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The following report has been prepared by the Committee on Occupational Cancer of the Council on Industrial Health.

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OCCUPATIONAL CANCER

METHODS OF EPIDEMIOLOGICAL STUDY

The first form of cancer with an identified causal factor was described nearly two centuries ago. It occurred with unusual frequency among workers in a single occupation and, hence, became known as chimney-sweep's cancer. In spite of the fact that the first knowledge of the etiology of cancer can be traced to Percival Pott's¹ observation on chimney-sweeps, we have no reliable information today from which a reasonable estimate can be made of the proportion of cancers that have some causal relationship to an exposure of occupational or industrial origin. Although a number of specific types of cancer have been associated with occupational exposures since Percival Pott's original studies, there is no reason to believe that these exhaust the possible list of such cancers.

In recent years, an increasing amount of scientific literature has appeared on the subject, confusing, at times, both the physician in private practice and the full-time industrial physician. Part of this confusion arises from the fact that occupational cancer is different from many other well-known occupational diseases, more difficult to identify, and, hence, more difficult to study. Experience has demonstrated that the identification of occupational or industrial causes of human cancer is made difficult by certain characteristics of cancer itself, as well as by labor mobility. Occupational cancers can rarely be distinguished on morphologic grounds from those due to other causes. Furthermore, several years may elapse between the date a worker is first exposed to an agent capable of causing cancer and the time of development of a tumor to the stage where it can be clinically recognized.

From a study of 300 cases of mule-spinner's cancer reported in England and Wales from 1920 to 1928, Henry² found that the time elapsing from

the date of starting work as a mule spinner until the date of diagnosis of cancer ranged from 16 to 63 years and that for 67% of the cases this latent period varied between 35 and 54 years. Several of the workers were no longer employed in this occupation at the time of diagnosis. The average latent period for mule-spinner's cancer is appreciably longer than that for some other forms of occupational cancer. However, a latent period of several years is characteristic of most cancers. For example, the average interval from initial exposure to diagnosis of lung cancer among workers in United States chromate-producing plants was 17.2 years, with a range of 4 to 47 years.³

Finally, there is a "normal" or "expected" incidence of cancer, whereas most occupational diseases do not "normally" exist. Thus, if a man develops silicosis, it probably arose as a result of his occupation, since this disease does not have a "normal" incidence. Accordingly, it becomes necessary in the study of occupational cancer to establish that the disease occurs either at a higher than normal incidence in a given occupation or with a greater relative frequency of site or type, so that there is no doubt about the causal relationship between the disease and the occupation. For this reason, single case reports of silicosis, lead poisoning, or other occupational diseases may make significant contributions to our understanding of most occupational diseases, but individual case reports really contribute little to our understanding of occupational cancer. The same problems have arisen in attempts to relate trauma to cancer—and for the same reasons. These difficulties have led to vigorous debates in the scientific literature, which have perhaps been best summarized by Stewart.⁴

The past three decades have witnessed the birth and large-scale development of experimental methods for the study of carcinogenesis. This has permitted identification of an extensive list of chemical compounds capable of causing cancer in animals in specific experimental situations.⁵ A number of these compounds are encountered in various manufacturing processes. It is not correct to assume from these two facts that the risk of cancer developing

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among industrial workers thereby is either increased or left unchanged. This can be ascertained only by appropriately conducted investigations, and the answer ultimately must be derived from observations on workers in specific occupations and industries.

It is essential, therefore, for the investigator who would study occupational cancer, to have, for comparative purposes, reasonably reliable estimates on the normal incidence of cancer of various types and sites. The collection of such data is a difficult and time-consuming task, requiring almost constant work by a team of trained epidemiologists and statisticians. Cancer incidence increases with age, shows site-specific variations with sex and color, may be modified by geographic factors, and is being continually altered by the aging of the population. In addition, certain specific cancers, such as cancer of the stomach in males, may show unpredictable, unexpected, and unexplained changes in incidence with time. Finally, because of improved diagnostic techniques, greater awareness of cancer, changes in the reporting of disease occasioned by legislative or administrative action, and improved reporting of the cause of death, additional artifacts may be introduced into the calculations. At the present time, the best available rates of normal cancer incidence, prevalence, and relative frequency are those assembled by Dorn and associates.⁶ Annual and special reports of the National Office of Vital Statistics provide mortality statistics for the entire country and for various geographic subdivisions.⁷ Finally, certain states, particularly Connecticut and New York, have assembled similar data.⁸ It is to be hoped that such efforts will be continued and expanded in order that up-to-date, reliable figures will be available for the necessary comparisons, not only to aid occupational cancer studies but also to keep abreast of decade-by-decade changes in cancer incidence and distribution.

The physician of today, and increasingly in the future, will be called on to provide answers as to whether the increased use of a chemical or the introduction of a new chemical has increased old hazards or introduced new ones. If the advancement of the chemical age and the anticipated improvements in standards of living continue, it will be necessary for the physician to keep well in mind the caution so well phrased 10 years ago by Stewart⁴: "It is probable that with the development of chemical industry we will see new chemical cancers and medicine must be on the watch for such developments. But it must refrain from hastily ascribing to industry those tumors whose incidence falls well within the expectations for the population as a whole and from making premature conclusions based on lack of appreciation of statistical methods."

While the study of occupational causes of cancer is complicated, it is not impossible. Since the area of investigation is so broad, a great deal of time and energy can easily be spent in fruitless study unless some preliminary idea can be obtained of those occupations which appear to be associated with cancer hazards. The principal support for such ideas or hypotheses is clinical impressions derived from the study of individual cases of disease and the analysis of existing records of morbidity and mortality. Accordingly, it is believed worthwhile to describe various sources of data now available and to indicate, in summary fashion, certain approaches and techniques that may prove fruitful.

Official Statistics

The official certificate of death required for each deceased person in the United States provides for the entry of his usual (and probably last) occupation and industry. Very little use has been made of this source of information, largely due to uncertainty concerning the comparability of the entries for occupation and industry on death certificates with corresponding data from the census of population. Information on this point soon will be available from current study of the corresponding entries for occupation and industry found on the death certificate and on the 1950 census schedule for a sample of deaths.

At best, official mortality statistics provide a measure of the total effect of an occupation and the general level of living of persons following that occupation. Specific occupational hazards are not likely to be identified by a study of these records. Only one entry for occupation is requested, and frequently either no occupation or an entry of "retired" is reported for persons who have stopped working because of old age. Occupations are described only in general terms, so that it is not possible to identify specific groups of workers who are thought to have been exposed to a suspected health hazard. Furthermore, each industry, and usually each individual company, employs entirely different names for the same job assignment.

In spite of their many defects, mortality statistics, if analyzed with imagination, may provide clues to occupational or industrial hazards which can be explored by more specific studies. The following examples illustrate the types of studies that have been made with death certificates.

Mortality Rates by Occupation.—The information on cause of death and occupation and industry on death certificates and census reports can be used to compute death rates from different forms of cancer. The most extensive series of death rates are those published by the Registrar General of England and Wales. References to these data may be found in an article by Kennaway.⁹ A comprehensive study of occupational mortality in the United States has never been made. The National

Office of Vital Statistics has initiated a study based upon deaths occurring during 1950, the preliminary results of which have been reported.¹⁰

Mortality rates by occupation can be computed for the population of specific localities, for example, a city or county, provided the number of workers is large enough to yield reliable rates. The information needed for such studies is (a) the number of deaths of persons in each of the occupations to be studied, and (b) the total number of persons in each occupation classification by age and sex. The number of deaths can be obtained from the local or state office of vital statistics; unless special information is available locally, statistics concerning the number of workers by occupation must be obtained from the U. S. Bureau of the Census. Studies should be done for a period near the date of the census of population in order to avoid the necessity of preparing population estimates. A good illustration of this approach has been reported from Sheffield, England, by Turner and Grace.¹¹

Mortality Rates for Specific Areas.—The analysis of mortality statistics for cancer of specific sites for local areas, such as a county or group of counties, may be undertaken in order to determine whether an unusually high death rate or an unusually large proportion of deaths exists for a specific form of cancer. Available information concerning possible environmental hazards may be studied simultaneously to determine if there are any that appear to be associated with the known facts about cancer mortality.

These studies may be conducted by systematically studying the variation in cancer mortality among the counties of a state, as was done by Mancuso and others¹² in Ohio, or by analyzing mortality from cancer in an area where an industry whose workers are thought to be exposed to some cancer hazard is located. Projects of this kind are most likely to yield useful leads if a large proportion of workers in the area are employed in a single industry. Mortality rates for total cancer and for cancer of specific sites by age and sex can be computed for a period of several years. If the population under observation is too small to yield reliable age and sex specific death rates, an expected number of deaths can be computed by multiplying the population of the local area distributed by age and sex by the death rates for some appropriate standard population, for example, the population of the state in which the local area is located. The expected number of deaths is then compared with the observed number. For comparative purposes, similar computations should be made for other counties that do not have an appreciable number of workers in the industry in question.

If the deaths of persons who have been employed by a specific industry can be identified, a comparison of the causes of death in this group with those of the rest of the population can be

made. The study by Hill and others¹³ of workers in a factory handling inorganic arsenic compounds is an excellent example of this method.

Mortality from Specific Forms of Cancer.—Since most of the carcinogenic agents of occupational origin that have so far been identified cause cancer of a specific site, several studies have been made in Great Britain, based on death certificates, with a specific type of cancer, for example, cancer of the skin as the cause of death.¹⁴ The usual procedure has been to review all death certificates filed in a specified area for which population data are available and to compute death rates by occupation. The areas selected for study have been either the entire country or a specific local area where the existence of a cancer hazard is suspected.

Social Security Records.—The records maintained by the Bureau of Old-Age and Survivors Insurance, Social Security Administration, Department of Health, Education, and Welfare, include the employment history of all workers covered by the act since January, 1937. Information may be obtained concerning the name and address of each employer, the dates of employment and the industrial classification of each employer according to a four-digit code. These records may be used by themselves or in conjunction with official vital statistics for studies of mortality among persons who have worked in specific occupations.

For example, one could start with a list of persons who are known to have been employed in a given occupation or industry. Although detailed information usually will not be given out for persons who are still living, the date of death and employment history can be obtained for persons who have died. In this way the subsequent history of part or all of the workers who have left the occupation can be traced. Alternatively, one could start with a group of persons who have died from a specific form of cancer and obtain their previous work history. A control group of persons who died from causes other than the type of cancer being studied should be investigated simultaneously in order to judge whether the number dying from cancer who had worked in a given occupation was large enough to suggest the existence of an occupational hazard.

Occupational Disease Reports.—A survey conducted by the United States Public Health Service in 1953 found that only 28 states had statutes or regulations requiring physicians to report patients suffering from occupational diseases. No serious attempt is made to promote compliance, so that the regulations often are ignored.

A much larger number of occupationally induced diseases are reported in connection with claims for workmen's compensation. About one-half of such diseases are skin disorders. Among the remainder, complaints due to physical conditions of the working environment, systemic effects of chemicals, and

infectious diseases are the most common. At best, the claims give only a rough indication of the occurrence of the types of complaints reported. Even where awards have been sustained for occupational cancer, the validity of the alleged causal relationship frequently fails to satisfy critical and competent medical judgment. Neither official reports of occupational diseases nor claims for workmen's compensation have yet yielded useful information concerning the incidence of occupational cancer in the United States.

In contrast, the Factory Inspection System of Great Britain has been an important source of information about occupational cancer. The first medical inspector was appointed in 1898. As presently organized, the medical staff is responsible for the promulgation and supervision of regulations for various occupations, the investigation of cases of industrial poisonings, the study of new industrial processes that may be injurious to health, and the supervision of the work of physicians who give certificates of fitness for work.

A list of lesions that may be caused by known or suspected carcinogenic agents has been established, and these must be reported to the Chief Inspector of Factories. This information is supplemented by inspection of plants where possible carcinogens are produced or handled. Special studies have been made of cancers developing among workers engaged in the extraction, processing, or use of shale oil, petroleum products, asbestos, nickel, and dyestuffs. In 1947, for example, Henry¹⁵ published an analysis of 3,753 skin cancers in 2,975 persons reported to the Chief Inspector of Factories from 1920 to 1945 inclusive. Pitch, tar, or tar-products accounted for about 60% of these cases; shale oil, mineral oil, or bitumen caused most of the remainder.

Insurance Company Statistics

Life Insurance.—Life insurance company follow-up studies have the special merit that they usually deal with relatively large numbers of persons who can be automatically traced for long periods of time through the circumstance of their being insured. A suitable standard of comparison is available in the experience of the aggregate body of insured persons of the particular type. Moreover, in the absence of national mortality statistics by socioeconomic classifications, the experience of different groups of insured persons sheds some light on the relative prevalence of cancer in different socioeconomic classifications.

Life insurance companies maintain detailed records of death claims, disability claims, claims for hospitalization, surgical benefits, and medical expense benefits, as well as special records for medicoactuarial studies and, occasionally, records of periodic health examinations of their employees also. All of these can be tapped for information

regarding the prevalence of cancer. It is important to realize, however, that the records maintained by life insurance companies are prepared primarily for administrative purposes and only incidentally yield information about the prevalence of cancer among insured persons.

Generally speaking, from death claim records and records maintained on the insurance in force, it is possible to compute death rates by age, sex, and race for various classes of insured persons. The experience of industrial policy holders of the Metropolitan Life Insurance Company has been reported in a number of studies,¹⁶ which show for the years 1911-1955 the mortality rates by age, sex, and race from cancer of the following sites: digestive organs, female genital organs, breast, buccal cavity, skin, lungs and pleura, bladder, prostate, and other organs. Current information along these lines is published in the Statistical Bulletin of the Metropolitan Life Insurance Company.

Because the applicant's occupation is usually a major factor in determining the life insurance risk, such information is given on the application for insurance. It is often possible, therefore, to calculate the cancer mortality among insured persons by industry or occupation. However, occupation is usually available only to the insurance company at time of application for insurance or at time of death, intermediate occupations ordinarily being unavailable.

The records for group life insurance (that is, insurance issued to groups of employees generally with the cooperation of and contributions from the employer) have been used to calculate cancer death rates for all employees actively at work in particular industries. It should be noted that the cancer death rates for all employees actively at work in an industry so covered may not be significantly higher than average. Yet there may be some processes in that industry in which relatively small numbers of men are employed and which are associated with very high cancer death rates. However, it is frequently possible to determine cancer death rates for individual plants, and, if these plants concentrate on specific processes, the cancer death rate associated with such processes can be derived. A study covering the period 1927-1934¹⁷ indicated significantly higher than average mortality among felt hat makers, tube, rod, and pipe mill employees, paper manufacture employees, hotel and restaurant workers, shoe and light leather goods producers, and employees of electric and street railways.

In recent years a number of corporations have become interested in the mortality from cancer of specific sites among their employees, and such studies have been made in various industries or plants from group life insurance records. The customary procedure has been for the employer to approach the insurance company and request that

a study be made. Inasmuch as the relationship between the holder of a group life insurance contract and a life insurance company is confidential, a life insurance company is not free to publish the results for individual concerns. However, investigations made on an industry-wide basis are not subject to this restriction. At the present time, about 36 million persons are insured under group life insurance policies, and these include most of the employees of the larger companies in the major industries.

Industrial Insurance.—The records for industrial insurance (that is, insurance issued to individuals in small amounts on which premiums are payable weekly or monthly, usually collected at the home of the insured) can be used to compile cancer death rates according to the occupation of the insured at the time his policy was issued. It is usually also possible to ascertain the occupation of the policyholder at the time of his death. A large proportion of the adult males so insured are employed in industry. About 20 million adult males are currently insured under industrial policies, and these include, chiefly, the lower paid urban wage-earners.

From several studies made in the Metropolitan Life Insurance Company (based on the occupation at death), it would appear that the following occupations have been associated with higher-than-average death rates from lung cancer: copper-smiths and tinsmiths, painters and varnishers, and roofers and slaters. Less definite, but suggestive, have been the findings for such occupations as machinists and mechanics, railway enginemen and trainmen, proprietors and bartenders of drinking establishments, brick and stone masons, plumbers, steamfitters and gas fitters, and tailors and other clothing workers.

Special medicoactuarial records maintained by most of the larger life insurance companies on ordinary life insurance (that is, insurance issued to individuals in amounts of \$1,000 or more) lend themselves most readily to the computation of cancer death rates according to occupation of the insured at the time the policy was issued. However, the last intercompany study of mortality among persons with ordinary life insurance according to occupation was made in 1937. This and earlier investigations indicated that cancer mortality was high among waiters and cooks, hotel keepers, guards, watchmen and janitors, painters and brick and stone masons, and tailors and clothing operatives. When studies of this kind are undertaken in the future, they will probably be made under the aegis of the Committee on Mortality under Ordinary Insurance and Annuities of the Society of Actuaries. About 60 million persons are currently insured under ordinary policies, comprising mostly middle-class males in nonhazardous occupations.

It is important to bear in mind that the records maintained by life insurance companies can merely indicate the fact that cancer mortality has been high in certain occupations. It does not by any means follow that such cancers are occupational in origin. Additional investigations must be made to determine whether the association is causal.

The records of accident and health insurance companies on operations and treatments for cancer provide another starting point for investigations of cancer mortality. However, in such instances an elaborate and costly machinery would be necessary to obtain a reasonably complete follow-up. Such a follow-up is automatically obtained where a person carries life insurance. The disability claim records of life insurance companies can be used as a means of determining the survival and recovery rates among persons insured under ordinary life insurance policies who submit disability claims on account of cancer. Such disability claim records usually contain more detailed information as to the site and type of cancer than do claim records. Furthermore, persons insured under ordinary life insurance policies who submit disability claims on account of cancer can, as a rule, be traced after recovery to determine the rate of recurrence of cancer.

The records of periodic health examinations of life insurance company employees have a potential value for the investigation of the natural development of cancer in its preclinical stages, even though employment by a life insurance company does not carry any known occupational cancer hazard.

Industrial Records

The use of public health and insurance company statistics in the study of occupational cancer can at best only indicate areas in which detailed studies should be undertaken. These must be undertaken within the industry itself and require the careful cooperation of several different groups. Since exposure within industry is far more likely to be greater than outside of industry, it is probable that studies conducted in the primary producers of a chemical will be more productive than studies of secondary users. Such investigations are difficult and time-consuming to conduct, and unless planning for them is undertaken in advance, they may be impossible to complete.

The reason for the lack of such planning in the past is found in the history of industrial medicine. At the turn of the century, industrial medicine was primarily concerned with the treatment of accidental injuries. This state of affairs still exists in many industrial plants, although the more progressive industrial physician is increasingly recognizing the importance of preventive and constructive health measures. Intensive safety campaigns and much safety engineering have reduced indus-

trial accidents to the point approaching the infinitesimal. Thus, only 3% or less of absenteeism in industry is due to in-plant accidents. The increasing importance of preventive-constructive measures in industrial medicine is attested by the recent recognition granted occupational medicine as a section of the American Board of Preventive Medicine.

Suspicion for the existence of an occupational cancer may also arise from the clinical judgment of the physician. Many medical advances have arisen out of the "clinical hunches" of well trained and observant physicians. It is necessary only to point out that the clinical hunch can do no more than arouse suspicion, it neither proves nor disproves the existence of occupational cancer. However, when the clinical hunch serves as the basis of careful, detailed study, it may lead to significant advances in our knowledge. Such clinical hunches may arise out of a physician's being impressed by the number of cases he sees in a relatively restricted group, by corollary clinical findings in individual cases, or even by inquiries from the workers themselves, the answers to which he may not know but yet feel obligated to develop. The increasing potential significance of occupational cancer arising from the increased quantity and diversification of chemicals used in or made by industry places an increasing responsibility on the industrial physician, full or part-time.

When a suspicion has arisen, from studies of public health or insurance statistics as outlined above, by clinical judgment, or from an unusual location of a cancer, such as scrotum or bladder, that an occupational cancer may exist in a given industry, subsequent studies follow a pattern which it may be helpful to outline. The first step is to obtain all of the cancer cases of that industry for a period of time (perhaps 5 or 10 years) and to analyze them for over-all incidence in the industry. It is recognized immediately that the first requisite is that some system of cancer reporting within the industry is necessary. Let us assume, for example, that in a given industry 50 cases of cancer have been reported over the past 10 years. If this occurred in an industry in which there was an average annual employee census of 200, this would represent an incidence of 2,500 cases per 100,000 per year, which would be distinctly abnormal. If this incidence happened in only one year, it could well be a statistical artifact, hence, it is important to have the study encompass more than one year. On the other hand, if this occurred in an industry in which the average annual census was 2,000, this would represent an incidence of 250 per 100,000 per year, which would be just about the anticipated rate. If it happened in an industry with an average annual census of 20,000, this would represent an incidence of 25 per 100,000 per year. Such a result would clearly be so much below the expected that

it should be immediately evident that only about 10% of the cases are actually being reported with the system used. Such a result should lead to a critical evaluation of the effectiveness of the reporting system. More detailed studies would be futile in this stage unless the cancer being studied is of an unusual site, such as the scrotum or bladder.

Let us assume, however, that an incidence of 250 per 100,000 per year has been determined. The next step would be to analyze the cases by sex. Thus, if it were found that 40 of the 50 cases occurred in men and that about 80% of the employees were male and 20% were female, the incidence rates of the sexes would be approximately the same. On the other hand, if 40 of the 50 cases occurred in men in an industry in which only 20% of the population were men, it would certainly be suggestive of two situations: first, that the incidence in men was suggestively high (i. e., 1,000 per 100,000 per year) and second, that the incidence in women inordinately low (i. e., 60 per 100,000 per year). Both situations would warrant further study in an attempt to understand the causes.

The next step in the procedure would be to pull out the medical record of each of the 50 cases reported and study it in great detail. The importance of an adequate medical record, containing a maximum of information and documented by originals or copies of laboratory reports, x-ray reports, biopsy reports, summaries of hospitalizations, autopsy records, and death certificates (when death has been the result), now becomes apparent. In looking to the future, every physician, and particularly every industrial physician, can understand the importance of the maintenance of adequate industrial medical records. It is apparent that if the industrial medical record is inadequate the promise of rewarding results from the detailed study of them is indeed remote.

However, after the medical records have been found adequate, detailed studies of them will now permit the proper classification of cases. For instance, such studies may reveal that cases reported as lung or liver cancer are, in reality, metastases of cancers of different primary sites. They should, therefore, be reclassified as to the primary site of origin. In addition, it may be found that certain conditions initially believed to be cancer and reported as such have been found on detailed study to be some disease other than cancer. The initial report on such cases may never have been changed and the cases carried erroneously as cancer cases. Such detailed study, therefore, may lead not only to an alteration of the total cases reported but also to changes in the distribution of cancer cases in organ systems.

This detailed study of the medical record also permits all cases to be classified by age at apparent onset of the disease. This study may be rewarding

because if it is found that the average age at onset of cancer, either in general or in site-specific situations, is significantly lower than in the general population this itself may be justification for pursuing the studies further.

The next step in the procedure is to obtain an occupational history on the individuals with cancer. This is not an easy task, since the individual himself, if still living, may not remember all of the various occupations he has been involved in, even within one industry. At this point, the personnel and/or payroll office may be of great assistance to the investigator. Because it is necessary for industry to know the cost of its finished goods, cost accounting records are usually maintained. Since different jobs may demand different rates of pay, it is frequently possible by reviewing such records to follow a man's career within an industry in quite specific detail, at least as far as different departments and the major classifications within each of these departments are concerned. A study of such occupational records may then provide a further clue for the continuation of these studies. Thus, if an inordinate number of cancers appear among one group of workers or if cancers of a specific site all occur in men with a long service in one department, further detailed studies again may be warranted.

At this stage, the numerator of the incidence equation is available, but the denominator is not. This equation is as follows: Incidence (cases per 100,000 per year) = total number of cases for n years $\div$ population at risk $\times n \times 100,000$. Let us assume that, at this point, examination of the records shows that there are 10 cases of lung cancer among gadget wreckers. Further review of the records discloses that among these 10 persons the minimum service as a gadget wrecker is nine years. Two more men have had 10 years of such service, one 11, two 13, one 15, one 18, one 23, and one 25 years. It would then be extremely helpful to the physician if he were able to obtain from the personnel department the number of men who have worked nine years or longer as a gadget wrecker. This figure would supply him with the denominator in the above equation. Thus, if our study encompasses 10 years, ending Dec. 31, 1955, and 100 men have worked nine years or more as a gadget wrecker by that date, the equation becomes as follows: Incidence = $10 \div 100 \times 10 \times 100,000 = 1,000$ per 100,000 per year. This incidence of lung cancer is some 30 times the expected incidence in men of all ages and about 14 times the expected incidence in men over 45 years of age.

It might appear that the study is now complete, but actually it should proceed further. The next step would be to obtain from the personnel department the names of all men who have ever, regard-

less of the duration of such work, worked as a gadget wrecker. Then the medical records of each of these men should be reviewed in order to insure that no cases of cancer have been overlooked. Experience in occupational cancer studies has shown that this review may frequently uncover proved cancer cases among these medical records, which, for one reason or another, may have escaped reporting. It is conceivable that such studies will reveal cases with an exposure time which is less than the previous minimum uncovered in the reported cases and, hence, may require revision of the population at risk. This type of analysis of medical records will insure that no cases have been missed. The collection of data on total employment in the department will permit analysis of cancer data in a variety of ways, most of which will give negative results which only serve to establish more firmly the significance of the positive results in the more selected groups. Thus, analysis of incidence rates for all men employed one day or longer, 5 years or longer, 9 years or longer, and 15 years or longer may show no statistically significant increased incidence until employment has exceeded 9 years, and an increasingly significant increase the more employment has extended beyond 9 years. It is obvious from what has been said that when the incidence rates have been determined they should be analyzed for statistical significance in comparison with the expected rates in the general population. This analysis should generally be performed by someone well acquainted with statistics as applied to biological problems. This is important because a four-fold or five-fold increase in incidence, which may appear on the surface to be significant, may really not have any significance statistically because of the small number of cases.

In addition, consideration should be given to the possibility that a difference in the characteristics of the industrial population and the general population with which it is compared may account for the observed difference in incidence. The incidence of cancer of specific sites is known to vary by age, sex, race, and geographical region, so that the possible effect of these factors should be investigated in the interpretation of differences in incidence rates.

Finally, when these rates have been determined, one last step may be worthwhile. This is to go to the foreman of the operation involved and inquire about the existence of shift books. A careful study of such shift books may reveal a pattern of occupation by subdivisions in the department which cannot be determined from the records maintained by the personnel and/or payroll office. It may be found that, although 100 men work in a department, perhaps only one-half or one-quarter of them are involved in one particular operation of the de-

partment and that all of the specific cancer cases are to be found among those men performing this specific operation. This final study may be of great importance from two standpoints: first, it may increase the significance of the incidence rates, and second, it may serve to pinpoint the exposures and, hence, lead to the easier detection of the carcinogenic agent and, thus, to its ultimate control.

It is necessary to point out that, in small industries with a heavy labor turnover and also in certain industries with problems peculiar to the industry, such as the construction industry, industrial medical records may be quite incomplete or even lacking. In such cases, obviously, the above techniques cannot be applied. Other methods, such as the use of social security records or high-caliber union medical services, may need to be developed for statistical, epidemiological studies of this nature. In these cases, again, the first requisite will be the collection and periodic analysis of adequate medical records.

From what has been said above, it can be seen that occupational cancer studies even within an industry can be laborious, time-consuming procedures. There are no real shortcuts to such adequate studies, and attempts to perform "quickie" or ill-conceived studies may lead to very misleading results. Adequate studies require the services of a physician who is interested in such studies and trained well enough to determine the adequacy of medical records. He must also have enough familiarity with the industry being studied in order that occupational histories will have some meaning to him. He must, in the course of such studies, enlist the support of the personnel and/or payroll departments, a competent biostatistician, the foreman, and other groups within the industry, including, particularly, engineers and chemists who are familiar with the operations being studied. Finally, he needs, for comparative purposes, age, sex, and site-specific incidence rates for the general population and for segments of the population more comparable to those he is studying, if his group differs in any significant way from the general population.

The above comments outline certain requirements for the future which will greatly assist in the performance of occupational cancer studies. First, and most important, are adequate industrial medical records. Second is a mechanism of recording and reporting disease which is capable of periodic analysis. This suggests McBee sort cards and IBM or other mechanical methods of analyzing data. Third is a mechanism of recording occupations and the occupational exposures of various segments of the working force. These occupational data must be capable of mechanical analysis so that a periodic running survey of occupational exposures, including their length, may be correlated with the medical data. If industry and industrial

physicians become cognizant of the demands which will be made of them in the future and plan at this time for the recording of data so that they can be analyzed, it will be possible for them to become aware of any significant shifts in the incidence of disease, including occupational cancer, in the working force. The earlier such shifts are recognized, the sooner can their causes be studied and understood. This in turn will lead to the control of significant exposures and the genuine fruition of industrial medicine, whose confines lie within the preventive-constructive framework of medicine. These comments, although true of occupational cancer, are equally valid for all occupational disease. The methodology can be applied equally successfully by the industrial physician, the private physician, the public health physician, and the union physician, but, because of the need for assistance from other groups within industry, it will probably be most successfully applied by the industrial physician. It will become important for industry to know that its engineering controls are keeping pace with its technological developments, and this can most effectively be done through studies comparable to those outlined above.

Summary

In the majority of cases, occupational cancer cannot be distinguished, morphologically, from cancer not due to occupation. As a result, the diagnosis of occupational cancer is more difficult than the diagnosis of many other occupational diseases.

The suspicion for the existence of an occupational cancer hazard may arise from clinical observations, from public health statistics, or from the statistics available from insurance companies. The value and limitations of each of these must be realized. Failure to realize the limitations of these methods may lead to misleading conclusions. Failure to appreciate their value may result in overlooking important leads for further detailed studies.

In modern industry, with the tremendous expansion in the manufacture and use of chemicals, some of which may be carcinogenic, the responsibilities of the medical profession for detecting new occupational cancers have been increased. The first requisite in such studies is the maintenance of adequate medical records by competently trained physicians. In addition, it will be necessary to maintain adequate employment and occupational records. The correlation of cancer with occupation must be made from these records with a full appreciation of the natural history of nonoccupational cancer, such as its age, sex, and site distribution.

Specific increases in age, sex, and site-specific cancer incidence above normal incidences for the same age, sex, and site represent the only reliable

evidence for the existence of an occupational cancer hazard. The importance of normal incidence rates in the general population, to serve as a base-line control, is therefore self-evident. Further, a careful methodology for occupational cancer studies from industrial medical and occupational records is required.

The important aspect of occupational cancer studies lies in the fact that an understanding of the disease will permit its control and, ultimately, its complete prevention. With modern engineering methods and control and protective devices, prevention can be achieved at reasonable cost.

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BLOOD SUGAR DETERMINATIONS.—Blood sugar in the majority of clinical laboratories is determined by obsolete analytical methods which yield false values. Instead of the actual glucose content of the blood, these values represent glucose equivalents of the combined copper reducing power of glucose plus other substances—such as glutathione, ergothioneine, uric acid, amino acids—which are entirely unrelated to blood sugar. The reducing power of these substances varies with the several reagents employed, so that the sugar values are distorted to variable degrees. Thus the non-sugar reducing matter adds to the actual sugar content 10-15 mg. percent in the Hagedorn-Jensen method, 15-25 mg. per cent in the original Folin-Wu method 25-35 mg. per cent by the old Shaffer-Hartmen method. In consequence, different laboratories report for the same sugar concentrations a variety of figures which allow no basis for comparison. This situation has been, and still is, the source of much confusion and misunderstandings. For 28 years now we have been using methods which give the true, correct sugar values. Since these are at least as simple as the methods which yield false values, there is no justification whatever for the inertia that keeps false values in circulation.—Michael Somogyi, Ph.D., *Sugar Tolerance Tests: Their Relation to Diabetes and the Nature of Diabetes*, Proceedings of the Forty-fifth Annual Meeting of the Medical Section of the American Life Convention in New York, 1957.

man of the department should accompany each application. Requests for accommodation should be made to Dr. Lalich at the same time.

Meeting on Electroencephalography in Atlantic City.—The 12th annual meeting of the American Electroencephalographic Society will be held June 12-15 at the Hotel Traymore, Atlantic City, N. J. Dr. Robert S. Dow will give the presidential address the morning of June 14 and will serve as chairman for a symposium on "Electrophysiology of the Cerebellum," which will include the following topics and participants:

Introduction and Historical Survey, Dr. Dow.
Cerebellar Responses to the Stimulation of Afferent Connections, Dr. Ferdinando A. Morin, Detroit.
Electrical Activity of the Cerebellar Cortex and Nuclei and How It May Be Modified, John M. Brookhart, Ph.D., Portland, Ore.
Efferent Discharges Resulting from Electrical Stimulation of the Cerebellar Cortex and Nuclei, Ray S. Snider, Ph.D., Chicago.
Significance of Electrophysiological Studies in Relation to the Localization of Function in the Cerebellum, Dr. William W. Chambers and James M. Sprague, Ph.D., Philadelphia.
Relation of the Cerebellum to Sensory Mechanisms, Dr. Dow.

Twenty-five papers are scheduled and a symposium on EEG of the "Premature, Newborn and Young Infant" is planned for June 15. Speaker at the annual banquet (June 14, 7 p. m.) will be Donald B. Lindsley, Ph.D., who will discuss "Lindsley's Folly: Reminiscences About the Early Days of EEG During the Depression Era (1930-1940)." For information write Dr. Jerome K. Merlis, Secretary, American Electroencephalographic Society, EEG Laboratory, University Hospital, Baltimore 1, Md.

FOREIGN

International Meeting of Gynecologists and Obstetricians.—The International Professional Association of Gynecologists and Obstetricians will meet in Brussels, Belgium, under the presidency of Dr. Francisco Luque Beltrán, of Madrid, July 18-19. Two main subjects to be discussed are: "Criteria and Processes of Specialization in Gynecology and Obstetrics" and "Economic Classification of Fees for Obstetric and Gynecologic Functions According to the Hierarchy of Values." Registration fee is 500 Belgian francs to be deposited to the account of l'Association Professionnelle des Obstétriciens et Gynécologues Belges: Dr. Stocq, 23 Drève du Caporal Ucle, Banque de la Société Générale de Belgique, Brussels, Belgium. Information can be requested from the General Secretary of the Congress, Dr. Geeraert, 211, Avenue Louise, Brussels, Belgium.

DEATHS IN OTHER COUNTRIES

Tobias Levitt.—Formerly surgical first assistant at the thyroid clinic, New End Hospital, Hampstead, England, Tobias Levitt, F. R. C. S., died in Charing Cross Hospital Feb. 22. He was elected to give a

Hunterian Lecture at the Royal College of Surgeons (1952), was author of "The Thyroid: A Physiological, Pathological, Clinical, and Surgical Study," and was attached to the Royal Marsden Hospital in a research capacity (since 1956). He was awarded a travelling fellowship by the Kellogg Foundation and by the International College of Surgeons, spending a year in the U. S. lecturing on diseases of the thyroid.

CORRECTIONS

Occupational Cancer.—In the report to the Council on Industrial Health in the April 26, 1958, issue of The Journal, Page 2177, column 1, second new paragraph, the equation starting on line 3 should read as follows: "Incidence (cases per 100,000 per year) = [total number of cases for n years ÷ (population at risk × n)] × 100,000." The equation starting on the fifth line from the end of the same paragraph should read: "Incidence = [10 ÷ (100 × 10)] × 100,000 = 1,000 per 100,000 per year."

Aero Medical Association.—In the Washington News in THE JOURNAL, Feb. 22, 1958 issue, front advertising page 27, and April 5, 1958 issue, front advertising page 27, it was stated that the Aero Medical Association was "now nine years old" and was "formed ten years ago," respectively. These statements were erroneous. The Aero Medical Association was founded in 1929. The 30th anniversary will be observed at the association's annual meeting in Los Angeles, April 27-29, 1959.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: The American medical qualification examination to be given henceforth twice a year for foreign medical graduates. Medical Schools in the United States and Foreign Countries, Sept. 23. Final date for filing application is June 23. Executive Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Illinois.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Written. Parts I and II.* All medical centers in the United States and Canada, June 17-18. Sec., Dr. John P. Hubbard, 133 S. 36th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 17-19. Sec., Dr. D. G. Gill, State Office Building, Montgomery 4.
ARIZONA: * *Examination.* Phoenix, July 16-18. *Reciprocity.* Phoenix, July 19. Sec., Dr. Thomas N. Bate, 826 Security Bldg., Phoenix.
CALIFORNIA: *Written Examination.* San Francisco, June 16-19; Los Angeles, August 18-21; Sacramento, Oct. 20-23. *Oral Examination.* San Francisco, June 14; Los Angeles,