An Epidemiological Study of Cancer Among Employees in the American Petroleum Industry

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THE KETTERING LABORATORY

in the

Department of Preventive Medicine and Industrial Health

College of Medicine

UNIVERSITY OF CINCINNATI, CINCINNATI, OHIO

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Summary and Conclusions

Between 1949 and 1957, an industry-wide effort was made to describe the occurrence of various kinds and sites of cancer in persons employed in refineries and certain other installations of the petroleum industry, in association with occupations concerned This epidemiological study was undertaken as one phase of a larger project that included the biological testing of many products of the industry, and the exploration and further development of physical and chemical methods for detecting the presence of carcinogenic substances in petroleum products and for the identification of individual substances and classes of substances of this type in petroleum.

As the information received from the cooperating companies did not permit the calculation of attack rates, reliance had to be placed upon simple comparisons of the relative frequency of different kinds and primary sites of tumors as reported. In this investigation, the variables included, among others, were the major occupational assignments of employees, the principal type or source of their contact with petroleum products, and their geographic location. The experience of the populations of ten large U,S. cities, as reported by the U.S. Public Health Service, was employed as the "expected" or "normal" occurrence.

No significant differences were found in the limited and very small sample of cases available for study in this fashion. This finding must be interpreted with unusual caution. The reports received were not only few but there was very definite bias in their selection. However, the fact that there was reasonable correspondence in the relative frequencies both as to primary site and kind of cancer seems noteworthy.

Introduction

Some twenty years ago, various procedures for the catalytic cracking and reforming of petroleum came into commercial use in certain large units of the American oil industry. Out of these processes come side streams and products of crude petroleum in which the reformed and original hydrocarbons are so distributed as to create mixtures with new physical and chemical characteristics. Certain of these, particularly in the high boiling ranges, proved capable of producing cancers of the skin of mice. Further, these materials contain appreciable amounts of polycyclic hydrocarbons identical or similar in their chemical structure to those incriminated earlier as having a possible causal relationship to human skin cancers and generally accepted today as potential carcinogens.

The recognition of these facts, suggesting that the hazard of skin cancer in petroleum workers might assume significant proportions, led the Medical Advisory Committee of the American Petroleum Institute to recommend a comprehensive study of this problem. After the necessary and appropriate negotiations, the Kettering Laboratory was authorized to undertake this investigation. Chemical and biological testing of various fractions began in 1948.

While these experimental studies were developing, it was reported from England that "cuts" obtained from thermally cracked petroleum had proved to be carcinogenic for both mice and rabbits. This early observation was acted upon by the British Medical Research Council, under whose sponsorship a "Special Committee on the Carcinogenic Action

of Mineral Oils" was formed in 1948. Under the direction and stimulation of this Committee, several groups of investigators undertook coordinated and integrated explorations of this problem. These well controlled studies are still in progress, but, in general, the attack has been centered on the chemical and biological testing of crude petroleum samples and extracts obtained without severe thermal cracking.

The British efforts are to be considered essentially as complementing rather than duplicating the investigations authorized by the American Petroleum Institute, since the latter were directed primarily at the hazard of contact with catalytically cracked oils. Furthermore, the British program did not provide for epidemiological studies nor the recording of the incidence or prevalence of cancer among petroleum workers.

In neither country was any great apprehension felt until the modern catalytic processes began to replace thermal cracking. Reports of the occurrence of cancer among refinery workers had not been noteworthy save for those cases associated with exposure to crude waxes and oils in pressing out paraffin. In limited reviews of their experience, two U.S. companies had found rates of occurrence seemingly lower than those of the general population. It is evident, therefore, that these investigations were directed toward the appraisal of a potential or future hazard than they were to the elucidation of an actual or demonstrable incidence of neoplastic disease.

At the inception and throughout the planning of the experimental program sponsored by API, it was recognized that, beyond exhaustive

biological and chemical investigations, it would be desirable to determine, if possible, the prevalence and incidence of neoplastic disease among the employees of the petroleum industry according to occupational class and period of employment. Industry-wide epidemiological investigations with such goals are not entered into lightly, especially when directed at a disease such as occupational cancer, for the induction of which a long period of significant exposure to the etiological agent is required. New techniques must be developed and special channels of reporting improvised. Furthermore, there being no legal or other compulsion in these arrangements, the success or failure of the mechanisms of reporting depends upon the extent of the interest and cooperation of the various participating groups.

Planning and Development of the Investigation

The technical aspects of this attempt to estimate the hazard of neoplastic disease of petroleum workers were discussed repeatedly and at length with the Medical Advisory Committee of the American Petroleum Institute, its Subcommittee on Carcinogenicity, and individually with a majority of the medical directors of the companies that had signified their intention to support and participate in the investigation. It was thoroughly explained and emphasized on many occasions that the securing of any results whatsoever, either positive or negative, would demand prolonged investigation and the complete cooperation of the participating companies.

The apparent lack of a readily demonstrable increased incidence or prevalence of cancer in the industry seemed to indicate that any hazard

would be of a low order of magnitude. On the other hand, it was recognized that the concentration of carcinogenic materials, both in amount and kind, was usually low in the products of thermal cracking, and the contacts of workmen with these products, even under the primitive condition said to exist earlier in the petroleum industry, apparently were not sufficiently severe to be actually hazardous.

Human skin cancers related to polycyclic hydrocarbons occurred in the past only after long and close contact with soot, coal tar, shale waxes and lubricating oils, and crude paraffin waxes and oils. The experience of the workers with the catalytically cracked extracts was, of necessity, recent and of relatively short duration. Further, the fast moving developments in modern petroleum technology could be relied upon to produce a constantly changing situation.

It was recognized at the same time that the results obtained by chemical methods in correlation with the responses of experimental animals could be used only guardedly to predict or explain human reactions. By means of modern technological methods, complex mixtures, such as crude petroleum, can be separated with varying degrees of completeness into their major components and fractions. These can then be described as to their composition, and their biological activity can be compared with that of a known carcinogen under predetermined and uniform experimental conditions. By combinations of such means, the potential hazards of petroleum products, from the aspect of cutaneous cancer, may be explored and located and, at least in terms of relative severity, can be given a tentative or

inferred rating. In this as in other fields of animal experimentation, great caution is justified in any attempt to apply the results to human experience either before or after the fact. Such interpretations become even more difficult with the recognition that workers are subjected only rarely to the stringent conditions which in the laboratory are purposely designed to produce reactions within a limited period of time.

After careful consideration, the sponsors in 1949 established certain desirable objectives. These were:

1. To ascertain the incidence and prevalence rates of neoplastic disease in the employee population of the various participating petroleum companies;

2. To compare their experience with that observed in the general population and other industries, particularly those in the same geographical areas;

3. To evaluate, insofar as possible, with available methods and records, the present programs of hygiene control; and

4. To suggest improvements and changes in methods of environmental control in accordance with the results of the field investigations.

With the setting of these goals and with general agreement that the experience of the participating companies in regard to cancer should be assembled in as precise and comprehensive a manner as could be devised and supported by the Medical Advisory Committee, the first steps were taken during 1950 to explore possible methods for the conduct of epidemiological investigations. From the many ideas, varying concepts, and special needs of the medical directors and the individual companies advanced and discussed during the early months of this project, it was

apparent that it would be necessary to scrutinize minutely and weigh thoroughly all approaches. On the other hand, it was acknowledged that only those objectives and procedures could be implemented that seemed to offer at least a reasonable chance of success within a finite period of time.

In this planning, The Kettering Laboratory sought advice and guidance from many sources. Among these were the members of the API Medical Advisory Committee, Governmental agencies such as the National Cancer Institute and several State health departments, and finally other epidemiologists who had undertaken a similar solution of one or another of the complex problems of chronic disease. These apparently prolonged consultations and discussions were justified by the realization that this venture would require extraordinarily careful planning, if it were to be brought to a satisfactory conclusion.

Seven possible approaches were submitted to the Medical Advisory Committee for their review, with the full realization that not all would be acceptable or feasible within the limits of the financial support and the time available for this aspect ot the API project. It was also recognized that other limiting factors would also play a part in the decisions both from short and long range points of view. The avenues offered for their consideration are given below. The justification for these recommendations is discussed in detail in Appendix I. It is obvious that the feasibility, value, and priority of the several proposals vary widely. In this ordering, they are listed, without reference to their desirability or practicability, in the pattern established in earlier reports.

1. Historical Survey - To assemble and review the records of known cases in the files of the participating companies.

2. Current Registry - To create by mutual agreement a central file for receiving and tabulating cases as they occur among the employees of the oil companies.

3. Insurance Records - To investigate and utilize insurance and health benefit records for intra- and extramural comparisons.

4. Controlled Field Studies - To repeat and expand investigations that have indicated the existence of hazard due to certain cutaneous contacts.

5. Contact Control Programs - To survey and evaluate for the industry as a whole the programs of personal hygiene that have been instituted.

6. Consultation Service - To offer for the use of the participating companies such services as may be required to establish adequate medical records, and to aid in planning individual investigations.

7. Literature Survey - To collect and review critically the medical literature in the field of occupational and environmental carcinogens.

At the April 1950 meeting of the Medical Advisory Committee and their technical advisors, general approval in principle was given to the several approaches as outlined. For many cogent reasons, acceptance was asked and granted at that time for only two of the suggested studies, namely the "Historical Review" and "Current Registry." It was acknowledged that both would be of little immediate value and that embarking on the latter approach particularly implied a long range effort. The others were held for future consideration, pending better definition of the methods and techniques to be employed and assurance that they would be acceptable to the cooperating companies. (See Appendix I.)

With this limited authorization, clinical and occupational history record forms were devised, based essentially upon the format and the inclusion of items customarily required for notification of occupational cancers to State health departments. Instruction books outlining the reporting mechanisms and the objectives were prepared and distributed in the late fall of 1950. (See Appendix III.) The reports trickled in slowly during the winter of 1950-1951, mainly because many of the companies found that their records did not lend themselves readily to this reporting procedure. Others had to arrange entirely new channels and systems in order to secure and extract the necessary data. Several special field trips were made to further explain the objectives and methods to be employed.

Taking advantage of this necessarily slow progress, and postponing exploration of the remaining approaches, 1951 was used largely to observe at first hand the work of the English investigators and to establish working relationships that would insure ready access to their results. This activity was carried on without reducing the funds available for the investigation, as part of a fellowship program of the World Health Organization project, thereby furnishing an unusual opportunity to bring to the Medical Advisory Committee the findings and underlying philosophies of the British workers in this restricted area of occupational cancer. Later events proved the value of the relationships so cultivated, in keeping open channels for additional information as to developments, particularly in England. The details of the trip are described in the interim report submitted in the fall of 1951.

The historical and current case records came in slowly. By March of 1952, 900 records had been forwarded from thirteen companies. A year later, a total of 1239 cases had been reported by fourteen participants. During 1952 and 1953, the information as received was coded and transferred to McBee Key Sort cards. All of the records were lacking in certain details, but most proved usable in the preparation of simple tabulations. Much time and energy was expended in attempting to complete the records, but in most instances this effort proved unproductive.

Later in 1954, when it seemed likely that a reasonably large segment of the industry would participate in at least the registration of current cancer cases, a major alteration was made in the handling and processing of the reports. The necessary manipulations of the key sort cards had become cumbersome, and the number of analyses possible was necessarily limited. It seemed wise therefore to shift to IBM equipment and utilize electronic sorting for the preparation of more complex tabulations.

Throughout 1955, the work was centered on the development and testing of the new code. The greater flexibility of the IBM permitted the inclusion of many more variables in much greater detail. On the other hand, this change forced discarding of the earlier key sort code and reediting of all the records. With this maneuver, it became apparent that many more reports were deficient, with particular reference to certain features of the occupational history. Additional clerical assistance was assigned to the project, but many of the coding problems finally proved insoluble.

By September 1955, 1877 reports had been received from sixteen companies. Geographical coverage of the industry was almost complete, and an additional company had begun to send in records. Steps had been taken (1) to improve the accuracy and completeness of the records, to insure reporting of all known cases, and to stimulate greater effort in individual companies to obtain information about cases; (2) to include a larger number of employees (ten of the participating companies indicated that their reports represented the cases found among approximately 120,000 workers, but others were sending in reports from only a single refinery); and finally, (3) to secure reporting from all of the major companies represented on the Medical Advisory Committee.

These efforts achieved some results and by April 1956, 2108 records were in the files of the central registry. Participation in the reporting seemed to be gradually widening, but it was evident likewise that many of the companies still had little or no knowledge of the occurrence or non-occurrence of cases of cancer within the bulk of their employees. This deficiency was reported to the members of the Subcommittee on Carcinogenicity of the Medical Advisory Committee. It was indicated that although the notification of cancer cases was not entirely satisfactory, the sample of cases might still be studied in a limited manner if this error proved entirely random. Further, it was pointed out that in order to get a sufficiently large group of cases a much longer collection period would be required.

During the winter of 1955-1956, all of the reports on file were recoded. The transfer of the clinical abstracts, while time-consuming and

laborious, proved to be far simpler than the classification of the principal occupation and the petroleum product with which contact occurred. Only half of the records could be readily separated by the clerks alone, according to occupation. For this reason, a "work assignment" glossary was formulated for the possible use of the personnel departments of the companies, utilizing the various job descriptions as listed on the reports. This was planned jointly with representatives of one of the participating companies who had become interested in the development of a morbidity reporting mechanism and had discovered a similar need for better classification of occupational assignments. It was believed that a carefully considered ordering of the occupations would prove useful to the industry as a whole and would be a significant additional benefit of this aspect of the project.

Late in April 1956, the Medical Advisory Committee, upon the recommendation of the Subcommittee of Carcinogenicity, decided to terminate the epidemiological investigations as of July 1, 1956. The justification for this action stemmed essentially from the failure of the Medical Advisory Committee to secure complete cooperation and greater participation in the reporting of cases. Since the sample would be limited, both in number and kind and the results forthcoming would be of doubtful validity, the Committee was unwilling to support the longer study period required to overcome the reporting deficit. Inasmuch as the occupational coding and transference to cards could not be completed in the two remaining months, it seemed wise to stop all work immediately and reassign the statistical staff to other ongoing projects of The Kettering Laboratory.

Meanwhile, it seemed wise to determine whether the Medical Advisory Committee could find means for supporting the tabulation of reports received through 1956 and the preparation of final summary tables. It was recognized that these comparisons would not be satisfactory, and that little reliance could be placed on the findings. However, so much time and effort had gone into this attempt to relate the site and kind of cancer to specific occupations that it seemed desirable to reexamine the tumor cases, employing the revised occupational classifications, if only to test the capacity of the procedure to reveal suggestive trends.

Late in 1956, this further support was granted, but the final recoding, punching, and preparation of summary tables had to be postponed until the spring of 1957, since the clerical staff of the statistical team was not available immediately. Furthermore, all doubtful or questionable records had to be reviewed individually by the professional staff of the Laboratory before they could be included or excluded. These maneuvers were finally completed late in 1957, with the assembling of the work tables required for the preparation of this final report.

Results

Study Period. When the decision to discontinue the support of the industry-wide registration of cancer cases and deaths was finally made by the Medical Advisory Committee, April 1, 1956, was selected as the closing date for this phase of the API Cancer Project. The study period, therefore, covered approximately six years, running from 1950 through 1955. Reports have and still continue to filter in from some companies and physicians.

These are filed but not processed and are not included in the tabulations and analyses herewith presented. The relative short period of collection and the admittedly small sample of the cases and deaths which occurred during this period also limited seriously the number of comparisons that could be readily made.

Reporting. As indicated earlier, special clinical and occupational record forms were devised for the use of the cooperating medical departments. The first forms were modified slightly after a short preliminary trial, but the information requested was not altered essentially during the study period. The forms were so arranged that the patients were identified solely by number, thus preserving the employer-employee and the professional relationships and protecting the legal responsibilities of the participating companies. The report blanks were modeled after the one designed originally by the New York State Health Department, since this form had been copied widely by other state cancer registries. It was hoped that this similarity would reduce the clerical effort required to assemble the needed data.

At the start of the project, the reports came in slowly, and the response was not uniform for what appeared at that time to be good and sufficient reasons. The first was that certain of the companies had no centralized medical department, no files of earlier cases, and usually no mechanism for notification of deaths or illnesses among their employees. Even in full time medical departments, the central recording arrangements

were recent and there were no past histories, or the recording system employed was not arranged to provide this type of information, or the information was not readily accessible.

Furthermore, this was a tradition-breaking venture. The companies and physicians were required to report regularly and accurately to an unofficial central agency. It has always been difficult to secure official reports from busy physicians, but in this instance additional clerical help and supervision were frequently required of the cooperating company. This made it almost impossible at times to secure the requested information. A few companies remained wary to the end and never released their case histories to the industry pool. Others sent in the cases already in their files and reported subsequently only a scattering or none of their current cases. Some furnished only current records for a year or two. The inadequacies of reporting are quite apparent even with only a superficial study of Table 1* of the Appendix II.

For example, one large oil company with an excellent medical department and an adequate followup among some 26,000 workers has reported 516 new cases within the five-year period of 1951-1955 - an average of 103.2 cases per year. In contrast, only 1367 cases were reported during a six-year period (1950-1955) from seventeen companies from an employee population of at least 100,000. At best, therefore, one will believe that less

*In this tabulation, the 1964 individuals with single neoplasms are distributed according to year of onset and reporting company. Those with multiple tumors are excluded because in some of these individuals the onsets were both before and after the starting date of the current registry.

than half of the cases were reported. It is also noteworthy, although not important to these analyses, that it proved impossible to determine the exact year of onset - as contrasted to the year of report - of more than a third of the cases.

Sex. In Appendix II, Table 2, the 2055 cases with both single and multiple neoplasms recorded in the historical and current registries are classified according to sex and race. Cancer among female employees accounted for only 99 or approximately 5 percent of the total reported. This disproportion obviously reflects the fact that males predominate among the employees of this industry. However, without exact knowledge of the proportion of females, one cannot draw any conclusion from these data.

The female cases both in the historical group and current registry (onset before and after January 1, 1950) are redistributed in Appendix II, Table 3, according to primary site. There were only 19 in the former and 71 in the latter category. Since the samples are so very small, further comparisons are not feasible. However, as one might expect, the distribution of primary sites of the tumors as reported in both classes do not differ greatly from that obtained by the Public Health Service in their 1947 survey.

Race. This is another important variable in carcinogenesis, but unfortunately the records from the petroleum industry as assembled do not permit ready evaluation of its force. Only 31 of the cases were listed as having occurred among negroes, but no information was available for 146. This inability to separate out racial groups stems from the terms of the

Fair Employment Practice Acts which prevent recording of this kind of information on official or company forms. It is particularly unfortunate that while the selection for disease has always a genetic component, the force of social and economic changes now hamper and probably in the future will prevent general investigations of this variable in industrial populations.

Clinical History. This portion of the record was usually filled in very well. Seldom was there need to seek additional information, but some editing and professional interpretation were required for approximately 25 percent of the reports. The questions usually raised concerned the primary site, histogenic type, stage of the disease, and the extent and number of metastases. It became apparent early that the date of diagnosis and the date and kind of treatment could not be readily confirmed or tabulated. When available, this kind of information was coded and transferred to the IBM cards, but acceptable answers were lacking in more than 50 percent of the forms.

Primary Sites. The primary sites were separated according to the classifications originally devised by Dr. Harold Dorn of the National Institutes of Health for the Maryland State Cancer Program. This code also indicates the stage of the disease, as well as the number and location of metastatic sites. It was difficult at times to classify clearly some of the cancers, particularly those of the skin and mucosal surfaces of the lip. Otherwise, the categories proved reasonably sound and adequate, and the cases were easily grouped.

Appendix II, Table 3, rearranges the cases, both historical and current, male and female, according to the primary site of the tumor as reported. A similar distribution (at all ages) of the cancer cases reported from the ten cities included in the study of the National Cancer Institute, is also provided for comparison. The major differences will be noted in the number of tumors of the digestive system and peritoneum among males with onset prior to 1950, and neoplasms of the skin and soft tissue with onset after that date. These variations have been noted in earlier reports. The relative proportions of cases with other primary sites, on the other hand, correspond reasonably well with the U.S. experience.

Type of Tumor. The histogenic types of the tumors reported were classified following the code devised and recommended by the American Cancer Society. This numerical system also permits separation as to the degree of malignancy. It proved very satisfactory for the purposes of the study, and all of the acceptable records were finally coded without undue difficulty.

The tumors reported were largely malignant. Among the cases reported as having their onset prior to 1950, 53 of 668 (7.9 percent) were benign, and of those occurring subsequently, 103 of 1367 (7.5 percent). All subsequent tabulations are limited solely to the distribution of the malignant neoplasms both as to site and kind. The number of benign lesions is far too small to justify a similar study. Eight individuals were reported with multiple neoplasms. Twenty-seven had multiple sites of the same type of tumor.

Occupational History. With the questions in this part of the report form, an attempt was made to secure an orderly chronological listing of the patient's various occupations as well as his specific work assignments in the petroleum industry. This information was sought with the goal of assembling sufficient data to permit the classification, of the affected persons, at the onset of the tumor, according to employment status and work assignments in the petroleum industry, and also as to other contacts with possible irritants, and similar variables. It was recognized that only very gross separations would be possible, and that the severity and duration of exposure could only be approximated. However, it seemed desirable to divide into a few broad categories the hazard patterns of the reported cases for correlation with the type and primary site of their tumors.

The answers received proved most troublesome, both in coding and in the preparation of work tables. As can be seen in the accompanying summary (Table 1), a fairly sizeable proportion (35 percent) of the cases could not be categorized even with the use of very broad occupational groupings. This was true of those having their onset either before or after 1950.

Geographic Location. As the reports were received and processed, they were classified according to the geographic location of the refinery or plant where the employee was working at the time of onset of the tumor. This was done in order to ascertain if climatic factors influenced in any way the relative frequencies either as to primary site or type of cancer among petroleum workers. These data would also permit adjustment of the observed differences that might be related in some way to residence. It has been

MALES WITH MALIGNANT NEOPLASMS

TABLE 1

PETROLEUM OCCUPATION	BEFORE 1950		AFTER 1950	
	NO.	%	NO.	%
KNOWN	367	62.7	744	64.2
UNKNOWN	218	37.3	415	35.8
TOTAL	585	100.0	1159	100.0

shown in many other studies that skin cancers are far more frequent in the South.

In the table on the following page (Table 2), the geographical distribution of the reported cases has been summarized. They have been grouped into four large areas, North, South, Central, and West. Of the 1867 cases reported, 1448 could be so located. It will be noted that more cases having their onset prior to 1950 came from the South, whereas the West increased its proportion subsequent to that date. Cases among marine workers, pipe line crews, and production workers, and those arising outside of the U.S., accounted for 326 of the reports. Fifty-six had too little information to permit classification. As a whole, however, the records were sufficiently complete to permit distribution of the reported cases into these broad geographic categories for comparison with the U.S. experience.

Other Irritants. The record form included questions dealing with exposure to irritants other than petroleum, either in or out of the oil industry. These were phrased and arranged so as to give some information both as to degree, kind, and duration of contact. Unfortunately, most of these items proved too difficult to answer, and while the responses as given were coded and transferred to the IBM cards, no tabulations were prepared for this report. Without accurate knowledge of the work history and, in many cases, without access to the patient, the participating medical directors could not collect these data. It became evident early that only general statements could be made, particularly since most of these hazardous contacts do not occur in the plant environment.

PERCENTILE DISTRIBUTION OF CANCER
REPORTED ACCORDING TO GEOGRAPHIC LOCATION

TABLE 2

YEAR OF ONSET	NORTH		SOUTH		CENTRAL		WEST		TOTAL	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
BEFORE 1950	172	33.1	241	46.4	18	3.5	89	17.1	520	100.0
AFTER 1950	338	36.4	223	24.0	38	4.1	329	35.4	928	100.0

Primary Site. In Appendix II, Table 3, the reported cases with malignant neoplasms are distributed according to sex, date of onset, and primary site of the tumor. The U.S. experience, as collected by the Public Health Service, is included for comparison.

It will be noted that the proportion of tumors of the digestive system and peritoneum, having their onset among males prior to 1950, was much larger than that found in the U.S. as a whole and among the current cases reported after 1950. In the latter group, in turn, the relative number of cancers of the skin and soft tissues was greater. The distribution of other tumors differed only slightly from the U.S. values. No valid comparisons are possible because of the small number of cases reported, but it may be said that in general the U.S. pattern for sites of tumors was paralleled.

In Appendix II, Table 4, the malignant neoplasms having their onset prior to 1950 are redistributed both as to primary site and occupational assignment. The excess of neoplasms of the digestive system and peritoneum carries on through most of the job classifications, even including the unknown group. Thus it seems unlikely that this difference is related to any special occupational factor in the petroleum industry. This point of view is further supported by the finding that there is no concentration of such sites in association with any particular occupation among the cases reported after 1950.

Nearly all of the assembled cases, both historical and current, are derived from a male working population between 20-69 years of age.

With the thought that this biased age grouping might explain, in part, some of the differences in relative numbers of tumors of the digestive tract, the data concerned with U.S. experience were redistributed into the three pertinent broad groups. The results are given in text Table 3. It will be noted that there is much greater correspondence in the relative frequencies. To reinforce further this assumption, the figures of one company that has followed its tumor cases very carefully within recent years were also obtained. (These cases are not included in the API sample.) The pattern of primary sites again was found to be quite similar to the values for the older age groups in the U.S. (See text Table 3.)

The excessive proportion of tumors of the skin and soft tissues in the cases having their onset after 1950 also required some explanation. It will be noted again in Appendix II, Table 4, that there was no obvious association with any given occupational classification. An accounting of the age groupings (text Table 3) failed to explain the difference. Furthermore, the experience of Company X paralleled closely the distribution of the current cases reported by the petroleum industry as a whole. Accordingly, consideration was given to the possible effect of climate and solar exposure. Almost 25 percent of the API cases, as indicated in text Table 2, was reported from oil installations in southern states. In the tabulation of the U.S. experience, only four large southern cities were included. Of these, the climatic conditions in New Orleans and Dallas are similar to those to which the petroleum workers were exposed. These sub-tabulations are given in Appendix II, Tables 9 through 12 inclusive.

PERCENTILE DISTRIBUTION OF CANCER
REPORTED ACCORDING TO PRIMARY SITE

TABLE 3

PRIMARY SITE	U.S. MALES* PREVALENT IN 1947				WHITE MALE EMP. X CO.**	API MALE EMPLOYEES	
	ALL AGES	20-69	20-39	40-69		BEFORE 1950	AFTER 1950
BUCCAL CAVITY	6.9	7.3	6.3	7.3	3.3	3.3	4.1
DIGESTIVE SYSTEM	28.7	31.2	15.0	32.7	30.1	35.0	26.2
RESPIRATORY SYSTEM	12.6	14.1	6.0	14.8	15.2	14.5	15.7
BREAST	.2	.3	.2	.2	.3	.0	.2
GENITAL ORGANS	10.4	8.2	8.6	8.1	7.0	8.6	7.9
URINARY SYSTEM	6.9	7.2	41.2	7.5	5.1	6.5	5.6
SKIN AND SOFT TISSUES	19.3	16.6	21.7	16.0	29.2	15.7	28.5
BONES	.8	.7	2.1	.5	.6	2.1	.8
BRAIN	2.7	2.4	8.1	1.8	2.1	1.7	1.8
LYMPH. AND HEMA. SYSTEMS	6.7	7.6	20.7	6.0	4.0	6.5	5.0
OTHER SITES	4.8	4.6	7.8	4.3	3.1	6.2	4.2

*From "Morbidity from Cancer in the United States," Public Health Monograph, No. 29, PHS of DHEW (1947).
**Personal Communication (Cases reported between 1950 - 1956).

In Appendix II, Table 9, the U.S. experience for males aged 25-64 for the "Ten City" study has been compared with the API group of cases. It is obvious that there is a large difference between the southern and northern cities.

In Appendix II, Table 10, the API tumor cases are divided geographically, and the excess of tumors of the skin in the South, in both the "Historical" and "Current" categories, becomes even more apparent. In this tabulation it will be noted that the U.S. experience with skin tumors, when examined according to broad age grouping as well as geographical location, is essentially the same in all respects as that recorded in the petroleum industry.

A more detailed breakdown of these observations is given in Appendix II, Table 11. In this tabulation, the broad groups of tumors of the skin and the digestive and respiratory systems are separated according to the principal sites included within these categories and are arranged according to the geographical location of the case. The number of tumors that fell into each classification was not large and the differences found were not tested statistically. It is noteworthy, however, that once again the pattern of principal sites follows essentially the U.S. experience as adjusted for geographical distribution.

In Appendix II, Table 12, these same broad groups of tumors have been rearranged according to the major occupational classes and the date of onset of the tumor. It is interesting to observe that the failure

to provide sufficient information to permit occupational grouping was not limited to any particular primary site but was seemingly entirely random. There are some differences in the distribution of the historical and current cases. The tumors of the digestive system, especially those having their onset prior to 1950, stand out again. This phenomenon is smoothed out in the current group of cases.

Without valid data as to the size of the populations concerned, incidence rates cannot be calculated from the numbers of cases. Comparisons, therefore, can only be considered as speculative. Nevertheless, it is interesting to observe that approximately the same number of tumors of the respiratory system were reported among refinery workmen and executives. The very slightly higher proportion of skin tumors in the production and refinery workers might, perhaps, be considered indicative of greater occupational risk. All that can be said of these findings is that they are not remarkable or contrary to what might be expected.

Histological Type. Appendix II, Tables 6 and 8, are tabulations of the histological types of the malignant tumors reported according to sex, date of onset, and occupation. The proportion of non-glandular epithelial tumors is somewhat larger in the API group as compared to the U.S. values. This holds generally in all of the broad occupational classes and with respect to the cases reported before and after 1950.

In text Table 4 these data have been summarized and compared to U.S. experience adjusted for age. The observed differences are increased

PERCENTILE DISTRIBUTION OF CANCER
REPORTED ACCORDING TO HISTOLOGICAL TYPE

TABLE 4

TYPE OF NEOPLASM	U.S. MALES*				API MALE EMPLOYEES	
	ALL CASES AND AGES	NEW CASES 1947			BEFORE 1950	AFTER 1950
		20-64	20-34	35-64		
GLANDULAR EPITHELIUM	22.4	34.2	22.1	35.3	11.3	14.2
NON-GLANDULAR EPITHELIUM	60.1	51.7	43.0	52.5	66.5	69.9
LEUKEMIA	2.9	2.5	4.8	2.2	2.2	1.2
LYMPHOMA	3.8	3.6	8.6	3.1	4.8	4.1
NERVOUS TISSUES	2.0	1.3	3.7	1.1	.7	1.5
VASCULAR TISSUES	.2	.2	.6	.1	.0	.1
MUSCLE	.2	.4	.9	.4	.2	.2
NON-EPITHELIAL TISSUES	2.0	2.1	5.1	1.8	3.2	2.0
EMBRY.-MIXED TISSUES	1.5	.8	2.3	.6	1.0	1.8
NOT CLASSIFIED	4.8	2.6	8.4	2.0	10.1	5.2

*From "Morbidity from Cancer in the United States," Public Health Monograph, No. 29, PHS of DHEW (1947).

by this comparison. If they are valid, the explanation again lies in the biased geographic grouping of the API cases. As indicated in the discussion of the primary sites, the apparently excessive proportion of tumors of the skin could be accounted for by considering the geographic location. Although a similar tabulation was not made for histological types, it may be assumed reasonably that these differences would again disappear.

Discussion

From several points of view, this attempt to estimate by epidemiological techniques the hazard of occupational cancer from exposure to petroleum and its fractions cannot be considered an entirely successful venture. Only two relatively simple approaches were implemented, and neither was expected to do more than to indicate the presence of a possible hazard. Even though the limited objectives were selected, the number of old and current cases assembled proved far too small to permit detailed or elaborate analyses.

Accordingly, only a few pertinent variables were examined, although as many more were of equal interest and concern. On the other hand, the similarities demonstrated in the patterns of distribution between the U S. and the API cases were noteworthy. The apparent differences could generally be explained either because of the age group involved or because of the geographic location of the cases. It is unfortunate that the size of the sample so laboriously collected did not warrant employment of standard significance tests.

The epidemiological work, however, was productive of certain indirect benefits. The interest stimulated by this investigation of cancer among employees of the oil companies carried over into other areas. It pointed up the need for more and better medical supervision, coupled with adequate records of the medical and occupational history of each employee. As a matter of fact, in order to improve their reports, several companies took steps during the study period to insure that such services and information

would be provided. Impetus was given also to the movement for the creation and support of centralized medical departments.

It was recognized almost at once that the reporting mechanisms devised for the tumor studies dealt only with one occupational problem, while there were many other important hygienic matters facing the medical departments. As a consequence, impetus was given to the growing demand for a practical and systematic means of gathering and recording in a centralized agency the accessible data on morbidity and mortality. The benefits to be derived, within a single industrial organization, among the organized units of an industry as a whole, and within a still larger segment of our industrial population, are incalculable. No such data are available now, nor, with few exceptions, will they be in the future, despite the urgent need, unless numerous problems of this type, coming to a social or economic head, make a stern necessity of what is now an opportunity.

The inability to categorize occupational assignments also demonstrated the desirability of clarifying in one way or another "job titles." As indicated in the body of the report, marked differences were found in the terminology employed, as between installations of the same organizations as well as among the various companies. Since the definition of occupational hazard will depend in large part upon an orderly, painstaking recording of work assignments, the need for uniformity and specificity is obvious.

Adjustment for other hazards or stresses in the home, community, or prior (as well as coincidental) occupations remains a vexing and possibly

insoluble problem. It does not seem likely that any adequate mechanism for recording and appraising such influences will be devised readily or soon. It must be recognized that industry cannot demand or otherwise insure reporting of such hazards by all employees despite their potentially important role in the causation or aggravation of disease. The same is equally true of other physical and climatic factors, such as solar radiation, which in relation to the problem under investigation in this instance is of unquestioned importance.

The most important product of this study, especially for the investigators and for the medical and technical personnel of the petroleum companies that have been intimately concerned with it, has been the sharpening of their appreciation of the many and varied problems of occupational health which are amenable to attack by appropriate epidemiological methods when coupled with adequate techniques for medical and environmental appraisals. It became apparent at once that the successful conduct of these studies depends directly upon the industrial physician and his place in the activities of his company. Such a physician must recognize that the provision of the primary data of such investigations is an essential part of his task. Routine procedures and records must be designed to permit easy access to pertinent information for methodical compilation. In so doing, an active, resourceful industrial physician, with the wholehearted cooperation of his management, can participate in fruitful studies far beyond the capabilities of any outside agency. Finally, investigative and advisory organizations can help, but in no way supplant, the industrial medical department in the appraisal of their special health hazards.

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Experimental Work and Report by:
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Date: March 15, 1958

APPENDIX I

Selection of Study Methods

In opening a discussion of the reasons for the selection of methods utilized in this study of cancer among employees of the petroleum industry, it seems appropriate to point out that the investigation dealt essentially with a pure problem in "chronic disease" epidemiology. This usage of the term "chronic disease" excludes such problems as:

a. Residual conditions that may follow acute infectious diseases or accidental injuries;

b. Infectious diseases that may have a prolonged period of clinical reaction or frequent relapses; and

c. Congenital lesions that may result from prenatal factors or intrauterine infections.

The principal objective is to determine the relationship between the occurrence of chronic or degenerative diseases and repeated but, apparently, as they occur individually, insignificant noxious insults. Among the major obstacles to be overcome are the tremendous and possibly insoluble problems - first, of adjusting or taking into account other "competing causes," and second, the importance of the single, versus the cumulative, effect of both "reactive" and "sub-reactive" stimuli. As for the former, consideration must be given to the roles of other extrinsic as well as intrinsic variables. These may be few or many, mild or severe, rare or frequent, depending upon the individual, his occupation, his habits, and his environment. In the latter instance, the repetition of minor infections, exposure to a variety of toxic materials, and other insults over a lifetime may either promote susceptibility or even finally produce the host reaction.

To illustrate these points better, a crude theoretical diagram of the potential chain of causes of one type or another that must be summated in such analyses, is given on the next page. This demonstrates in a somewhat exaggerated way the problem of relating in some fashion all the possible contributing factors Since they will vary in degree, kind, and relative importance at each point, adds only to the complexity of the problems of chronic disease epidemiology facing the investigator.

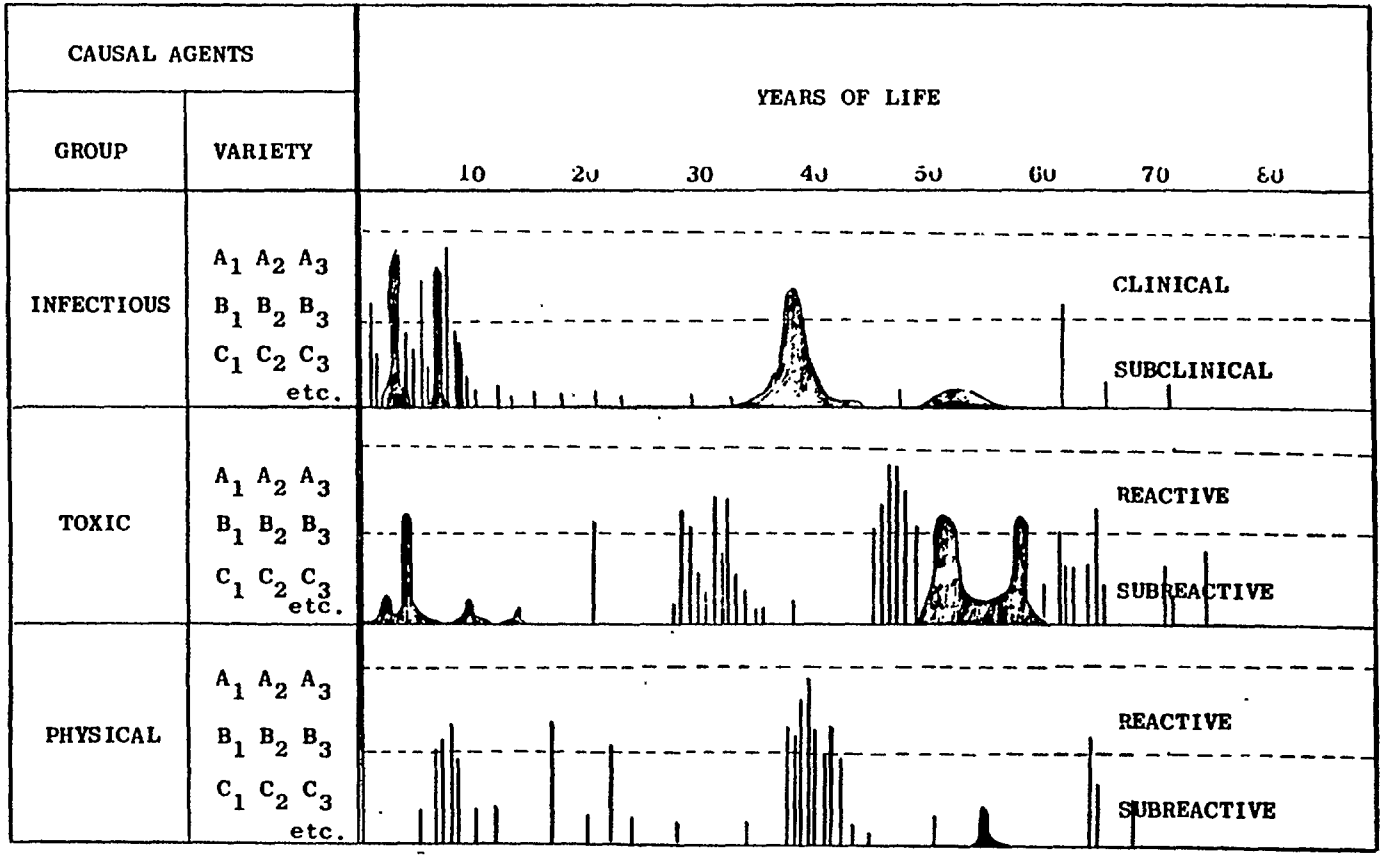
Accordingly, the choice of proper indices and the devising of means to secure the data required to describe and evaluate a particular occupational hazard is neither simple nor quickly accomplished. However, because epidemiological techniques have proved so successful in the elucidation of factors involved in the dynamics of infectious diseases and in the measurement of the effectiveness of control procedures, this approach is suggested more and more for use in the description and identification of causal factors of noninfectious processes.

These attempts can be successful only to the extent to which the degree and kind of exposure required to produce the reaction of the host can be defined accurately and distinguished from all the other possible factors. This becomes then the major problem in the design of an investigation. Some of the deficiencies and gaps commonly found in the medical facilities and in the knowledge of the hazards associated with the work of groups of employees include the following:

1. A lack of, and frequently an inability to provide, periodic, uniform comprehensive medical examinations and/or

POSSIBLE RELATIONSHIPS OF COMPETING CAUSAL AGENTS

DIAGRAM 1



supervision for all of the widely scattered employees of any given company, despite its maintenance of a full-time centralized medical department. Many companies rely entirely on local physicians answerable solely to the local supervisors.

2. A great dearth of accurate and satisfactory medical records, particularly of the type and detail that might be expected to furnish information as to the incidence and prevalence of cancer or any chronic disease, either past or present. This is especially true where a modern medical service has been formed only recently. In many instances, even companies with good all-inclusive medical programs do not maintain record systems by which the diseases that occur among their employees can be enumerated readily.

3. The complete impracticability of describing and categorizing the precise occupational hazards of the employees. This will always be a barrier to the estimation of proper incidence rates according to occupational exposure not only for cancer but any other chronic disease. This obstacle is due generally to the lack of a practical mechanism for recording the occupational assignments of all employees. Such data are usually obtainable from the reported cases, but there is no way to determine the number of individuals with a similar history in any given plant, large industrial company, or the industry as a whole. This situation becomes even more confused by the employment and seniority policies. Furthermore, the technological advances constantly made prove to be equally important variables since they change markedly the nature and the degree of hazard within very short time periods.

Similar questions of equal or greater difficulty can be anticipated in the effort to assemble cases for the numerators of the desired incidence and prevalence rates. This proved particularly true in this special study of industrial carcinogenesis. Among those uncovered during the investigation were:

1. The inability to secure the records of all cancer cases, particularly those with skin neoplasms and/or precancerous lesions. This stems from the customary methods employed by physicians in the treatment of such lesions. A large

majority of these tumors will be diagnosed and removed as a simple office procedure. There will be no request for a pathological study, and the individual employee will not think of reporting the incidents.

2. The availability of only a variable proportion of the cases of cancer among employees that have left employment or retired. Some information can be had if the company maintains or supports a retirement program. However, all too frequently, these records are held by the insurance carrier and are not readily accessible or available. Also, the information generally recorded, such as a death certificate, is not verified. Moreover, usually no feasible mechanism can be utilized or developed for tracing any large number of persons who leave the employ of a given industry.

3. The impossibility of adjusting or accounting in any reasonable fashion for "competing causes" and "cumulative effects." In addition to the occupational contacts, the employees have prior and even coincidental work, community, and home risks. Local climatic conditions, such as sunlight, may play a large part. Many of the employees have other occupations or hobbies. They have significant contacts with other known carcinogens. All these possible variables must be taken into account, especially in relation to environmental or occupational cancer with its long incubation period and a great number of possible etiological agents acting individually, conjointly, and possibly synergistically.

4. The lack of reliable and acceptable evidence as to the relative importance of:

   a. the period and kind of exposure required to induce a cancer. The latter variable will probably be given much more consideration in the future than in the past as knowledge and understanding of the biological activity of carcinogens and particularly the role of accelerators grows;

   b. the difference in reactivity and responses of the individual worker at various ages and situations;

   c. the possible differences in the genetic susceptibility of certain worker groups, especially as related to skin pigmentation; and

   d. the possible variation in susceptibility that may arise from the nutritional status.

These difficulties in the selection and collection of data for the calculation of proper incidence and prevalence rates generally force the investigators of chronic disease, particularly in industrial situations, to rely instead upon "Relative Frequencies," that is the comparison of the proportions of certain types, kinds, or sites of lesions in the various groups. The decision is usually reached reluctantly, since this latter statistic can only indicate and not evaluate the importance of any given hazard. Furthermore, proper controls are not easily found. Ordinarily, the experience of the general or some other industrial population in the same area must be used. Furthermore, the validity of any conclusions that are drawn depend definitely upon the size of the sample and this must be accordingly quite large.

Epidemiologists concerned with the description of factors governing the spread of acute infectious diseases can easily calculate incidence rates since the time and period of exposure in most instances may be disregarded and there is usually no need to take into account other variables. Likewise, while differences in susceptibility are also recognized as a factor, it can be assumed to have an "all or none" role. These limitations also govern, to a large extent, the population groups and the period to be studied. For chronic disease problems, three approaches usually are considered, namely, "retrospective," "prospective," and "closed population or cohort" studies. All three can be carried out by following only a sample of the total group involved.

In a "retrospective" survey, the investigator customarily initiates the observations with individuals or groups who are ill or have died and works backward in time to determine if their habits, living places, or other environmental conditions could have had any causal relationship This method has great advantage in that, providing the patients or groups involved can be easily defined, a search is not required for individuals reacting clinically to the exposure or responding in a way that an objective laboratory test can identify them. Further, since the study extends back in time, the results are more quickly obtained, particularly if a long incubation or latent period is involved. The great disadvantage is that any conclusions that may be drawn depend essentially upon the comparison of the cases under study with the experience of a selected control: Thus, much time must be spent in determining and providing a satisfactory unbiased control group to be studied in a similar fashion. The proper choice of this group all too frequently proves to be a major stumbling block.

In a "prospective" or forward epidemiological survey, selected individuals or a group with common exposures with full prior definition and knowledge of their characteristics and composition are followed for predetermined periods of time accompanied by controlled observations of the particular variables under study. The advantage of this method is that the frequency or incidence as well as the prevalence of reactions, clinical or subclinical, can be readily described in the experimental group. If a sufficient number of workers or subjects can be followed, further and more minute subdivisions and studies according to age, sex, race, and similar

variables are possible. The major obstacle generally is the length of time that may be required to obtain the desired answers. If a long latent or incubation period is involved, observations must be planned for ten or twenty years. Such experiments are not only costly, but the initial size of the sample chosen is determined not only by the expected differences, but must be large enough to allow for the unavoidable losses due to migration or deaths from other causes. Socio-economic variables may also change greatly during the observation period, and in dealing with industrial problems there is always the ever-present danger of great changes in the exposure due to technological advances.

The "cohort" type of study demands an entirely different approach. In it, a group is arbitrarily selected by definition and the total experience is recorded, not only for those individuals who react, become ill, or die, but also all others as well. Knowing when the period of observation begins, the number and time of occurrence of the reaction, valid morbidity and mortality rates can be calculated and compared with those observed in the community. This approach requires access to records that furnish sufficient information to enter and remove individuals from the time period of the study in a reasonably accurate manner in order to calculate "person years." This is not unreasonable for most industrial situations. Recognition of cases is more of a problem unless the reaction is readily recognizable. However, "exposure" can be described far better since it can be sharply defined in the planning and implementation of the investigation.

In considering definitions for use in industrial epidemiological studies, it has been found that "work contacts" as described by an occupational history are influenced greatly by the customary company-union relationships, in that the job assignments and length of such employment depend primarily upon the seniority attained and the frequency with which vacancies occur. In other words, the individual progresses gradually up the ladder, beginning usually as a laborer and mounting step by step to the better positions. There usually is no order in this advancement and, furthermore, no marked specialization as one might expect in highly technical operations.

It was quickly discovered as various industrial situations were studied also that job titles differed greatly from company to company and indicated little if any relationship to the degree and kind of hazard. Men charged with the actual operation of the equipment, for example in the petroleum industry, may have very little or no contact with either petroleum or the various refined products, but the samplers and maintenance personnel may have frequent and heavy exposures. At the same time, maintenance and labor classifications may work in all parts of the refinery or, equally common, be assigned for a significant period of time to a single area. In reviewing the effect of technical changes in the refining processes on the exposure factor, one is immediately impressed by the fact that this is an extraordinarily fluid and dynamic industry. New processes evolve constantly, and this has been particularly true in recent years as companies moved rapidly from "batch" type of operations to essentially "assembly line"

procedures. With this evolution, the degree and kind of contact change markedly. Maintenance problems are reduced, and even the presently widely-spaced "turn arounds" are being subcontracted by many companies.* Consequently, even if accurate and reliable occupational records were obtainable, the local situations are constantly changing and improving so that the exposures of today are much less than those ten years past, and it can be predicted confidently that they are probably much greater than those of ten years hence.

These problems and other likely difficulties to be encountered should long-range epidemiological studies be attempted in the petroleum industry, were discussed broadly and thoroughly. At the November 1949 meeting the objectives were finally described by the Medical Advisory Committee of the A.P.I. and their technical advisors. There was general agreement then that the only way to achieve a uniform understanding of the problems and to insure satisfactory working relationships would be through individual interviews and discussions with the interested medical directors, their scientific advisors, representatives of management, and the responsible investigator. Only by complete cooperation in an over-all joint effort could one be sure of successfully mobilizing their experience in and knowledge of the industry and its medical problems in the organization and implementing logical and feasible studies.

*It must be admitted that, although this development may diminish the exposure hazard for the refinery worker, it may be concentrating and augmenting the danger to the employees of companies specializing in this service-type operation.

During the remainder of 1949 and the next two years, field trips were arranged so that all of the participating medical directors had an opportunity to contribute not only to the basic planning but also to assist in the development of satisfactory reporting mechanisms. It was found desirable to spend much time on the clarification of the legal aspects of the proposed studies to be conducted by The Kettering Laboratory as the companies would be releasing their abstracted but private records to an outside agency. At the same time, similar projects of private and governmental agencies were reviewed such as the National Cancer Institute of the Public Health Service; State and local Cancer Control Units; Medical Centers; and other Research Institutions concerned with various aspects of the cancer problem. Such contacts were directed primarily at determining their interest and participation, past, present, or future, in research on occupational carcinogenesis; to establish working relationships with investigators concerned with this possible health hazard; and to insure that their observations were utilized to the fullest extent in the planning of the A.P.I. project.

From this welter of discussions, meetings, and interviews, some seven approaches were crystallized out for study and evaluation by the participating companies. All had certain advantages and disadvantages, but none could be expected to furnish final and definitive answers to the questions posed by the petroleum industry. These are described briefly in the paragraphs that follow:

1. Historical Review

This required all of the cooperating companies to forward to a central agency (in this instance, the University of Cincinnati) the clinical and employment histories of all the known proved or suspected cases of neoplastic disease that had occurred among their employees in the past. It was conceded that, due to the great differences in the availability and accessibility of such records in the various Medical Departments, the number of cases reported and the period covered could not be the same for all companies.

It was acknowledged also that these reports would not be sufficiently uniform, since they would be sent in from so many sources and arise from an unknown population base, both as to time and exposure, to permit even crude estimations of past hazards. The principal returns expected from the completion and assembling of detailed clinical and occupational forms for cases in the files of the companies would be primarily:

a. the indication of the kind and amount of information that was readily available for inclusion in study, and an indication of additional items that might be required in the future recording of such cases;

b. the training of the staffs of the respective Medical Departments in the mechanics of handling and filing uniform reports and participating in this unique industry-wide recording system. It was hoped that this preliminary "seasoning" exercise would insure better records for the proposed "Current Registry;"

c. the testing of a standardized form as to content and format, with particular attention directed at the development of methods that would permit a reasonably accurate description of the occupational history, and a rough estimation of the degree and kind of work contact not only to petroleum and its products, but other possible "competing" irritants; and

d. that although it could be predicted confidently that the deficit in skin cancer reports would not permit any evaluation of the risk in work exposures under refinery conditions, the relative frequencies of cancer of other types and sites might point to other problems or, in turn, demonstrate that future efforts should be focused alone on skin contact.

2. Current Registry

This second approach envisioned the expansion of the central registration of the historical cases (at the University of Cincinnati) to include reports and occupational histories of cancer patients as they are discovered by and/or reported by physicians to the Medical Departments or any similar responsible and designated office of the participating companies. The pretested standardized and corrected record form would be used, and it was believed that the information obtained in this manner would be much more reliable since the questions would be answered immediately upon notification of the occurrence of a case.

The absolute risk of an individual or a particular population group for a given disease is best measured always by a morbidity or attack rate. The assembling of current cases still would not permit the calculation of such incidence or even crude prevalence rates. Even if all of the companies reported all of their cases and if satisfactory mean populations by broad occupational grouping could be sketchily estimated, the values thus obtained could not be considered accurate descriptions of the actual exposure risk. As indicated earlier, this situation arises from the inability to describe the "worker exposure" in any workable terms for these refinery populations.

However, particularly for chronic and degenerative diseases such as cancer, the "relative frequency" of different types and sites for the lesions in individuals with some common characteristic such as age, sex, race, nutritional status, or occupational history can be expected to give some indication of the presence or absence of some unusual cuasal factor, even though such statistics are known not to be near as sensitive as incidence rates.

It was believed, therefore, that if satisfactory channels for sending and receiving the reports could be arranged with the individual companies through their medical departments, then the comparisons of the relative frequencies of types and sites of cancer occurring in the workers' refineries with similar values for the general population and/or other industrial groups in the same geographical area might indicate unusual hazards. The inherent dangers and difficulties in this approach were fully appreciated, but the proposal merited very serious consideration.

The crux of the problem would be the number of cases that could be assembled and the completeness of the coverage of the industry. To secure a reasonable and worthwhile sample meant that a majority of the participating companies had to report all of their known cases for a significant period of time. At least 10,000 records had to be assembled if the analyses were to be valid, and it was estimated that this would require at least ten years at the rate cases were being seen in a reasonably large segment of the industry.

The only practical solution to the problem of securing adequate reporting would seem to be a slow, persistent, patient approach, gathering what can be assembled from time to time and gaining the trust and cooperation of the groups involved. This is acceptable when long range support is assured and the immediate attainment of a definite and final objective is not essential. It must be reemphasized that the validity of epidemiological observations depends entirely upon the accuracy and completeness of the available medical supervision and records. It follows then that there can be no sound appraisals of occupational hazards until facilities and methods are made available in industry not only for the detection of clinical reactions but for the recording of them in an orderly manner. Occupational assignments and hazardous contacts must be similarly noted for possible future correlations. Even in enlightened interested medical departments, entirely satisfactory mechanisms and procedures have not yet been devised or perfected. Unfortunately for medical science, the acceptance of this need is likely to be slow for some time to come. However, some acceleration may be expected from the impact of health insurance programs and the widening recognition of the importance of industrial exposures for certain chronic diseases.

As a supplementary activity of the central registry, it seemed wise for several reasons to plan the provision of a pathological service. First, because the availability of and easy access to this assistance would insure uniformity in the tissue diagnosis. Second, because of the definite need to stimulate the interest and cooperation not only of the various Medical Departments, but also the local part-time plant and private physicians. Finally, because this action would emphasize the desirability of microscopic examination of all suspicious lesions no matter when or where they occur, as well as serve to standardize the nomenclature used to report their occurrence.

3. Health Benefit and Insurance Records

Most of the participating petroleum companies had health benefit and retirement insurance programs of one kind or

another. One maintained a complete medical care program not only for the employee but also his family as well, supported by joint contributions. All of the medical claims of employees of this company, regardless of kind or degree, were recorded. Like arrangements can be found in other industries operating in the same geographical area and drawing from the common labor pool. Furthermore, a wide variety of industries and different work exposures will carry their insurance coverage with a single company.

Utilization of these records seemed to offer a real opportunity for comparisons of the effect and force of "competing causes." These would include such factors as usual or unusual geographical and community risks, outside plant exposures, and personal habits. However, before an experimental design for this approach could be drawn, ready access had to be assured not only to the health benefit and insurance records of the participating companies but also those of at least one or two other major industries or plants operating in the same geographical area. It was thought that this might be arranged either directly by using the records in the company files or indirectly with their permission, obtaining the required information from the insurance files. The success of this approach would depend essentially upon company policies, the types of medical programs, management interest, and employee-employer relationships. If it proved workable in the petroleum industry, it would result in an exceptional "cohort" type of study with unusual controls. An investigation of such records could be far more extensive and cover more occupational assignments than the "prospective" type of field studies under consideration.

Several major obstacles immediately arose. The first was the need to assemble far more information than customarily required for an ordinary insurance claim. Most insurance carriers do not verify the cause of death since this introduces a serious error and further search for death certificates would be necessary. A second bias, and one always inherent in this problem, arises because skin carcinomas, due to early detection and minor local treatment, will not result in lost time or a medical claim, and so would be undercounted. The third point worthy of emphasis is that in all likelihood only crude mortality rates can be calculated if this approach is applied industry-wide since some of the companies have death but not health programs. Finally, it would still be very difficult to take into account those employees who have left or leave the company rolls for any reason other than retirement.

4. Controlled Field Studies

Two types of field studies had to be considered seriously as possible avenues to be explored in an attempt to ascertain directly the hazard of various degrees of skin exposures. Both require periodic field observations of selected groups of employees with proper controls over a significant period of time. These would be essentially "prospective" investigations and would require support for a significant period of time.

a. Slack Wax Workers

The first of these was the proposal for a repetition of the studies that had demonstrated the increased risk of scrotal cancer among employees involved in processing slack wax. These could be redesigned to take into account process variations as well as climatic differences and answer certain criticisms that had been brought forward in regard to the earlier observations. Racial susceptibility as well as skin pigmentation would also be taken into account. The approach contemplated was a joint effort of The Kettering Laboratory staff, including competent dermatologists, and the clinicians of the Medical Departments of the interested companies.

Insofar as the employees are concerned, these studies could be justified as part of the routine periodic physical examination, and the Laboratory participation would be confined essentially at insuring a standard procedure for the identification and recording of the skin and scrotal lesions. It has been found that the various medical departments were not at all consistent or uniform in their diagnosis and handling of such cases. It was also known that one or two companies had undertaken independent investigations of the probability and risk of skin contact not only in slack wax processes but also other refinery procedures, and it seemed not only desirable but wise to bring together this information from many different sources for the benefit of the industry as a whole.

The principal obstacles, granting that management interest and cooperation was forthcoming, were the technological advances that have been made in this process by the installation of solvent extraction. It is apparent that any prospective study would be too limited to give valid rates for the older methods. Furthermore, the evidence already gathered amply demonstrates the hazard that was present in the past and had already indicated the need for changes in plant and personal hygiene practices.

b. Exposures to Catalytic Cracked Residuals

The second "prospective" field investigation warranting consideration was observation of those individuals exposed to skin contact with petroleum fractions known through the chemical and biological tests to have a high concentration of possible carcinogens and/or accelerators or to be comparatively potent in the production of skin tumors in mice. This method would require careful periodic examinations and notation of the appearance of retrograde, hyperkeratotic or malignant lesions. Again, it would be necessary to take into account variations in processes, as well as climatic conditions, racial susceptibility, and personal hygiene.

As in the instance of the slack wax investigations, the dynamic, almost fluid, state of modern petroleum refining technology would seriously interfere with any attempt to define accurately, for any significant period of time, the degree and kind of work exposure save in the broadest of terms. When this variable is weighed in the light of the relatively long and severe exposure to carcinogenic materials that was required to produce neoplastic disease in man in the past, then process changes become quite important and are difficult to evaluate. Furthermore, this situation is even more complicated by the long interval that may elapse between the termination of exposure and the appearance of a tumor.

It is obvious, therefore, as in the investigation of the slack-wax problem, that the observation of the test and control groups in the refineries would have to be continued and maintained for a long period if one wished to measure the risk of the newer processes. It was to be hoped that the evaluation of the older refinery method could be terminated much earlier, provided adequate occupational histories could be obtained from the workers as they were examined and accepted into the study groups.

5. Survey of Personal Hygiene and Contact Control Programs

Each company differed widely in refinery practices, and it was proposed that arrangements be made for The Kettering Laboratory to assemble, collect, and summarize this information for the industry as a whole. Several reasons were offered in justification of this activity. First and probably most important was the need for a compilation of the contact control programs. A second is the value of classifying in an orderly fashion the probable work exposures that would be

recorded in the occupational histories. The results of such a survey would also be valuable in the planning of special studies such as have been proposed. These data would guide and assist in the selection of plants and/or processes to be studied. Further, the bringing together of this information in a usable form would be helpful in raising the refinery and personal hygiene standards of the industry as a whole.

The items suggested for inclusion in this study were:

a. Manufacturing Activities - i.e., a list of the various processes at that particular plant or refinery;

b. Employee Population - i.e., race, sex, occupational classification, etc.;

c. Employee Facilities - i.e., number of showers, locker rooms, toilet facilities, eating areas, etc.;

d. Hygiene Program - i.e., degree and type of supervision regarding personal hygiene, changing of clothing, etc.;

e. Contact Control - i.e., provision of protective clothing, special equipment or procedures, etc.;

f. Health Education - i.e., objectives, methods employed, degree and type of supervision, etc.;

g. Medical Care - i.e., personnel, equipment and resources, therapeutic and preventive programs; and

h. Insurance Programs - i.e., accessibility of records; extent and type of Medical Care, Hospital Care, Sick Benefit, Retirement Benefit, and Death Benefit Programs.

6. Medical Record Consultation Service

As soon as epidemiological techniques are considered for an attack on medical problems in industry, the clinical and occupational records of the employees as made and maintained by the medical and personnel departments become all important. Yet even a very superficial survey of the situation in this instance uncovered the fact that there were great gaps and serious deficiencies not only in the records themselves but also the mechanisms for tabulating, summarizing, and analyzing the observations. Even though the petroleum industry as a whole is much further advanced in the provision of medical services than industry in the USA in general, it is obvious that a great deal more remains to be accomplished, particularly in relating the medical problems of the employees to occupational factors.

The importance of this point was repeatedly emphasized in the discussion of the various approaches. Accordingly, it appeared wise to provide in some fashion advice or assistance in the devising of medical records and the planning of facilities for their proper analysis. The interest and concern of the industry as a whole with the possible cancer hazard had pointed up the desirability of maintaining adequate medical departments with proper clinical records and occupational histories. This, in turn, had generated a demand for competent assistance in the planning of such facilities, particularly in the preparation and tabulation of medical records.

Moreover, there are other needs of the medical departments to be satisfied with such records beyond the simple question of occupational carcinogenesis. These include the causes of absenteeism and injuries, the incidence of acute and chronic disease as related to the employee, the plant environment, and job requirements. There is no question that the value and many applications of standardized recording methods, uniform tabulations, and evaluation of various indices were generally recognized by the medical directors and their companies.

Consequently, it was proposed in this approach that the University of Cincinnati furnish guidance and advice upon request to any of the participating companies. This could include suggestions as to contents and format of the medical records, first as they concern the cancer problem and later to take in other medical problems. It was believed that the channels developed for the current reporting of cancer cases to a central agency could be utilized in the future for expansion into other areas.

7. Literature Survey

As the importance of occupational carcinogenesis grew and the varied sources of information on this subject were tapped, it seemed desirable to collect and critically abstract scientific articles as they appeared in the medical literature. Abstracts were to be prepared, duplicated, and circulated periodically to the members of the Advisory Committee.

Consideration of this activity could be justified although there are at least two major compilations of this material available. Most of the published information had never been interpreted critically and put in the proper perspective. It would be worthwhile, therefore, as one aspect of the API project, to provide the Medical Directors of the participating companies with current summations and critical reviews of the various investigations in the field of occupational carcinogenesis.

As indicated in the report, these proposed attacks, while considered generally acceptable, were never completely implemented. Only two, namely the Historical Review and Current Registry, were selected finally for exploration. Between 1952 and 1955 the remaining suggested approaches were reviewed many times. Methods and applications were discussed freely and minutely not only at the meetings of the Medical Advisory Committee but with individual medical directors. Active steps could not be taken for two principal reasons. First, all outside or unusual investigations were postponed because of the high priority of technological changes in refining operations brought about by the Korean emergency. Consequently, it proved impossible to secure serious consideration of simple requests for access either to records or workers. Secondly, between 1950 and 1953 there were many innovations in the medical programs of the participating companies, including major shifts in personnel and policies. All in all, it seemed desirable not to insist on expansion of the epidemiological investigations until the entire situation stabilized.

As the project progressed during the later years, the exploration of the possible use of health benefit and insurance records was postponed also time and again because of the cost of this type of review and the great differences in the type and kind of insurance coverage offered by the companies.

During 1954 the medical and occupational records of two major oil companies were carefully reviewed with their medical directors. It

was hoped that at this time an opportunity had been presented to develop feasible methods for the utilization of routine medical and insurance records. Unfortunately, it was found that they did not contain sufficient information nor were they in a form that would permit valid or useful studies.

All thought of "prospective" field studies among refinery populations was dropped almost at once because it became apparent early that investigations of this kind can only be carried out by the individual companies with their own staffs and could not be undertaken readily as a group effort.

Until the discontinuance of the epidemiological phases of the project, advice and help was solicited and provided for the planning of records and record keeping systems in various situations. The literature review proposal was rejected early by the Medical Advisory Committee.

The failure to employ all of the proposed avenues in this essentially exploratory investigation should not preclude trials with such methods in other fields in the future. It was recognized that the selection that was made would not permit the calculation of rates and at best only permit the comparison of "Relative Frequencies." It seemed wiser and far more practical, however, to begin with the records immediately at hand and proceed to the more complex approaches as they appeared feasible.

APPENDIX II

Summary Tabulations

NUMBER OF INDIVIDUALS WITH SINGLE TUMORS AND SITES
ACCORDING TO THE YEAR OF ONSET
AS REPORTED

APPENDIX II - 1

COMPANY	BEFORE 1950	AFTER 1950									ALL CASES REPORTED
		1950	1951	1952	1953	1954	1955	1956	UNKNOWN	TOTAL	
1					NO REPORTS						
2	3	2								2	5
3					NO REPORTS						
4						4	5		3	12	12
5					NO REPORTS						
6	107	74	48	1					20	143	250
7	34	4	9	9	9	13	7		27	78	112
8	80	4	6						4	14	94
9	24	1		4	4				29	38	62
10		2		2	3	5	3		3	18	18
11	15	2		2					6	10	25
12	3	2	1	10	10	15	23		13	74	77
13					NO REPORTS						
14		6	10	8	16	18	18		3	79	79
15	2	2	2	5	4	12	1			26	28
16					NO REPORTS						
17	49	8	13	11	29	30	31	1	48	171	220
18	31	3	2	3	8	8	3		190	217	248
19	14	11	18	16	13	10	4		10	82	96
20					NO REPORTS						
21					NO REPORTS						
22					NO REPORTS						
23	232	15	14	5	9	8	12	1	48	112	344
24	27	5	5	16	10	26	9		15	86	113
25	24	9	12	7	19	16	18		76	157	181
TOTAL	645	150	140	99	134	165	134	2	495	1319	1976

NUMBER OF NEOPLASMS ACCORDING TO
SEX, RACE, MALIGNANCY, AND REGISTRY STATUS
AS REPORTED FROM 17 COMPANIES

APPENDIX II - 2

SEX	RACE	ONSET PRIOR TO 1950			ONSET SUBSEQUENT TO 1950			TOTAL NEOPLASMS REPORTED		
		MALIGN	BENIGN	TOTAL	MALIGN	BENIGN	TOTAL	MALIGN	BENIGN	TOTAL
MALE	WHITE	558	48	606	1100	68	1168	1658	116	1774
	COLORED	20	0	20	11	0	11	31	0	31
	NOT GIVEN	37	4	41	75	30	105	112	34	146
	OTHER	0	0	0	5	0	5	5	0	5
	TOTAL	615	52	667	1191	98	1289	1806	150	1956
FEMALE	WHITE	20	1	21	67	1	68	87	2	89
	COLORED									
	NOT GIVEN	0	0	0	6	4	10	6	4	10
	TOTAL	20	1	21	73	5	78	93	6	99
TOTAL BOTH SEXES		635	53	688	1264	103	1367	1899	156	2055

MALIGNANT NEOPLASMS ACCORDING TO SEX, REGISTRY STATUS, AND SITE OF TUMOR
(ONLY INDIVIDUALS WITH SINGLE NEOPLASMS-SINGLE SITE)

APPENDIX II - 3

SITE	MALE					FEMALE				
	USA * 1947	PRIOR TO 1950		SUBSEQUENT TO 1950		USA * 1947	PRIOR TO 1950		SUBSEQUENT TO 1950	
		NO.	% **	NO.	% **		NO.	% **	NO.	% **
BUCCAL CAVITY 00-0X	6.9	19	3.3	48	4.1	2.2	0	0.0	0	0.0
DIGEST. SYS. AND PERIT. 10-1X	28.7	205	35.0	304	26.2	19.8	5	26.3	8	11.3
RESPIRATORY SYSTEM 20-2X	12.6	85	14.5	182	15.7	2.3	2	10.5	0	0.0
BREAST 30	0.2	0	0.0	2	0.2	22.0	5	26.3	26	36.6
GENITAL ORGANS 40-4X	10.4	50	8.6	91	7.9	25.5	3	15.8	21	29.6
URINARY SYSTEM 50-55	6.9	38	6.5	65	5.6	3.1	0	0.0	2	2.8
SKIN AND SOFT TISSUES 60-6X	19.3	92	15.7	330	28.5	13.1	1	5.3	8	11.3
BONES 70-75	0.8	12	2.1	9	0.8	0.5	1	5.3	0	0.0
BRAIN 76-78	2.7	10	1.7	21	1.8	1.9	0	0.0	1	1.4
LYMPH. AND HEM. SYSTEM 80-8Y	6.7	38	6.5	58	5.0	4.2	1	5.3	2	2.8
OTHER SITES 90-9X	4.8	36	6.2	49	4.2	5.4	1	5.3	3	4.2
TOTAL	100.0	585	100.0	1159	100.0	100.0	19	100.0	71	100.0

* From "Morbidity from Cancer in the United States", Public Health Monograph No. 29, U.S.P.H.S..
** Columnar percentage totals may vary slightly from 100% due to .5 adjustment in each computation.

PERCENTILE DISTRIBUTION OF MALIGNANT NEOPLASMS IN MALES WITH ONSETS BEFORE TO JANUARY 1, 1950, ACCORDING TO SITE OF TUMOR AND PETROLEUM OCCUPATION
(INDIVIDUALS WITH SINGLE NEOPLASMS, SINGLE SITE ONLY)

APPENDIX II - 4

PRINCIPAL PET. OCCUPATION / SITE	UN-KNOWN 00	PRODUCT-ION 01-09	REFINING							TRANS-PORT 80-89	EXEC. AND MARKET 90-98	OTHERS 99
			CRACK-ING 20-29	LUB. AND GREASE 30-35	PARAFFIN 36-39	STR. RUN 40-49	SPEC. PROD. 50-59	MAINTEN-ANCE 60-69	OTHERS 70-79			
BUCCAL CAVITY 00-0X	(9) 4.1	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(3) 2.7	(2) 3.2	(1) 2.2	(3) 3.1	(1) 5.9
DIGEST. SYS. PERIT. 10-1X	(81) 37.2	(3) 15.8	(0) 0.0	(0) 0.0	(2) 40.0	(0) 0.0	(0) 0.0	(37) 33.0	(26) 41.9	(20) 43.5	(31) 31.6	(5) 29.4
RESPIRATORY SYSTEM 20-2X	(32) 14.7	(9) 47.4	(0) 0.0	(3) 50.0	(0) 0.0	(0) 0.0	(1) 100.0	(10) 8.9	(4) 6.5	(6) 13.0	(15) 15.3	(5) 29.4
BREAST 30	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0
GENITAL ORGANS 40-4X	(22) 10.1	(1) 5.3	(0) 0.0	(0) 0.0	(2) 40.0	(0) 0.0	(0) 0.0	(8) 7.1	(4) 6.5	(5) 10.9	(8) 8.2	(0) 0.0
URINARY SYSTEM 50-55	(12) 5.5	(1) 5.3	(0) 0.0	(1) 16.7	(0) 0.0	(0) 0.0	(0) 0.0	(5) 4.5	(4) 6.5	(2) 4.3	(12) 12.2	(1) 5.9
SKIN AND SOFT TISSUE 60-6X	(37) 17.0	(4) 21.1	(1) 100.0	(1) 16.7	(0) 0.0	(0) 0.0	(0) 0.0	(27) 24.1	(7) 11.3	(3) 6.5	(8) 8.2	(4) 23.5
BONES 70-75	(4) 1.8	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(5) 4.5	(2) 3.2	(0) 0.0	(1) 1.0	(0) 0.0
BRAIN 76-78	(5) 2.3	(0) 0.0	(0) 0.0	(0) 0.0	(1) 20.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(2) 4.3	(2) 2.0	(0) 0.0
LYMPH. AND HEM SYSTEM 80-8Y	(7) 3.2	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(11) 9.8	(8) 12.9	(4) 8.7	(7) 7.1	(1) 5.9
OTHER SITES 90-9X	(9) 4.1	(1) 5.3	(0) 0.0	(1) 16.7	(0) 0.0	(0) 0.0	(0) 0.0	(6) 5.4	(5) 8.1	(3) 6.5	(11) 11.2	(0) 0.0
* TOTAL	(218) 100.0	(19) 100.0	(1) 100.0	(6) 100.0	(5) 100.0	(0) 100.0	(1) 100.0	(112) 100.0	(62) 100.0	(46) 100.0	(98) 100.0	(17) 100.0

* Columnar percentage totals may vary slightly from 100% due to .5 adjustment in each computation.

Note: Items in parentheses are actual count total.

PERCENTILE DISTRIBUTION OF MALIGNANT NEOPLASMS IN MALES WITH ONSETS AFTER JANUARY 1, 1950, ACCORDING TO SITE OF TUMOR AND PETROLEUM OCCUPATION (INDIVIDUALS WITH SINGLE NEOPLASMS, SINGLE SITE ONLY)

APPENDIX II - 5

PRINCIPAL PETROLEUM OCCUPATION / SITE		UNKNOWN 00	PRODUCTION 01-09	CRACKING 20-29	LUB. AND GREASE 30-35	PARAFFIN 36-39	STR. RUN 40-49	SPEC. PROD. 50-59	MAINTENANCE 60-69	OTHERS 70-79	TRANSPORT 80-89	EXEC. AND MARKET 90-98	OTHERS 99
BUCCAL CAVITY	00-0X	(15) 3.6	(4) 5.5	(0) 0.0	(0) 0.0	(0) 0.0	(1) 14.3	(0) 0.0	(9) 5.0	(1) 1.5	(6) 4.8	(11) 4.7	(1) 2.8
DIGEST. SYS. PERIT.	10-1X	(109) 26.3	(14) 19.2	(3) 50.0	(1) 20.0	(3) 42.9	(1) 14.3	(1) 50.0	(55) 30.4	(13) 19.4	(32) 25.8	(68) 28.8	(4) 11.1
RESPIRATORY SYSTEM	20-2X	(62) 14.9	(11) 15.1	(2) 33.3	(2) 40.0	(0) 0.0	(1) 14.3	(0) 0.0	(28) 15.5	(9) 13.4	(20) 16.1	(40) 16.9	(7) 19.4
BREAST	30	(2) 0.5	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0
GENITAL ORGANS	40-4X	(27) 6.5	(4) 5.5	(0) 0.0	(0) 0.0	(1) 14.3	(0) 0.0	(0) 0.0	(13) 7.2	(7) 10.4	(18) 14.5	(17) 7.2	(4) 11.1
URINARY SYSTEM	50-55	(25) 6.0	(5) 6.8	(0) 0.0	(0) 0.0	(1) 14.3	(0) 0.0	(0) 0.0	(9) 5.0	(3) 4.4	(7) 5.6	(11) 4.7	(4) 11.1
SKIN AND SOFT TISSUE	60-6X	(124) 29.9	(25) 34.2	(0) 0.0	(2) 40.0	(1) 14.3	(4) 57.1	(0) 0.0	(51) 28.2	(27) 40.3	(30) 24.2	(56) 23.7	(10) 27.8
BONES	70-75	(3) 0.7	(1) 1.4	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(2) 1.1	(0) 0.0	(2) 1.6	(1) 0.4	(0) 0.0
BRAIN	76-78	(9) 2.2	(1) 1.4	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(4) 2.2	(0) 0.0	(0) 0.0	(6) 2.5	(1) 2.8
LYMPH. AND HEM. SYSTEM	80-8X	(24) 5.8	(5) 6.8	(0) 0.0	(0) 0.0	(1) 14.3	(0) 0.0	(1) 50.0	(5) 2.8	(5) 7.5	(3) 2.4	(10) 4.2	(4) 11.1
OTHER SITES	90-9X	(15) 3.6	(3) 4.1	(1) 16.7	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(5) 2.8	(2) 3.0	(6) 4.8	(16) 6.8	(1) 2.8
TOTAL		(415) 100.0	(73) 100.0	(6) 100.0	(5) 100.0	(7) 100.0	(7) 100.0	(2) 100.0	(181) 100.0	(67) 100.0	(124) 100.0	(236) 100.0	(36) 100.0

* Columnar percentage totals may vary slightly from 100% due to .5 adjustment in each computation.

Interactions in percentages are actual count totals

MALIGNANT NEOPLASMS ACCORDING TO SEX, DATE OF ONSET, AND TYPE OF TUMOR
(INDIVIDUALS WITH SINGLE NEOPLASMS, SINGLE SITE ONLY)

APPENDIX II - 6

TYPE OF NEOPLASM		MALE					FEMALE				
		USA *	PRIOR TO 1950		SUBSEQUENT TO 1950		USA *	PRIOR TO 1950		SUBSEQUENT TO 1950	
		1947	NO.	% **	NO.	% **	1947	NO.	% **	NO.	% **
GLAND EPITH.	00-09	22.4	66	11.3	164	14.2	31.1	3	15.8	27	38.0
NON-GLAND EPITH.	11-19	60.1	389	66.5	810	69.9	54.7	12	63.2	38	53.5
LEUKEMIA	20-29	2.9	13	2.2	14	1.2	1.7	1	5.3	0	0.0
LYMPHOMA	30-39	3.8	28	4.8	47	4.1	2.4	0	0.0	2	2.8
NERVOUS TISSUES	40-49	2.0	4	0.7	17	1.5	1.4	0	0.0	1	1.4
VASCULAR TISSUES	50-59	0.2	0	0.0	1	0.1	0.2	0	0.0	0	0.0
MUSCLE	66-69	0.2	1	0.2	2	0.2	0.4	0	0.0	0	0.0
NON EPITH. TISSUES	70-79	2.0	19	3.2	23	2.0	1.6	0	0.0	1	1.4
EMBRY. AND MIXED TISSUES	80-89	1.5	6	1.0	21	1.8	1.3	0	0.0	0	0.0
NOT CLASS.	97-99	4.8	59	10.1	60	5.2	5.0	2	10.5	2	2.8
TOTAL		100.0	585	100.0	1159	100.0	100.0	19	100.0	71	100.0

* From "Morbidity from Cancer in the United States," Public Health Monograph No. 29, U.S.P.H.S.
** Columnar percentage totals may vary slightly from 100% due to .5 adjustment in each computation.

PERCENTILE DISTRIBUTION OF MALIGNANT NEOPLASMS IN MALES WITH ONSETS PRIOR TO JANUARY 1, 1950, ACCORDING TO TYPE OF NEOPLASM AND PETROLEUM OCCUPATION (INDIVIDUALS WITH SINGLE NEOPLASMS, SINGLE SITE ONLY)

APPENDIX II - 7

PRINCIPAL PET. OCCUPATION / TYPE OF NEOPLASM	UNKNOWN 00	PRODUCTION 01-09	REFINING: CRACKING 20-29	REFINING: LUB. AND GREASE 30-35	REFINING: PARAFFIN 36-39	REFINING: STR. RUN 40-49	REFINING: SPEC. PROD. 50-59	REFINING: MAINTENANCE 60-69	REFINING: OTHERS 70-79	TRANSPORT 80-89	EXEC. AND MARKET 90-98	OTHERS 99
GLAND EPITH. 00-09	(24) 11.0	(2) 10.5	(0) 0.0	(1) 25.0	(0) 0.0	(0) 0.0	(0) 0.0	(18) 16.0	(5) 8.1	(4) 8.7	(10) 10.3	(2) 11.1
NON-GLAND EPITH. 11-19	(150) 68.8	(17) 89.5	(1) 100.0	(3) 75.0	(4) 57.1	(0) 0.0	(1) 100.0	(62) 55.4	(35) 56.5	(33) 71.7	(71) 73.2	(12) 66.7
LEUKEMIA 20-29	(2) 0.9	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(4) 3.6	(2) 3.2	(1) 2.2	(4) 4.1	(0) 0.0
LYMPHOMA 30-39	(7) 3.2	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(7) 6.3	(7) 11.3	(3) 6.5	(3) 3.1	(1) 5.6
NERVOUS TISSUES 40-49	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(1) 14.3	(0) 0.0	(0) 0.0	(1) 0.9	(0) 0.0	(1) 2.2	(0) 0.0	(1) 5.6
VASCULAR TISSUES 50-59	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0
MUSCLE 66-69	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(1) 1.0	(0) 0.0
NON-EPITH. TISSUES 70-79	(7) 3.2	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(2) 1.8	(3) 4.8	(4) 8.7	(3) 3.1	(0) 0.0
EMBRY. AND MIXED TISSUES 80-89	(3) 1.4	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(1) 0.9	(0) 0.0	(0) 0.0	(2) 2.1	(0) 0.0
NOT CLASS. 97-99	(25) 11.5	(0) 0.0	(0) 0.0	(0) 0.0	(2) 28.6	(0) 0.0	(0) 0.0	(17) 15.2	(10) 16.1	(0) 0.0	(3) 3.1	(2) 11.1
* TOTAL	(218) 100.0	(19) 100.0	(1) 100.0	(4) 100.0	(7) 100.0	(0) 100.0	(1) 100.0	(112) 100.0	(62) 100.0	(46) 100.0	(97) 100.0	(18) 100.0

* Columnar percentage totals may vary slightly from 100% due to .5 adjustment in each computation.

Note: Items in parentheses are actual count totals.

PERCENTILE DISTRIBUTION OF MALIGNANT NEOPLASMS IN MALES WITH ONSETS SUBSEQUENT TO JANUARY 1, 1950, ACCORDING TO TYPE OF NEOPLASM AND PETROLEUM OCCUPATION (INDIVIDUALS WITH SINGLE NEOPLASMS, SINGLE SITE ONLY)

APPENDIX II - 8

PRINCIPAL PET. OCCUPATION / TYPE OF NEOPLASM	UN-KNOWN 00	PRODUCT-ION 01-09	REFINING							TRANS-PORT 80-89	EXEC. AND MARKET 90-98	OTHERS 99
			CRACK-ING 20-29	LUB. AND GREASE 30-35	PARAFFIN 36-39	STR. RUN 40-49	SPEC. PROD. 50-59	MAINTEN-ANCE 60-69	OTHERS 70-79			
GLAND EPITH. 00-09	(56) 13.5	(8) 11.1	(0) 0.0	(1) 16.7	(1) 16.7	(0) 0.0	(1) 50.0	(25) 13.8	(5) 7.5	(26) 21.0	(35) 14.8	(6) 16.7
NON-GLAND EPITH. 11-19	(288) 69.4	(54) 74.0	(4) 66.7	(4) 66.7	(3) 50.0	(6) 85.7	(0) 0.0	(125) 69.1	(50) 74.6	(87) 70.2	(167) 70.8	(22) 61.1
LEUKEMIA 20-29	(7) 1.7	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(1) 50.0	(1) 0.6	(1) 1.5	(0) 0.0	(2) 0.8	(2) 5.6
LYMPHOMA 30-39	(18) 4.3	(5) 6.8	(0) 0.0	(0) 0.0	(1) 16.7	(0) 0.0	(0) 0.0	(4) 2.2	(4) 6.0	(5) 4.0	(8) 3.4	(2) 5.6
NERVOUS TISSUES 40-49	(6) 1.4	(1) 1.4	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(3) 1.7	(0) 0.0	(0) 0.0	(6) 2.5	(1) 2.8
VASCULAR TISSUES 50-59	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(1) 0.6	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0
MUSCLE 66-69	(1) 0.2	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(1) 0.6	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0
NON-EPITH. TISSUES 70-79	(5) 1.2	(1) 1.4	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(7) 3.9	(2) 3.0	(1) 0.9	(5) 2.1	(2) 5.6
EMBRY. AND MIXED TISSUES 80-89	(4) 1.0	(2) 2.7	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(0) 0.0	(3) 1.7	(2) 3.0	(2) 1.6	(7) 3.0	(1) 2.8
NOT CLASS. 97-99	(30) 7.2	(2) 2.4	(2) 33.3	(1) 16.7	(1) 16.7	(1) 14.3	(0) 0.0	(11) 6.1	(3) 4.5	(3) 2.4	(6) 2.5	(0) 0.0
* TOTAL	(415) 100.0	(73) 100.0	(6) 100.0	(6) 100.0	(6) 100.0	(7) 100.0	(2) 100.0	(181) 100.0	(67) 100.0	(124) 100.0	(236) 100.0	(36) 100.0

* Columnar percentage totals may vary slightly from 100% due to .5 adjustment in each computation.
Note: Items in parentheses are actual count totals.

APPENDIX II - 9

COMPARISON OF PERCENTILE DISTRIBUTIONS OF CANCER REPORTED WITH TEN REPRESENTATIVE CITIES*

PRIMARY SITE	API MALE EMPLOYEES		U.S. MALES 25-64									
	BEFORE 1950	AFTER 1950	ATLANTA	SAN FRANCISCO	NEW ORLEANS	DENVER	PITTS-BURGH	CHICAGO	DALLAS	BIRMING-HAM	DETROIT	PHILA-DELPHIA
BUCCAL CAVITY	3.3	4.1	7.1	10.4	5.0	6.5	6.4	8.4	5.4	6.6	6.7	6.7
DIGESTIVE SYSTEM	35.0	26.2	18.9	25.7	23.4	24.8	31.6	36.8	15.8	21.3	32.5	34.3
RESPIRATORY SYSTEM	14.5	15.7	10.1	12.4	20.0	10.2	14.6	15.2	11.2	11.9	17.7	16.2
BREAST	.0	.2	.3	.4	.1	.8	.1	.2	.3	.0	.3	.2
GENITAL ORGANS	8.6	7.9	7.8	5.9	5.5	2.8	7.5	6.1	7.3	5.4	6.6	6.2
URINARY SYSTEM	6.5	5.6	4.8	6.2	7.2	6.5	7.6	7.8	4.5	3.5	7.9	7.8
SKIN AND SOFT TISSUES	15.7	28.5	35.6	22.9	25.8	26.5	14.7	9.2	40.0	33.1	11.0	11.5
BONE	2.1	.8	.5	.8	.9	.8	.9	.7	.7	.8	.7	.7
BRAIN	1.7	1.8	3.3	2.1	2.0	4.9	2.9	3.2	3.3	4.4	2.4	2.0
LYMPH. AND HEMA. SYSTEMS	6.5	5.0	7.0	8.0	5.5	8.1	7.3	7.5	6.7	8.6	10.5	8.6
OTHER SITES	6.2	4.2	3.9	4.6	4.0	3.3	5.8	4.1	6.5	3.6	4.6	5.2

SKIN, DIGESTIVE, AND RESPIRATORY CANCERS AS REPORTED
COMPARED WITH U.S. EXPERIENCE AS TO AGE AND GEOGRAPHIC LOCATION

APPENDIX II - 10

PRIMARY SITE	AGE	U.S. MALES*						API MALE EMPLOYEES							
		NEW CASES				ALL REGIONS		BEFORE 1950				AFTER 1950			
		ALL REGIONS	NORTH	SOUTH	WEST	ALL CASES	DEATHS	NORTH	SOUTH	CENTRAL	WEST	NORTH	SOUTH	CENTRAL	WEST
SKIN	20-69	16.4	13.0	32.0	24.9	15.9	1.5	6.9	20.7	5.5	16.8	14.2	37.2	18.4	26.4
	20-39	15.3	11.7	37.4	28.2	18.4	2.2								
	40-69	15.6	13.2	31.3	24.6	15.7	1.5								
DIGESTIVE SYSTEM	20-69	33.0	47.8	18.1	27.0	31.7	44.6	36.6	33.6	27.7	22.4	33.7	21.9	28.9	23.1
	20-39	11.6	17.6	9.9	11.6	15.0	25.7								
	40-69	20.5	51.2	19.2	28.3	33.4	45.9								
RESPIRATORY SYSTEM	20-69	14.4	19.8	12.7	11.2	11.2	19.8	8.7	12.4	16.6	10.1	17.7	10.3	23.6	14.2
	20-39	4.7	7.4	4.8	2.0	6.0	10.0								
	40-69	15.1	21.2	13.7	12.0	11.7	20.5								

*From "Morbidity from Cancer in the United States," Public Health Monograph, No. 29, PHS of DHEW (1947).

APPENDIX II - 11

PERCENTILE DISTRIBUTION OF SKIN, DIGESTIVE, AND RESPIRATORY CANCERS REPORTED BY GEOGRAPHIC LOCATION

PRIMARY SITE	U.S. MALES 20-69*						WHITE MALE EMP. X-CO.**	API MALE EMPLOYEES							
	NEW CASES				ALL REGIONS			BEFORE 1950				AFTER 1950			
	ALL REGIONS	NORTH	SOUTH	WEST	ALL CASES	DEATHS		NORTH	SOUTH	CENTRAL	WEST	NORTH	SOUTH	CENTRAL	WEST
SKIN	16.4	13.0	32.0	24.9	15.9	1.5	29.2	6.9	20.7	5.5	16.8	14.2	37.2	18.4	26.4
LIP	8.9	7.2	11.6	11.3	9.4	2.5	17.0	16.6	22.0	.0	26.6	12.5	15.6	42.8	10.3
FACE, HEAD, AND NECK	70.8	72.7	70.8	73.6	72.6	54.6	64.6	66.6	58.0	100.0	46.6	62.5	65.0	57.1	75.8
OTHER	17.6	20.0	17.5	15.6	18.0	42.8	18.4	16.6	20.0	.0	26.5	24.8	19.2	.0	13.5
DIGESTIVE SYSTEM	33.0	47.8	18.1	27.0	31.7	44.6	30.1	36.6	33.6	27.7	22.4	33.7	21.9	28.9	23.1
ESOPHAGUS	8.0	8.8	6.6	5.8	7.6	10.0		7.9	3.7	.0	10.0	4.3	2.0	.0	7.8
STOMACH	31.4	31.0	37.8	31.5	30.4	28.1		19.0	32.0	60.0	35.0	26.3	28.5	27.2	14.4
SMALL INT.	1.0	1.0	.4	1.8	1.0	1.0		.0	.0	.0	.0	.0	2.0	.0	1.3
LARGE INT.	21.6	44.6	23.1	21.2	22.4	23.3		34.9	23.4	.0	35.0	27.1	16.3	27.2	30.2
RECTUM	20.0	20.8	18.2	22.1	22.3	16.0		22.2	18.5	.0	5.0	19.2	16.3	9.0	13.1
BILE PASS.	4.8	4.6	8.3	4.5	4.2	6.0		1.5	1.2	.0	5.0	1.7	2.0	.0	3.9
LIVER	2.0	2.6	2.4	1.6	1.9	2.5		4.7	4.9	.0	5.0	5.2	14.2	9.0	5.2
PANCREAS	8.7	8.1	14.0	9.8	8.0	10.5		1.5	7.4	20.0	5.0	11.4	12.2	18.1	21.0
OTHER	1.9	2.5	2.8	1.6	1.7	1.9		7.9	8.6	20.0	.0	4.3	6.1	9.0	2.6
RESPIRATORY SYSTEM	14.4	19.8	12.7	11.2	11.2	19.8	15.2	8.7	12.4	16.6	10.1	17.7	10.3	23.6	14.2
LARYNX	18.6	18.3	20.1	18.8	27.0	12.4		4.7	30.0	33.3	.0	13.3	17.3	.0	8.5
LUNG AND BRONCHI	77.8	78.1	76.1	76.9	67.3	84.3		76.1	63.3	33.3	100.0	75.0	78.2	100.0	78.7
OTHER	3.3	3.5	3.7	4.1	5.6	3.2		19.0	6.6	33.3	.0	11.6	4.3	.0	12.7

*From "Morbidity from Cancer in the United States," Public Health Monograph, No. 29, PHS of DHEW (1947).

**Personal Communication (Cases reported between 1950 - 1956).

MALIGNANT NEOPLASMS OF SKIN, DIGESTIVE, AND RESPIRATORY SYSTEMS
AS REPORTED ACCORDING TO OCCUPATION IN THE PETROLEUM INDUSTRY

APPENDIX II - 12

	CANCER CASES	PETROLEUM OCCUPATION														
		TOTAL UNKNOWN		PRODUCTION		REFINING		TRANSPORTATION		EXECUTIVE AND MARKETING		OTHERS		TOTAL KNOWN		TOTAL
		NO.	% TOTAL	NO.	% KNOWN	NO.	% KNOWN	NO.	% KNOWN	NO.	% KNOWN	NO.	% KNOWN	NO.	% TOTAL	
BEFORE 1950	SKIN AND SOFT TISSUES	37	40.2	4	7.3	36	65.5	3	5.5	8	14.5	4	7.3	55	59.8	92
	DIGESTIVE SYSTEM	81	39.5	3	2.4	65	52.4	20	16.1	31	25.0	5	4.0	124	60.5	205
	RESPIRATORY SYSTEM	32	37.6	9	17.0	18	34.0	6	11.3	15	28.3	5	9.4	53	62.4	85
AFTER 1950	SKIN AND SOFT TISSUES	124	37.6	25	12.1	85	41.3	30	14.6	56	27.2	10	4.9	206	62.4	330
	DIGESTIVE SYSTEM	109	35.9	14	7.8	77	39.5	32	16.4	68	34.9	4	2.1	195	64.1	304
	RESPIRATORY SYSTEM	62	34.1	11	9.2	42	35.0	20	16.7	40	33.3	7	5.8	120	65.9	182