pathogenesis of pancreatic cancer by morphological and biochemical methods.

This commitment to develop an expanding program in carcinogenesis at the NCI and the availability of funds to support collaborative research in this area presented an opportunity to initiate and maintain a coordinated effort toward the study of this important form of cancer. Through workshops, meetings of investigators, advisors, and NCI staff, a number of interrelated studies have been initiated and guided by the most relevant and pertinent information. Projects in model development of exocrine pancreatic cancer induction in laboratory animals, techniques of enhancing delivery of carcinogens to the pancreas, and studies to culture the organ and the ductal and acinar epithelial cells were initiated in June 1972.

Separate and distinct from this coordinated program on pancreatic carcinogenesis, there existed a program to study the carcinogenic activity of nitrosamines and their derivatives in laboratory animals. Since this class of chemical carcinogens is known for its wide spectrum of organ specificities, it was expected that these studies would contribute to the identification of several organ-site models of carcinogenesis. This program, largely conducted at the Eppley Institute for Research on Cancer, University of Nebraska, resulted in a hamster model for pancreas carcinoma, a report of which is included in the series of papers that follow.

It is significant to say that, in just a little over 3 years since inception of these investigations, a number of models for pancreatic carcinogenesis have been identified and are now actively being refined for systematic use in more detailed studies. The results are of such import within a field that only 1 year ago was struggling to succeed that a single session during the Third Annual Carcinogenesis Conference held by the NCI in Orlando, Fla., on February 3 to 5, 1975, was devoted to this 1 subject. Papers were presented that formed the bases for the articles in this publication.

Three short communications, not formally presented at the Carcinogenesis Conference but having import to the

¹ Presented at the symposium "Current Progress in Pancreatic Carcinogenesis Research," February 4, 1975, Orlando, Fla., as part of the Third Annual Carcinogenesis Conference.

² Presenter.

³ The abbreviation used is: NCI, National Cancer Institute.

Table 1
Incidence rates, by race and sex, for cancer of the pancreas

Race and sex	1937	1947	1969
White male	7.0	9.3	11.3
White female	4.9	5.5	6.7
Black male	5.0	11.6	15.0
Black female	3.4	6.4	14.5

Pancreatic Carcinogenesis Program, are appended to this series of articles. These are authored by Dr. Murrell, Dr. Hay, and Dr. Elkort.

It should be acknowledged that success of an NCI program can occur only in direct proportion to the capabili-

ties of competent investigators who are challenged by and are willing to study these difficult problems. Their cooperation with one another and the NCI staff and their application of high standards to quality research are facets of this program that are highly appreciated by the NCI and the community that it represents.

References

1. Druckrey, H., Ivankovic, S., Bucheler, J., Preussmann, R., and Thomas, C. Erzeugung von Magen- und pankreas-krebs beim Meerschweinchen durch Methylnitroso-harnstoff und-Urethan. *Z. Krebsforsch.*, 71: 167-182, 1968.
2. Third National Cancer Survey. National Cancer Institute Monograph 41. Washington, D. C.: U. S. Government Printing Office, 1974.