[I]

CONCEPT AND SIGNIFICANCE OF OCCUPATIONAL TUMORS

1. THE NEW ARTIFICIAL ENVIRONMENT

THE great majority of disease conditions results from an interaction of the cells of an organism with some animate or inanimate, exogenous, environmental agent. Until the early part of the nineteenth century the general knowledge concerning the nature and causative mechanism of these etiological factors was highly deficient for most of the diseases known to occur up to that time. The deep ignorance prevailing in such matters was hidden behind the vague concept of miasma.

A fundamental change in this deplorable condition was brought about during the latter half of the past century through the discovery and subsequent intense study of the numerous pathogenic micro- and macro-organisms, such as bacteria, protozoa, viruses, and worms. Since then, and until rather recent times, the chief interest and energy of medical research has been expended upon the elaboration and accumulation of data regarding the characteristics and properties of, and the pathogenic effects produced by, these animate constituents of our natural environment.

The remarkable achievements contributed in this respect by the various and, in part, newly developed branches of medical science (clinical medicine, bacteriology, parasitology, immunology, pathology, physiology, pharmacology, and hygiene), aided by the simultaneously rapidly advancing basic sciences of chemistry and physics, have led to the institution of protective, preventive and therapeutic measures controlling effectively a great number of the formerly dreaded and often fatal or disabling infectious diseases.

However, during the same period in which these noteworthy advances concerning the animate pathogenic environment were made, a revolutionary change in our inanimate, external environment took place through the development of modern industry and the general use of its products in daily life, transforming thereby the former state of an agricultural civilization into an industrialized one.

While the inanimate, exogenous environment, to which man and animals are exposed, depended through the preceding ages mainly upon the locally prevailing geological and climatic conditions determining the type of fauna and flora and represented in this sense a part of the natural environment, the gigantic growth of modern industry occurring in its main portion within the lifetime of men now living, i.e., within the last one hundred years, has intro-

MEDICAL

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/1

duced numerous artificial, heretofore unknown, exogenous factors in constantly increasing number and variety. The creators and beneficiaries of the industrial development are thereby made potential victims of health hazards which cause numerous and diverse acute as well as chronic and insidious diseases never observed before. This powerful impact of the rapid rise of modern industry upon the inanimate exogenous environment affects mainly and primarily the industrially employed parts of the present-day population, but extends also to a considerable degree upon practically all other portions of the population and influences all branches of human activity, including personal and public hygiene, nutrition, clothing, living quarters, habits and customs (Zangger).

The rise of industrialization during the past century has vastly expanded the production and use of formerly known substances and manufactured goods and has resulted as well in the manufacture of innumerable new ones, entailing the employment of new techniques of production, handling, and consumption, and necessitating the application of many new physical and chemical agents. There have appeared entirely new methods and means of power production, transportation, communication, lighting, heating, water supply, disposal of industrial wastes and municipal sewage, road construction, printing and illustration, food production, processing of foodstuffs, clothing, mining, metallurgy, and other forms of industrial production.

The chemical industry especially has excelled in the creation of this new artificial environment by producing new synthetic substances in never-ending number and for ever-increasing purposes (dyes, mordants, explosives, plastics, fertilizers, insecticides, fungicides, solvents, rubber, resins, lacquers, pigments, paints, finishes, textile fibers, fuel and lubricants for motors and machines, refrigerants, building materials, radioactive substances, food components, drugs, toilet articles, pharmaceuticals, household supplies, and innumerable other articles.

The introduction of air pressure tools, air pressure chambers, biologically highly active rays (roentgen-rays, radium rays, ultraviolet rays), the use of airships and airplanes, etc., has widened greatly the influence of occupational conditions of a physical nature upon the health of the modern industrial worker.

The growth of metallurgical establishments has brought about an intensified utilization of the various metallic natural resources, many of which were unknown and never before used for industrial purposes, such as aluminum, magnesium, chromium, nickel, vanadium, and radium. This has increased the number of potential health hazards, and also is responsible for a greatly augmented exposure of the industrially employed as well as general population to substances of marked toxicity, such as arsenic, lead, mercury, antimony, manganese, chromium, and radium, used industrially or released as waste products into the environmental air (carbon monoxide, sulfur dioxide, arsenious

oxide, etc.), or into the waters of lakes and rivers (phenols, arsenicals, etc.) serving as water supply of adjoining communities.

Additional sources of chemical pollution of water supplies can be traced to the discharge of wastes from chemical factories, paper plants, cellulose manufacturing establishments, gas works, rayon plants, textile dyeing plants, tanneries, etc., and to the introduction of tarry substances from freshly tarred or oiled roads with the rain water, or of arsenicals used for the spraying or dusting of fields, orchards, and woods, or released from copper and iron smelters into the air and carried down by the rain. The use of chemical insecticides on fruits and vegetables containing lead, arsenic, copper, nicotine, etc., and the employment of numerous organic and inorganic chemicals in the processing of foodstuffs for various purposes (preservation, coloring, consistency, etc.) have added greatly to the number of exogenous agents composing this new artificial environment whose biological effect upon the human organism is often unknown or little appreciated.

This very incomplete list of new environmental agents may suffice as an illustration of the degree and character of the changes which the inanimate exogenous environment has undergone during the last five to ten decades (Dublin; Zangger; Koelsch; Johnstone; Sappington; Martland; Martineck; Aikman; Goodman and Sulzberger; Williams; Störring; Ruf and Fluck; Jephcott; Voss; Baader; and many others). While thus the factors composing the old natural environment are still present and active to some measure in a more or less modified form, the agents constituting the new artificial environment are superimposed upon them to an increasing degree, not only producing diseases of purely industrial origin but, through interaction with the pathogenic influences of the natural environment, also giving rise to disorders of complex etiology.

The immediate and great significance which this situation possesses from the standpoint of medical care and public health is reflected to some extent in the legislative measures taken in various countries in the form of food and drug acts and industrial health laws as well as in the increasing interest industrial diseases have aroused in the medical profession in recent years. It must be admitted, however, that these reactions can be considered only as *the first steps* toward an adequate and general appreciation, knowledge and control of health hazards which have arisen as the result of this industrialization and which produce diseases neither properly understood nor recognized in an appreciable number of instances.

The situation existing in this respect is less alarming with regard to the acute industrial poisonings than to the chronic poisonings, especially those of metatoxic type. It is in general neither very difficult to determine the nature of the various causative agents responsible for the majority of the acute industrial poisonings nor is it hard to recognize the etiologic character of the symptomatic manifestations produced by them, because of the special circum-

stances which, as a rule, surround such events. The often rapid onset of impressive symptoms following a usually accidental exposure to rather massive amounts of a particular agent of known toxic qualities furnishes in general the conclusive evidence.

The various possible sources of acute poisonings are obvious in well conducted industrial establishments when medically properly supervised, where adequate precautions for prevention under ordinary working conditions, as well as appropriate therapeutic facilities in case of their accidental occurrence, are provided. It must be noted, however, that less favorable conditions are apt to exist in this respect in plants which employ only a small number of men or where products with proprietary names and of unknown chemical nature are handled. Serious difficulties in regard to a correct and prompt diagnosis of acute industrial poisonings may be encountered in those cases in which the initial symptoms are rather mild and uncharacteristic, while being followed only after a more or less prolonged period of delay by manifestations of more severe nature.

It is obvious that the diagnostic obstacles offered by chronic poisonings are often greatly magnified, as the symptoms elicited by a prolonged exposure to comparatively small amounts of toxic agents are not infrequently neither characteristic nor appreciable for a varying period and may be considered even as "insignificant" from a medical standpoint, especially in the presence of metatoxic effects. Serious manifestations appear in many instances only after many months, or years, of exposure, or may be noted only many years after cessation of exposure to the injurious agent. The proper recognition of the causes and symptoms of many of these medically as well as socio-economically highly important diseases occasioned by the agents of the new artificial environment represents one of the chief problems with which the medical profession, public health agencies, industrial managements and legislative bodies will be confronted in the near future. At the present time, an appropriate progress, which may be considered as commensurate with the already existing tremendous significance of these environmental diseases, is obviated by various factors.

There exists among the members of the medical profession an inadequate knowledge and appreciation of these sources of disease conditions and of the symptoms produced by these environmental agents. In addition to the lack of proper training in this respect during the years devoted to medical education, the average physician has little opportunity to familiarize himself with the nature and possible biological action exerted by the multitude of substances used, produced or handled in the various industrial operations. His patients employed in such establishments are frequently not able to provide him with reliable or adequate data upon inquiry, while the plant management may be reluctant to divulge such information to a physician not connected with the industrial organization.

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/4

Environmental diseases of industrial origin present, moreover, not infrequently marked diagnostic difficulties, as an appreciable number of these disorders may masquerade symptomatically under the disguise of known infectious diseases or are readily and often complicated by such conditions, so that the primary, occupational, etiological aspect becomes obscured.

Some industrial diseases, on the other hand, exhibit symptoms simulating closely those found in certain diseases of unknown etiology (so-called "idiopathic diseases"), or are mistaken for organic changes observed with the "physiological" aging of the organism. The following examples may serve as illustrations of these points:

The occupational exposure to benzol and to certain benzol derivatives may lead to the development of a great variety of *hyperplastic and hypoplastic reactions* of the blood and blood-forming organs resembling in many respects those caused by some infectious, endocrine, or unknown agents. *Certain disorders of the central and peripheral nervous system* which are elicited by contact with a great number of industrial poisons (carbon monoxide, hydrogen sulfide, carbon disulfide, chlorinated aliphatic hydrocarbons, aromatic hydrocarbons, organic and inorganic compounds of lead, mercury, arsenic, manganese, etc.) may mimic closely those accompanying infectious diseases or appearing as degenerative manifestations of unknown etiology (Baader). The inadequate knowledge as to the existence of such causal connections is the reason that the industrial factors producing nervous disturbances often remain unappreciated, resulting in the institution of ineffective therapeutic measures and in the complete omission of essential preventive procedures. The causal role which an occupational exposure to noxious gases and vapors (sulphur dioxide, nitrous oxide, etc.) as well as to various kinds of organic and inorganic dusts (manganese, soot, iron oxide, and especially silica) plays in the production of *chronic inflammatory conditions of the respiratory organs*, is not rarely more or less obliterated by the secondary onset of a bacterial infection, for which the industrial agent has prepared the soil. The occurrence of *peptic ulcers* in individuals exposed to carbon disulfide vapors is generally little considered in the diagnosis of gastric disorders. Likewise is the production of degenerative and fibrosing lesions of the liver by aliphatic chlorinated hydrocarbons, aromatic hydrocarbons, etc., not taken into account in determining the causation of *cirrhosis of the liver*. A considerable number of *irritative or allergic cutaneous lesions occurring among the industrially occupied*, as well as among the general population, can be traced to an exposure to some of the innumerable new chemical compounds employed in industry and incorporated in articles of every-day use. These manifestations are not infrequently mistaken for bacterial or fungal infections which, however, are often superimposed upon, or activated by, the chemical agents.

Apart from these medical difficulties which impair the proper advancement in the knowledge and recognition of these environmental diseases there exists a fundamental and serious lack of information concerning *the biological effects exerted by many of the new synthetic compounds*. While the manufacturers of such chemicals, as well as the users of new and old substances for new purposes,

are usually well acquainted with, or anxious to determine over a wide range, the various chemical, physical, and technical properties of these agents, they do not, in general, feel obliged, or consider it apparently less important, to conduct equally thorough and detailed investigations in regard to the possible injurious effects which their products may produce in the human organism, prior to their introduction into large scale industrial operation or before they are offered for sale to the public.

This increase in the number and types of industrial and environmental diseases following upon the rise of the modern and artificial environment furnishes the background for the prominence which occupational neoplasms and related hyperplastic cellular responses of exogenous origin have now attained. Industrial tumors and allied diseases constitute an integral part of the pathological reactions resulting from the change which the inanimate environment has undergone during the past century (Teutschlaender). While a few of the industrial cancers have been known or have existed without correct recognition prior to the advent of the modern industrial era (pulmonary cancers of the Schneeberg and Joachimsthal miners, scrotal cancers of the chimney sweeps and arsenic workers in England), the great majority of the occupational blastomas appeared after the start of modern industrial development. In fact, the overwhelming number of occupational neoplasms has been placed on record during the last forty years. During this period there was not only a constant rise in the absolute number of these disorders, but also a marked increase in their organic types and in the exogenous sources. It must be pointed out, however, that the different occupational cancers participated in a very irregular fashion in this evolution. While some of them regressed in frequency in practically all countries in certain occupations, such as roentgen cancer of the skin among the medical profession, after the hazard had been properly appreciated and adequate precautionary and preventive measures had been instituted, they did not take the same course in other occupations into which they had more recently gained access to an increasing degree.

Other industrial neoplasms, such as aniline cancers of the urinary bladder, exhibited a decreasing incidence in some countries in which their development was originally favored by special industrial conditions (Germany, Switzerland), and where effective preventive measures were first developed. On the other hand, the same cancers appeared with increasing frequency during more recent years in other countries (England, Italy, United States), following the establishment of etiologically important chemical industries.

The promoters and managers of such newly developed manufacturing industries apparently neglected to profit from other countries' adverse experiences. It may be noted that the technical changes which resulted in an amelioration of the industrial cancer situation in some instances were prompted mainly, until rather recent times, by a desire of plant management to reduce

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/6

production costs and to improve the quality of the manufactured goods for sales reasons, and were not instituted primarily to provide better working conditions and protection to the workers.

The variations which the numerical and organic incidence of industrial neoplasms have displayed in recent decades and in different countries and industries, reflect, to a certain extent, the general and local growth of modern industrial enterprises. It may be conceded that occupational risk represents only one of several predisposing causes of cancer which may be operative in different instances or under different circumstances, as it is not uncommon to find in occupations an excessive mortality from cancer in certain sites for which no apparent explanation can be found in the industrial risks (Young and Russell). While it may be possible that in some occupations the excessive indulgence of habits, like smoking and drinking, may play a predisposing role, this conception should not be unduly encouraged in view of the serious ignorance existing concerning the cause or causes of cancer in general and industrial cancer in particular. Past experiences suggest that such observations regarding an unexplainable high organic incidence of cancer in certain professions can be traced more likely to an industrial source than to habit factors.

The medical, medico-legal, sociological, and scientific significance of occupational tumors extends far beyond the limited importance these proliferative reactions possess as an industrial disease. Industrial neoplasms are, at present, with the exception of a few tumors of non-occupational, environmental origin, the only blastomas in man of which the approximate cause is known. Occupational cancers represent, because of this fact, a challenge to the industry as well as to public health agencies, as they are the only malignant neoplasms the development and occurrence of which can be largely or completely eliminated, if proper precautionary measures are taken to prevent any undue contact of the workers with the offending agents, or if the cancerigenic factors are excluded from industrial operations (Hoffman, W. J.; Hoffman, Fr. L.).

Occupational cancers have attained additional importance as the study of these neoplasms has resulted in the discovery and synthesis of a large number of chemical carcinogens (dibenzanthracenes, cholanthrenes, etc.), some of which were found to be closely related to substances occurring normally in the body (bile acids, sex hormones), or forming constituents of our food and our cells, such as cholesterol and vitamin D. (Kennaway; Cook; Hieger; Cramer; and others [England]; Fieser and coworkers; Shear; Andervondt; Loeb; and others [United States]; Butenandt [Germany]; Yoshida and coworkers [Japan]). Occupational cancers have thus furnished the basis for one of the greatest advances ever made in the knowledge of cancer in general.

Inasmuch as the crude cancer death rate has markedly increased in all civilized countries, the increase in the United States being nearly 65 per cent between 1900 and 1933 (Rector), and considering the fact that cancer ranks now second as a cause of death, killing every tenth individual dying after the

age of forty years, any addition to existing information on the causation and causative mechanism of cancer is a highly important matter. This statement receives additional emphasis from the fact that in spite of definite advances made in the diagnosis and therapy of malignant diseases, and in spite of the increased cancer-consciousness of the general public, there has not been noted any appreciable reduction in the rate of cancer mortality (Wood). The far-reaching practical significance of the study of industrial cancers is derived from the light which such investigations shed upon the importance of preventive measures in the fight against cancer and upon the causes and causative mechanism responsible for these growth manifestations.

2. DEFINITION AND CLASSIFICATION OF OCCUPATIONAL TUMORS

The term "occupational tumor" is applied to blastomatous reactions originating in individuals during the course, and as the result of, the regular and usually prolonged exercise of certain occupational activities entailing contact with some exogenous, physical or chemical, carcinogenic agent acting in proper intensity. These occupational neoplasms proper are caused in general by specific factors which form an integral part of ordinary working conditions. They must be distinguished from accidental occupational tumors which result from or follow upon some extraordinary, unforeseen, accidental injury sustained while at work. The blastogenic factors allegedly responsible for these accidental neoplasias are of nonspecific nature, and consist primarily and usually of a single or repeated physical or chemical trauma unrelated to regular occupational influences.

Occupational tumors thus represent a variety of the environmental neoplasms, i.e., blastomatous responses to the action of certain specific extraneous cancerigenic factors of natural or artificial origin. The existence of non-occupational environmental cancers provides not only additional proof of the importance of exogenous agents in the causation of malignant and benign growths, but represents also a material source of information for the study of occupational blastomas. Non-occupational environmental tumors and related manifestations are, like the occupational variety, the result of extraneous influences of various kinds, such as *habits* (carcinoma of the oral cavity in betel nut chewers; carcinoma of the skin of the abdominal region in carriers of kangri [Kashmir] or kairo [Japan]); carcinoma of the penis due to uncleanliness and the use of caustic therapeutics in Chinese; *customs* (keloids in colored races caused by decorative scarring); *climatic factors* (skin cancers among light pigmented inhabitants of dry and sunny regions [Australia, Argentina, Midwestern States]); *geological influences* (cancer of the skin among inhabitants of areas in which the water supply is contaminated by arsenic from arsenic-containing ores [Silesia, Argentina]); adenomas and carcinomas of the thyroid among inhabitants of regions in which endemic goiter occurs because of *iodine deficiency of the soil* (Switzerland, Great Lakes

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/8

region); *endemic parasitic infections* (cancer of the bladder due to schistosomiasis in Egypt; primary cancer of the liver in many tropical and oriental countries caused by endemic helminthic infestations). Similar observations as to the occurrence of environmental blastomas on the basis of endemic infections with worms and viruses have been made in a number of animals (rats, rabbits, monkeys, frogs, fishes, chickens).

A tumor, in order to be classified and acceptable as of occupational etiology, must fulfill two conditions:

1) The clinico-statistical evidence must show that the incidence rate of a tumor of a certain type and site is appreciably and significantly in excess among workers engaged in a particular operation entailing contact with a more or less well-defined agent, of the rate observed for the general population. Proper consideration must be given in such an analysis to the relative age distribution and cancer incidence in the two groups compared, for the purpose of excluding not only the possibility of an apparent, age-conditioned excess, but also for determining whether younger age groups are more greatly affected in the occupational groups than in the general population, as a shift of the peak of incidence of a particular cancer into younger age groups favors an exogenous and specifically occupational influence operative in its genesis. Additional evidence of clinico-statistical nature supporting an occupational causation of a particular tumor may be obtained, if it can be demonstrated that a high, while not always statistically significant, incidence increase of the particular cancer exists among those workers who have either less intimate contact with the suspected agents, while working in the same operation, than the individuals most often affected, or who are employed in the environmental zone and thus sustain only an indirect and less intense exposure. Circumstantial evidence of this nature has been considered as sufficiently conclusive in numerous instances for extending official medico-legal recognition to neoplastic conditions of occupational origin before ultimate proof of such an etiology has been provided by a successful experimental reproduction of the particular neoplasm in animals.

2) The existence of adequate experimental evidence possessing conclusive value is essential not only from a scientific viewpoint, but is of decisive influence in all those instances in which the clinico-statistical data are not quite definite and permit, therefore, merely suggestive conclusions.

In the establishment of adequate and reliable clinico-statistical, as well as experimental associations, certain difficulties have to be overcome or taken into account to insure accurate results. Inasmuch as the information obtainable from death certificates is usually not only deficient, but also notoriously unreliable, especially as to the cause of death, it is indispensable that the diagnosis of the neoplastic nature of an allegedly occupational disease is based, in at least the great majority of cases investigated, upon the results of histo-pathological examinations of the suspected new growth. Similarly, uncertainty must be eliminated concerning the matter of occupation. Data

regarding the latter must be defined accurately, as there occur not only marked variations in the intensity of exposure to certain occupational agents among the members of the same occupation, but also among those employed in the same operation. An additional source of error may enter into the clinico-statistical studies by the tendencies of workers to change their occupation during the course of life and thus to become exposed to occupational hazards of varying nature, while the death certificate usually lists only the last occupation engaged in. In view of this fact and considering that occupational neoplasms have, as a rule, a long latency period extending over 40 years or more in instances, it appears of utmost importance that reliable data on the occurrence, sources and incidence of occupational neoplasms must be based on the entire occupational history of workers suspected of having industrial tumors.

In appraising the relative value of the experimental reproduction of a particular industrial neoplasm from a scientific as well as medico-legal standpoint, consideration must be given to the fact that any occupational tumor is, by its very nature, equivalent to an unintentionally produced experimental tumor in man. The clinico-statistical evidence thus may provide under favorable circumstances, as convincing proof of the occupational origin of a tumor as that which can be supplied by its experimental reproduction. The great and immediate significance of a successful experimental reproduction of occupational neoplasms in animals consists for this reason often not so much of a conclusive demonstration of a well-defined, industrial etiology, but of furnishing a suitable and practical method for the intelligent study of their causes and causative mechanisms. It must be emphasized in this connection that only positive experimental results possess conclusive value, while a negative outcome of experimental approaches frequently holds the problem merely in abeyance. Whereas failures in this respect may be caused occasionally by the use of an improper, noncarcinogenic agent, incorrectly suspected as the causative factor, past experiences have shown that negative results followed not infrequently upon the employment of the actual causal agent under unsuitable experimental conditions (insufficient intensity and duration of exposure, improper administration of agent, selection of a completely or markedly refractory species, etc.). It is a well-established observation that the reactivity of different species to some carcinogenic agents varies considerably and may influence, therefore, decisively the outcome of experiments of this kind.

Occupational neoplasms can be classified into certain groups according to the relation which the site of a particular occupational tumor possesses to the type of contact with a given carcinogenic agent:

1) Direct contact tumors.

a) Cutaneous neoplasms caused by a direct local action of mineral oil, crude paraffin, creosote, anthracene, solar rays, ultraviolet rays, roentgen-rays,

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/10

rays from radioactive substances upon the cellular components of the skin.

b) Pulmonary blastomas resulting from the exposure to and inhalation of radio-active material, chromates, asbestos, nickel carbonyl, tarry substances.

c) Tumors of the nasal passages and sinuses following upon the exposure to radioactive substances, chromates, nickel carbonyl.

d) Cancers of the upper alimentary tract exhibit statistically causal relations to certain industrial cancerigenic agents acting most probably directly upon the mucous membranes of these passages.

2) Excretory contact tumors.

a) Epithelial neoplasms of the skin following the ingestion of arsenicals.

b) Blastomas of the urogenous tract resulting from an exposure to certain aromatic amines, excreted in the urine.

c) Cancers of the liver, intestinal tract, female genital organs provide, theoretically, a possibility of proliferative manifestations of this type.

3) Depository contact tumors.

a) Cancers of the skin associated with the deposition of arsenicals in the cells of this organ.

b) Sarcomas of the bony tissues following the storage of radio-active material in the bones.

4) Tumors in tissues possessing a special affinity or sensitivity to a particular cancerigenic agent.

a) Blastomatoid and blastomatous reactions of the hematopoietic tissues following an exposure to roentgen-rays, radioactive substances, benzol, and chemically related substances.

b) Cancers of the urinary bladder and liver caused by an infestation with certain helminthic parasites exhibiting an affinity to these organs.

It is in the nature of any classification of biological manifestations that the dividing lines between the different groups are not always sharp and that a certain amount of overlapping occurs, or that several factors are operative and combine in bringing about a neoplastic response in a particular case. Thus, arsenicals are not only deposited and stored in the skin, but they are also excreted through its various component parts (epidermis, hairs, sweat). A depository and excretory mechanism may, therefore, be active in the development of arsenic cancers of this organ. Malignant neoplasms of the lung, on the other hand, may be elicited not only by a primary contact with radioactive substances inhaled in the form of gases or dust, but may also be caused by the exhalation of gaseous members of this chemical group representing degradation products of solid radioactive substances which may originally have entered the body through the mucous membranes of the digestive or respiratory tract.

The nature of the ensuing neoplasms depends moreover on the type of contact with a particular carcinogenic agent. Radioactive substances may thus produce cancers of the skin following a prolonged localized exposure to the rays emitted by these chemicals, while osteogenic sarcomas may result when these chemicals are deposited in the bony tissue, pulmonary neoplasms when

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/11

they are inhaled, and leukemias when a generalized exposure of the body to these substances exists. Similarly, the leukemic action of benzol may not entirely be an expression of a specific cellular affinity of the myeloid marrow cells to benzol, but it may be, in part, a product of an accumulation of this chemical in the fat tissue composing the bone marrow (Schrenk).

In addition to the definitely precancerous and cancerous lesions, occupational health hazards may produce a large number of proliferative reactions displaying more or less blastoma-like, or blastoma-near, qualities. Manifestations which belong to this group of tissue responses to exogeneous, occupational agents are transitory and reversible erythrocytoses and leucocytoses, sometimes associated with heterotopic hyperplastic proliferations of the corresponding hematopoietic tissues, adenomatoid hyperplasias of the liver accompanying an industrial cirrhosis of this organ, and similar reactions of a regenerative, compensatory or irritative nature. Nonspecific, traumatic, occupational influences are especially active in the production of such conditions (traumatic epithelial cysts caused by tissue misplacement, sarcomatoid granulomas, metaplasias of various kinds, traumatic ossifying myositis, Dupuytren's contracture, ganglions, keloids, warts, etc.).

The accidental occupational tumors may be grouped as follows:

1) Tumors following upon a single trauma resulting in
   a) an acute formation of a neoplasm.
   b) a delayed development of a blastoma.
2) Tumors following after repeated injuries of nonspecific, but sometimes occupational nature.
3) Tumors preexisting at the time of the traumatic episode, but aggravated in their further course by the accidental injury.

Specific occupational cancerigenic influences and non-specific traumatic accidental factors sometimes combine in eliciting a neoplastic reaction, or in modifying the time of its manifestations, or in affecting its course (mechanical or chemical trauma acting on a chronically roentgen-injured skin; thermic burn in a skin having chronic tar dermatitis with precancerosis, etc.).

An intermediate position between occupational tumors proper and accidental occupational neoplasms is occupied by those blastomatous reactions which arise, apparently or allegedly, as the result of a prolonged or repeated action of nonspecific occupational influences, of physical or chemical nature, causing a chronic traumatization or irritation of the tissues.

3. HISTORICAL, INDUSTRIAL AND GEOGRAPHICAL ASPECTS

Already the writings of Andreas Vesalius (1543) and of Peter von Forest contain allusions that certain occupations may be related to the formation of tumors (Ullmann, K.). Bernardino Ramazzini (1700) seems also to have entertained similar thoughts (International Labour Office Reports). However, not until much later were such vague suspicions placed on a firmer and factual

basis, when Percival Pott (1775) advanced good evidence connecting the appearance of scrotal cancers in chimney sweeps with their occupational exposure to soot. The number of recognized occupational cancerigenic agents, and of occupational neoplasms, has increased steadily since then, especially during the last five decades. A few of the diseases accepted among the occupational neoplastic disorders (pulmonary cancer of the miners of Schneeberg and Joachimsthal in Saxony and Bohemia, respectively) have been known symptomatically for several hundred years, others (carcinoma of the urinary bladder due to infections with Schistosomum haematobium among the fellahs of Egypt) possibly even for several thousand years without their actual nature and etiology being recognized.

Following the description of the first occupational cancer, almost four decades passed before a second source of industrial neoplasia was discovered. Ayrton in 1820, and Paris in 1822, recorded the frequent occurrence of scrotal carcinomas among the workers employed in the copper and tin smelters of Cornwall and suggested the existence of an etiological relationship between these lesions and the occupational exposure to arsenic fumes. Of these two occupational tumors belonging to the pre-industrial era, the cancer of the chimney sweeps is still observed in England, while the arsenic cancer of the copper and tin smelters in Cornwall has been extinct for many decades following the cessation of these operations.

Fifty more years elapsed, and the industrialization of the western and central European countries had been in full swing for several decades, before the first occupational neoplasm was described which can be called a product of this modern development and of the new artificial environment. In 1875, von Volkmann reported the first three cases of occupational paraffin cancer of the skin in workers employed in the newly-established lignite industry in Saxony. Only one year later (1876) Bell made a similar discovery among the paraffin workers of the shale industry of Scotland, and Manouvriez placed the first cases of tar and pitch cancer of the skin on record, which were observed among the workers of a patent fuel plant in France. The neoplastic nature of one of the oldest occupational tumors, the bronchial carcinoma of the Schneeberg miners, was established in 1879 by Härting and Hesse. Ten years later, Derville and Guermonprez called attention to the occurrence of skin cancers among the workers of crude oil refineries in northern France. In 1893, Unna described the cutaneous cancers in sailors which were attributed by Dubreuilh (1896) to the action of an excessive solar irradiation. During the preceding year (1895) Rehn made his first report on the excessive incidence of cancers of the urinary bladder ("aniline cancer") among the workers of the German dye industry, which had been established about thirty years previously. Thus, within twenty-five years, six new sources of industrial malignancy were added to the list of occupational tumors before the turn of the century. Four of these six sources were outgrowths of the industrial development.

Since that time a great many new types of industrial neoplasms have been placed on record. In 1902, the first case of roentgen-carcinoma of the skin was recorded by Frieben and Albers-Schönberg. The presence of a causal interrelation between vesical Bilharziasis and bladder carcinoma was noted by Ferguson in 1911. In the same year von Jagič, Schwarz, and von Siebenrock reported the first cases of leukemia attributable to chronic exposure to roentgen-rays. The last addition to this list before the World War was made by Rambousek in 1913, who observed the occurrence of cutaneous malignancies among workers handling crude anthracene oil.

Following this event Leitch and Sequeira described, in 1920, the first case of cutaneous malignancy caused by an occupational exposure to radioactive substances. Two years later, Southam and Wilson added the occupational carcinomas of the skin occurring in mule spinners in England resulting from the contact with certain lubricating oils. In 1924, Cookson placed creosote upon the list of occupational carcinogenic agents responsible for the development of epitheliomas of the skin. The occurrence of leukemia referable to the chronic occupational exposure to benzol was noted by Delore and Bergamo in 1928. During the following year, Löwy finally succeeded in placing the centuries old pulmonary diseases prevalent among the uranium miners of Joachimsthal among the occupational malignancies, while Martland added, in 1931, osteogenic sarcomas to the list of malignant neoplasms caused by an occupational exposure to radioactive substances. Alwens called attention to the high frequency of pulmonary cancer in chromate workers in 1932, while Bridge and Stephens recorded cancers of the nasal passages and of the lung among the workers employed in certain nickel refineries. The occurrence of pulmonary carcinomas among the employees of plants and laboratories handling radioactive substances was noted by Neitzel in 1935. During the following year, Kawahata described the high incidence of pulmonary malignancies among workers of generator plants who were exposed to the inhalation of hot tar fumes. After Wood and Gloyne (1934) as well as Lynch and Smith (1935) had reported the occurrence of pulmonary cancer in workers of asbestos plants, Horning, in 1938, claimed, when noting several new cases of this type, that causal relations exist between pulmonary asbestosis and the subsequent development of malignancy of the lung.

This chronological enumeration of the various occupational cancers, according to the different etiological factors and sites, reflects clearly the recent marked increase in the incidence of these industrial disorders. This fact is brought out still more strikingly by the continuous spread of these neoplastic diseases among the workers of an increasing number of different industries producing, using, or handling known carcinogenic occupational agents, and among the workers of such industrial establishments in different countries to the degree in which they participated in the modern industrial development.

The marked expansion of occupational contact with carcinogenic agents

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/14

upon new branches of industry is well illustrated by the wider distribution of tar and pitch cancer upon the various industrial groups of workers. While these occupational neoplasms were observed primarily among men employed in briquette factories, they have been seen later among workers of gas plants, tar distilleries, cork stone plants, manufacturers of dry battery cases, calkers of boats, road construction and repair men, fishermen and sailors, etc. Similarly, oil and paraffin carcinomas, found originally in workers of oil refineries, in mule spinners, employees of lignite and shale distilleries, have made their appearance in engineers, mechanics, oilers of machines, gunsmiths, employees of the automobile production and service trades, etc. Whereas arsenical epitheliomas were described first in smelters of tin and copper, they have now been seen in workers manufacturing or handling sheep dip, insecticides, arsenical pigments, agricultural laborers, silver miners, and among other workers with arsenicals. While other industrial cancers exhibit similar, but less striking developments, there remains the peculiar fact that the absolute number of occupational neoplasms is relatively low in comparison with cancers of unknown etiology, in spite of greatly increased occupational contact with carcinogenic agents. Then, too, many industries in which such exposures are definitely or probably present have failed to record any cases of occupational neoplasia.

This observation permits several explanations. The inference can be drawn that the actual existence of such neoplasms has not been recognized, or has been disregarded and has not been made property of public knowledge. The great discrepancies in the extent and character of the laws on industrial health prevailing in different countries may account readily for at least a part of those occupational blastomas which have escaped public recording. There exist, on the other hand, marked variations in production methods, in type and extent of precautionary and protective measures and medical supervision, as well as in the nature of the basic material used for the manufacture of identical or dissimilar end products. These variations are of sufficient significance to influence the incidence or appearance of occupational blastomas in different factories, industries and countries. Oil cancers of the skin, for instance, are particularly frequent in England because of the widespread use of a lubricating oil prepared from Scottish oil shale in certain industries. Similarly, the occurrence of cancers of the nasal passages, and of the lung in workers employed in nickel refineries, has remained so far restricted to Wales, apparently because of the use of refining methods, adapted to certain nickel ores. A special type of coal, the use of fireplaces and the existence of tortuous and narrow chimneys, together with special cleaning methods and bad hygienic conditions, seem to represent the etiological complex responsible for the prevalence of scrotal cancer in chimney sweeps in England. Chromate cancer of the lung as well as pulmonary malignancy among miners of radioactive ores have been observed thus far only in Germany. The reasons under-

lying this localized occurrence, however, are not clear, as similar occupational conditions seem to exist in the corresponding industries of several other countries.

The marked variations in the distribution, type and size of industrial establishments in different countries represent an additional important cause for the varying geographic incidence of occupational tumors. Highly developed industrial countries, such as England, Germany, Switzerland, Italy and the United States, possess a comparatively large number and more different types of industrial neoplasms than countries which are more agricultural (Denmark, Holland, Hungary, and Sweden, for example). The unusually low incidence of occupational neoplasms recorded in highly industrialized countries, such as Belgium and Japan, constitutes probably an apparent exception from this rule. As the industrial development in Japan is of relatively recent date, industrial cancers have been observed there only since the last ten years (Koinuma, 1931). Nagayo and Kinosita (1940), on the other hand, attributed the extreme rarity of industrial cancers in Japan, particularly among the workers employed as oilers in the textile industry, or in gas, tar, and tar by-products manufactures, to the fact that Japanese workers are very clean, taking a hot bath daily and change clothes frequently, thereby lowering the intensity of exposure. The cause for the scantiness of occupational neoplastic manifestations among the industrially active population of Belgium is not readily apparent. It may be possible that a certain deficiency in the number of post-mortem examinations as well as in the control of industrial health conditions plays a role in this respect, because medical surveys conducted recently among workers employed in Belgian pitch and tar plants revealed the occurrence of a considerable number of tar and pitch cancers during the last few years (Uytdenhof; Firket and Malter). An extraordinarily low rate of industrial tumors is reported also from France and Luxemburg, both countries possessing a very well developed industry.

There are a few additional factors which exert a certain influence upon the regional distribution of occupational cancers. Racial factors, for instance, contribute to the incidence of skin cancer in regions having an intense solar irradiation and being inhabited by members of light pigmented races. Industries located in countries where colored labor is available for operations entailing the contact with tarry and oily substances, on the other hand, are apt to show a low incidence of occupational tar and oil cancer, as the skin of Negroes is less susceptible to such reactions than that of white people. Occupational cancer caused by endemic parasitic infections (bladder cancer on the basis of Bilharziasis) displays also a locally restricted occurrence (Egypt). Similar considerations apply to industries depending upon the occurrence of rare minerals (radioactive substances [Schneeberg, Joachimsthal]).

No encouragement, however, can be given to the reasoning advanced by Hoffman (1928) in an attempt to explain the existence of marked variations

in the incidence of occupational neoplasms in different countries. This investigator contended that the scarcity of recorded industrial cancers in the United States was attributable to the fact that the workers in America are unusually intelligent and susceptible to educational influence; that they desire to know the truth and facts of a given situation and frequently govern their conduct accordingly; that this observation applies to no class of workers more than to those who are connected with the chemical industries in which malignant growths are unusually frequent in other countries. It is idle to speculate on, or argue about, the relative intelligence and self-reliance of industrial workers of different countries and their alleged influence upon the incidence and prevention of occupational malignancy. Then, too, it is more than doubtful whether American chemical workers are more thoroughly informed concerning the biological properties of the substances they come in contact with, or have a better opportunity to acquire such information, than their colleagues in other countries. But this is certain, the chemical industry of the United States has contributed its fair share or even more than that to the number of "recorded" industrial cancers. Hoffman's claim is highly objectionable, as it is apt to produce a spurious feeling of safety and superiority, which is especially ill placed in view of the fact that adequate industrial health legislation and laws on occupational diseases in many states of our country are of very recent date, or still non-existent.

4. STATISTICAL RELATIONSHIP BETWEEN OCCUPATION AND GENERAL CANCER INCIDENCE

The general and increasing interest in the problem of malignant neoplasms, prevailing since several decades, has fostered relatively early statistical investigations into the relative incidence of cancer in various occupational and social groups (Braithwaite; Newsholme [1881-1890, England]; Connel [United States]; Behla [1908]; Wolf; Weinberg; Aschoff [1887-1899]; Loth [1900]; Karupp; Gollmer [Germany]). Aschoff, as well as Loth, found a rather high mortality from cancer, especially epithelioma of the skin, among gardeners, which Loth suggested was caused possibly by contact with chemical fertilizer or by parasitical infection contracted from infested soil. Similarly, a high cancer mortality among English and Hungarian farmers was noted by Braithwaite and Jacobs, respectively, while Newsholme's analysis put this occupational group into second place as to relative cancer mortality, the highest place being occupied by chimney sweeps, where the ratio was found to be 70:156.

Connell, on the other hand, listed farmers in eighth place, with workers, sailors and fishermen, smiths, nurses, clergymen, servants, and masons preceding them, and merchants and gardeners following them in the order of relative incidence of cancer deaths. In the statistical studies reported by Behla, members of the literary profession exhibited the highest cancer mortality. They

were followed by members of the clothing trades, sanitation and medicine, lumber trades, etc., the farmers being well in the middle of the list, and workers employed in metallurgic, chemical, building and mining industries having the lowest cancer death rate. Oliver, in 1902, stated that glass makers, ironstone miners, tin miners, wool workers, shoemakers, and especially chimney sweeps display an excessive mortality from cancer, while miners in general were found to have a death rate 16 per cent below the average.

These few examples of the early efforts in this field may suffice, as the results obtained were not only contradictory (Jacobs), but the analyses were made without proper consideration of age groups and site of neoplasms, and were for this reason unreliable (Arnstein). Staemmler characterized these studies as defective and primitive beginnings in the establishment of interrelations between occupational exposures and cancer susceptibility by the statistical method. In commenting on these data, Koelsch called attention to several additional factors which made the information conveyed by these early investigations untrustworthy and misleading.

This investigator pointed out that it is difficult to obtain representative occupational groups, that is, groups of individuals exposed to the same occupational conditions to approximately the same degree and duration. A group such as "metal workers," for instance, includes persons having the most varied contact not only with different metals and metallic compounds, but also with numerous other substances, such as silica, lubricants, chemical fumes, and gases of varying kinds. Thus they form a group of individuals which is by far too crude and comprehensive for any significant and reliable statistical evaluation.

Similar, and perhaps even stronger, objections can be raised against the group of "chemical workers," as this is composed of individuals exposed to an even much greater number of substances possessing the most varied biological properties and acting at the same time under very different conditions and intensities upon the individual members of this group. Statistics on general cancer incidence, as well as organ cancer incidence based on an occupational grouping of such vagueness, are not infrequently absolutely valueless.

In addition to the lack of proper consideration given in these early studies to the age grouping in different professions, to the sites of the tumors and to the sex of the workers, practically no attention has been paid to the fact that many workers, especially the unskilled type, exhibit a more or less definite tendency to change the nature of their occupational activities. The inclusion of such workers and their relative proportion in the different occupational groups introduce additional sources of error, because these individuals are listed, as a rule, in that occupational group to which they were attached when the malignant neoplasms were first noted or to which they belonged at the time of their death. There are, moreover, certain non-occupational factors, such as condition of living quarters, diet, habits, hobbies, customs, and regional

and social influences which may play a more or less important role in the causation of malignant diseases occurring in members of the different occupational groups.

In spite of these adverse critical observations, the different groupings and standards used and the wide variations in the results obtained in the various statistical studies of this early period (Behla [Prussia, 1907-1908]; Kolb [Bavaria, 1905-1908]; English statistics, 1900-1902; data of the Sickness Insurance Company of Leipzig, 1887-1901, and similar investigations from Norway, Austria, Hungary, and the United States), general agreement seems to exist on the point that agriculturists exhibit a higher cancer mortality than industrially employed workers. Professions with a relatively high cancer mortality, according to Koelsch, are day laborers and maids, individuals employed in agriculture, forestry, lumber industry, hostelries, smiths, textile plants, governmental offices, and clergy, while a low cancer incidence is recorded for persons employed in mines, stone quarries, metallurgic industry, navy, and army. Inasmuch as not only the age grouping, but also the possible influence of non-occupational exogenous factors, vary greatly for these occupational classes, Koelsch concluded that the general statistical occupational studies made before and during the first decade of the present century were practically valueless.

There exist more recent statistical analyses dealing with the relationship between occupational activity and cancer morbidity and mortality; they come especially from English sources. In these some of the objectionable features of the older statistics are more or less absent. According to these studies, covering the period 1921-1923, the following occupations showed a high cancer mortality in England: wood workers, butchers, millers, dealers in liquors, barmen, stone masons, and chemical workers, while a low death rate from cancer was observed for soldiers, sailors, compositors, etc. (International Labour Office Reports).

A very comprehensive and thorough statistical survey as to the cancer mortality in the different trades and professions was made in England by Young and Russell (1926), based on an evaluation of 46,118 death certificates of the Registrar General of the years 1910, 1911, and 1912, giving sex, age, specific trade, and cause of death. These investigators divided the population for this purpose into 8 social classes and found the cancer death rates for these classes shown in the table at top of page 22.

The investigators concluded that special groups of workers show significant differences in cancer mortality. Thus, textile workers have a lower cancer incidence, and agricultural workers a still lower one, while miners (mainly coal miners) have the lowest cancer mortality among the eight social groups studied. Young and Russell believe that the statistical differences observed are of significance, if the data from which they are derived can be considered trustworthy. Similar marked differences in cancer mortality were demonstrated

Social Class	Standardized Death Rate for Persons Above 15 Years	Life Table Death Rate from Cancer
I. Upper and middle class	1.337	2.142
II. Intermediates	1.269	1.965
III. Skilled workmen	1.396	2.051
IV. Intermediates	1.283	1.957
V. Unskilled workmen	1.701	2.050
VI. Textile workers	1.397	1.864
VII. Miners	1.082	1.512
VIII. Agricultural workers	0.965	1.796
Coal miners	1.069	1.497
All males occupied and retired	1.355	1.983

by these investigators from an examination of the different trades and professions.

The comparative mortality figure (1910-1912) from cancer of all males in Wales was found to be 78, that of zinc manufacturers 178, barmen 137, patent fuel manufacturers 131, beer bottlers and cellarmen 126, brewers 125, messengers, watchmen and porters, as well as brass and bronze workers, 118, slaters 116, seamen and railway workers, each 110, tobacco manufacturers 38, coke burners 40, lithographers, tallow, soap and glue manufacturers each 41, printers and machine compositors 43, straw plait and hat manufacturers 44, clergy 45, maltsters 47, electric supply workers 49, plate layers 50. As the total figures available for zinc manufacturers, patent fuel manufacturers, coke burners, straw plait and hat workers, and electric supply workers were too small, the information obtained as to the cancer incidence in these groups was regarded as statistically unreliable.

It may be mentioned that Young and Russell also noted marked and significant differences in the mortality from cancer of various sites (skin, lip, tongue, esophagus, stomach, bowel, bladder, and larynx) related to certain trades and professions. In a study of the occupational incidence of cancer of the penis and of the scrotum in the general population by Kennaway (1928), this investigator also employed 8 social or occupational groups in his analysis (1. chimney sweeps; 2. textile workers; 3. all persons not included in 1 and 2, but especially likely to be exposed to carcinogenic agents such as tar, pitch, lubricating oils [workers in tar, patent fuel, coke and its by-products, fishermen, boatmen, drivers, stokers, and cleaners of engines]; 4. metal workers [may possibly also be exposed to lubricating oil]; 5. coal workers [miners above and below ground at the pit, coal boat loaders, trimmers]; 6. all manual occupations; 7. clerical and light manual workers; 8. agricultural workers).

Kennaway observed that the ratio of scrotal cancers to cancers of the penis is lowest in the class of agricultural laborers, whereas in the remaining classes

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/20

the ratio is lower in clerical workers than in manual workers and is lower in those doing light, than in those doing heavy, manual work. He suggested that cancer of the scrotum affects especially the classes who wash least and are most exposed to the dust of towns.

Two valuable statistical analyses on the occupational incidence and distribution of cancer were made in the United States, the one by Hoffman, the other by Haagensen (1931). Hoffman tabulated the deaths from cancer of the male generative organs (scrotum and penis) for twenty-three occupational groups according to the data obtained from the Bureau of Vital Statistics of the United States Census.

CANCER DEATHS—MALE GENERATIVE ORGANS
U. S. Registration Area—1926-29 (Hoffman)

	Penis		Scrotum	
	Deaths	Per Cent	Deaths	Per Cent
1. Laborers	131	18.4	22	16.5
2. Farmers	141	19.8	21	15.8
3. Gardeners	3	0.4	—	—
4. Fishermen and sailors	5	0.7	1	0.8
5. Army and navy	2	0.3	—	—
6. Transportation	25	3.5	1	0.8
7. Commercial and clerical	50	7.1	19	14.3
8. Professional	41	5.8	5	3.7
9. Machinists and mechanics	19	2.7	5	3.7
10. Textile	5	0.7	8	6.0
11. Painters	10	1.4	1	0.8
12. Blacksmiths	7	1.0	—	—
13. Carpenters	21	3.0	2	1.5
14. Plumbers	3	0.4	1	0.8
15. Shoemakers	5	0.7	—	—
16. Tailors	4	0.6	—	—
17. Bakers	2	0.3	1	0.3
18. Butchers	4	0.6	—	—
19. Printers	7	1.0	—	—
20. Miners	11	1.5	3	2.2
21. Chauffeurs	5	0.7	—	—
22. Electricians	7	1.0	—	—
23. Miscellaneous	72	10.1	23	17.3
24. Unknown and retired	130	18.3	20	15.0
	710	100.0	133	100.0

The occupational distribution of scrotal cancer, as recorded by Hoffman, shows much less variation than cancer of the penis. Nevertheless, there is a

definite parallelism between the absolute incidence of scrotal and penile cancer in the different occupational groups, the reason for which, however, is obscure. Hoffman felt that it is unlikely that social factors, such as special uncleanliness allegedly prevailing in certain occupational groups, would account for the high frequency of scrotal as well as penile cancer among laborers, farmers, commercial, and clerical workers.

Analyzing his data for the influence the state of marriage played in regard to incidence, Hoffman made the surprising observation that both types of cancers are significantly more frequent in married males than in unmarried males over 15 (scrotum: married 1.1, unmarried 0.4, per one million; penis: married 6.1, unmarried 1.9). Hoffman's studies of occupational groups on the basis of 3,462 deaths from cancer among males during the years 1920-27 (San Francisco Cancer Survey, Seventh Report, Prudential Press, 1931) did not render any significant information that would connect any particular occupation with some special type and site of cancer.

Haagensen made statistical studies regarding the significance of the occupational factor on the incidence of skin cancer, especially of the penis and scrotum, among various occupational groups. He attempted to obtain more definite information by applying the following formula:

$$\frac{O}{P} \times P_m = E.$$

In his calculations H represents the population of New York, Jersey City and Newark; P is number of occupied in Metropolitan area; P_m is the total number of males with skin and mucocutaneous cancers listed by occupation on the records of the Memorial Hospital; O stands for the number of males in a particular occupational group; A is the actual number of patients from the occupational group in question; E is the expected number of cases. Haagensen reasoned that if the morbidity of cancer is the same in all occupational groups the expected number for the Memorial Hospital records could be expressed in the formula given. A and E are then compared and the percentage of excess or defect determined. The statistical significance of the data thus obtained can then be ascertained by ordinary statistical calculations.

With this procedure Haagensen found that a high excess of penile and scrotal cancer existed in machinists and mechanics occupationally exposed to lubricating oil. This observation confirmed a finding previously made by Young and Russell, who reported a high incidence of penile cancer among equally exposed millwrights, turners, fitters, etc.

There was, moreover, an excess of skin cancer in brick and stone masons in Haagensen's as well as in Young and Russell's statistics, which was attributed by the English investigators to an occupational exposure to solar rays and mechanical trauma. Occupational factors of physical or chemical nature (sun light, tar, etc.) are blamed by Haagensen for the highly excessive incidence of skin cancer observed among sailors and boatmen (420 %), locomotive

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/22

engineers (900%), gardeners (800%), fishermen (600%), and roofers (500%).

No plausible explanation of this type, on the other hand, could be proposed by Haagensen for the excessive frequency of cutaneous malignancy among janitors, sextons, clergymen, blacksmiths, painters, glaziers, and varnishers, as none of these groups showed an equally extraordinary susceptibility in the English statistics. It is remarkable that occupational groups, such as petroleum workers, and gas house workers, who are notoriously exposed to irritative and carcinogenic agents exhibited in the statistics of Haagensen only a minor or negligible excess of skin cancer (250% and 150%, respectively).

Weiss, reviewing 100,000 cancer deaths which occurred in Baden during a period of 50 years, and analyzing those 12,354 cases which were observed during the ten years preceding 1932 as to the influence of an occupational factor, found the highest liability for contracting cancer in the following occupations: smiths, flour millers, shoemakers, carpenters, brewers, artists, chimney sweeps.

While the number of statistical studies on this subject is much larger, no additional information would be obtained by citing such data. Inasmuch as the basic evidence upon which these investigations are based is taken from death certificates, the conclusions arrived at do not deserve too much trust. The best that can be said for them is that they provide in some respects presumptive and confirmatory evidence, while being unreliable and misleading in others as to the presence or absence of causal interrelationships between general or local cancerigenesis and occupational factors.

A considerable number of sources of potential errors were mentioned above, but the most serious factor depreciating the value of these studies is the use of the death certificates, in which the cause of death is recorded in most instances either on the basis of clinical medical evidence, or, which is worse, on data supplied by lay persons, such as undertakers, coroners, etc. It is a well known and often established fact that the recognition of cancerous growths in such material is often missed (20 to 40 per cent), as is evident from comparisons of the clinical diagnoses with the findings of post-mortem examinations, especially regarding to the cancers of internal organs, inaccessible to direct observation (Wells, Lubarsch, Wolff, and others).

The degree of discrepancy existing between the number of cancers recorded on death certificates and that actually present must have been more marked in former decades than during more recent ones. The reasons for this lie in the appreciable increase of the number of autopsies during this period, as well as in the fact that malignant diseases have lost more and more of the character which caused people to surround these disorders with a sort of "social" silence, and which sometimes induced physicians to falsify the diagnoses recorded in death certificates, in order to spare the feelings of the relatives.

Legislative measures taken in recent years requiring the registration of certain occupational neoplasms have contributed somewhat to the reliability of the information contained in death certificates. Nevertheless, these developments and improvements are not sufficient to make death certificates a reliable basis for the statistical study of the relationship between cancer and occupation.

It is obvious from this exposition that the statistical approach usually taken does not only supply relatively inaccurate information, but also does not prevent many occupational neoplasms from escaping recognition and recording (Carozzi). More conclusive and valuable data would be obtained, if detailed investigations and analyses were made of small, but more or less uniformly exposed groups of workers, among whom appears a slight excess in the number of certain types and especially unusual varieties of cancers from time to time, so as to determine whether such phenomena are merely coincidental in nature or related to occupational factors. The explanation is often made that isolated cases of cancer may be accounted for by the natural occurrence of the disease in the general population. This evidently follows the line of least resistance and is evidence of an irresponsible and destructive attitude in the absence of any attempt to supply proof or to adopt constructive suggestions (Henry and Irvine).

The institution of fundamental improvements in the character of the data on which comprehensive statistical analyses can be based with confidence depends upon the future introduction of certain radical changes in the governmental attitude toward this important problem of public health. It is essential that cancer be made a notifiable disease, and reportable by a statutory requirement. The official notification should contain in addition to the name, sex, race, age, and married status of the affected person, detailed data as to hereditary history, complete occupational history, habits, hobbies, diet (consumption of processed and preserved foodstuffs, especially those treated with aromatic compounds [dyes]), previous diseases and therapeutic agents used, use of cosmetics, etc.

Such a law must also convey to qualified and specially trained physicians the right to perform post-mortem examinations on all persons who were afflicted at some time of their lives by a cancerous growth. Only the establishment of accurate, complete, and reliable morbidity statistics on cancer, for which the data are collected while the affected persons are still alive and able to supply the necessary and essential information, can provide in any effective degree those data pertinent to the determination of the character and action mechanism of the environmental agents which cause cancer. Proper preventive, precautionary and sanitary measures, similar to those already in effect concerning contagious diseases, should be instituted and enforced to control this pathological manifestation of cellular growth, which has become one of the most important and urgent problems of our population structure.

[illegible] contradictory or unobtainable statistical evidence concerning

the relationship between cancer and occupational activity has given rise to the idea that other factors of a more general nature, such as environmental conditions connected with the social status or with some general extraneous factors, are of more importance in determining the variations in the incidence of cancer found in different groups of people. Brown and Mohan, as well as Heron, investigated the relationship of the social and economical status of different sections of the population to cancer incidence. Heron claimed that conditions of prosperity and culture which lead to a low birth rate were conducive also to a high cancer death rate, so that cancer incidence could not be taken as a measure of that unhealthy environment with which a high birth rate seemed to be associated.

Brown and Mohan, on the other hand, concluded from their analysis that cancer is less fatal among the higher social or economical classes; but the data on which these conclusions were based were somewhat irregular. In support of their statements, these investigators cited observations made in Hamburg, where the average income was found to be related negatively to the rate of cancer mortality. In 1923, Stevens commented that, generally speaking, there appeared to be evidence of a moderate increase in the cancer death rate down the social scale, while showing marked exceptions in favor of the very specially situated occupations of mining and agriculture. Maynard (1909) reported from American sources that the lowest death rates from cancer were observed among occupations belonging to the highest social status, while Dublin (1924) concluded, from the data of the Metropolitan Life Insurance Company (U.S.A.), that the cancer mortality rate at the ages where the cancer rate is significant decreases with the rise in the economical status.

Cramer revived, in 1927, the idea of the "social cancer" in contradistinction from the "occupational cancer." This investigator pointed out that the incidence of gastric cancer increases as one goes down the social scale, so that in the two lowest classes this type of neoplasm is responsible for two-thirds of the total cancer mortality, while it accounts for somewhat more than one-third in the highest social class. Cramer based his conclusions on data provided by statistical analyses of the cancer mortality in Bavaria (Hang, 1924-1928) for different occupations. The following tabulation by Cramer illustrates the relationships observed:

Social Class, Description of Occupation	Percentage of Gastric Cancer in Total Cancer	Absolute Number
I. Merchants, high officials, doctors	38.8	2084
II. Office workers	40.1	970
III. Publicans, brewers, small officials	48.5	2140
IV. Skilled workmen	56.8	4247
V. Unskilled workmen	63.4	2423
VI. Agricultural laborers	68.5	6907

Referring to the analyses with regard to the occupational occurrence of gastric cancer in individuals connected with the alcohol trades (Young and Russell), Cramer pointed out that some of the trades with an excessive rate of gastric cancer had no considerable exposure to alcohol consumption and that therefore the evidence implicating alcoholism in the etiology of gastric cancer was far from convincing. More recent English statistical investigations conducted on this subject (Editorial) seemed to indicate that the excessive incidence of gastric cancer in the social Class V was not caused by occupational agents, but probably by some other environmental influences. Cancers of the intestine and rectum, on the other hand, were outstanding among those cancers which exhibited for both sexes and all five social groups no definite relationship between cancer mortality and social class for persons 35 to 65 years old.

For cancers in sites most exposed to external irritation (skin, larynx, alimentary tract above pylorus), on the other hand, the cancer incidence increased continuously among the male members from Class I to Class V, while the female members did not participate in this movement (Class I, upper and middle class; Class II, intermediate; Class III, skilled workers; Class IV, intermediate; Class V, unskilled workers). Similar conclusions were reached by Stocks in 1936 from statistical data dealing with the marked variations in general and organ cancer mortality observed among the inhabitants of various parts of Wales and England. The evidence obtained indicated, in this instance, that, in addition to occupational factors, other influences of endogenous (sex, race, etc.) and exogenous nature played a role in bringing about the marked variations in the incidence of certain tumors in different localities.

The fundamental objections which can be raised against the value of these studies are identical with those previously mentioned in connection with ocupational neoplasms. Hoffman's comment, that cancer statistics related to the social and economic status must be dealt with in an extremely cautious manner if erroneous conclusions are to be avoided, must be heartily endorsed.

Variations in the incidence of cancer with regard to regions and social classes have been attributed to differences of a more general environmental nature. It has already been noted that Kennaway considered the excess of scrotal cancer among the members of the lower social classes to have been caused by a defective personal hygiene more common in the lower strata of society than among the higher ones, and to an exposure to the dust of towns.

Mention must here be made of two theories relating the higher incidence of cancer among the industrially occupied population to the production of substances released into the atmosphere, by many industrial establishments, in the form of gases or fumes, which exert their alleged specific carcinogenic influence upon the workers, as well as upon the civil population living within the fume zone of such plants. Meyers referred, in his discussion of cancer death rates, smoke, and topography, to the contention of Green, that sulfur dioxide fumes, generated in numerous industrial establishments, or resulting

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/26

from defective burning of coal in furnaces, were responsible for the excessive incidence of cancer among persons exposed to this substance for occupational or general environmental reasons (workers in aniline dye plants, paraffin factories, gas and pitch plants, breweries, metallurgical factories, etc.). The local crowding of cancer deaths in valleys, gulleys, or in such parts of the towns where uneven roof lines produced pockets in which the sulfur dioxide fumes could accumulate, was attributed by Green to this cause. From a study of three different parts of Manhattan with regard to their relative cancer death rates and environmental factors, Meyers reached the conclusion that the portions exempted or less affected by smoke, fumes, and gases had a lower cancer death rate than those in which these pollutions of the air were present. As Meyers could not trace the differences found to factors such as age, sex allocation, etc., environmental conditions of the type suggested by Green were considered to be responsible for the excessive cancer mortality in the polluted regions.

A similar conception was advanced by Stephens, who was inclined, however, to blame the inhalation of carbon monoxide, of occupational or environmental origin, for the excessive incidence of cancer in certain professions. Analyzing the cancer deaths recorded in the Registrar's General Decennial Supplement (1921), Stephens found the highest cancer mortality in occupations which he considered excessively exposed to inhalation of carbon monoxide (waiters, cutlery grinders, tin and copper miners, cellarmen, cotton spinners, hat formers, gas stokers, puddlers, and china ovenmen), while low cancer death rates were listed for occupations having little contact with this gas (ministers, clergy, bank officials, machine compositors, leather goods makers, stone miners, etc.).

These theories dealing with the nature of the various environmental agents and conditions allegedly incriminated in the causation of occupational and environmental cancer are mentioned not because they are considered as valuable and important, but as excellent illustrations of the confusion and uncertainty existing in the field of statistical cancer research. It appears to be very likely that statisticians may be able to establish many more statistically significant relationships between etiologically unrelated items, one of which being cancer incidence or etiology.

According to the existing statistical information, cancer contributes relatively little (0.9 per cent per thousand industrial disabilities per year) to the annual volume of chronic disability, owing to its low incidence. The average amount of disability per case for this disease, however, is relatively high and ranks on this basis in importance with the cardiovascular-renal diseases, nervous disorders, etc., as an important cause of industrial disability (Perott and Holland).

BIBLIOGRAPHY

AIKMAN, J., J.A.M.A. 103: 640, 1934.

ARNSTEIN, A., Wien. Arbeiten a.d. Geb. d. soz. Med. 2: 63, 1912.

ASCHOFF, L., Verbreitung des Krebses. Klin. Jahrbuch, 1902.

BAADER, E. W., Klin. Wchnschr. 18: 522, 1939.

BLUMENBERG, W., Arch. f. Hyg. 118: 142, 1937.

BROWN, A. C., and MOHAN, L., J. Hyg. 14: 186, 1914.

CAROZZI, L., Some Observations Upon Occupational Cancer. Report International Conference on Cancer, London, 1928, p. 311.

CRAMER, W., Am. J. Cancer 29: 1, 1937.

DUBLIN, L. I., and VANE, R. J., Bull. United States Bureau of Labor Statistics, No. 582, 1933.

EDITORIAL, Am. J. Cancer 36: 110, 1939.

FIRKET, J., and MALTER, M. A., Arch. méd. soc. et d'hyg. 2: 797, 1939.

GOODMAN, J., and SULZBERGER, M., J. Allergy 9: 136, 1937.

GREEN, C. E., The Cancer Problem. 3rd ed., Chicago Medical Book Co., 1914.

HAAGENSEN, C. D., Am. J. Cancer 15: pt. I, 641, 1931.

HENRY, S. A., and IRVINE, E. D., J. Hyg. 36: 310, 1936.

HERON, D., On the Relation of Fertility in Man to Social Status, etc. London, 1906, Dulan & Co.

HOFFMAN, FR. L., Statistics of Occupational Cancer, Report International Conference on Cancer, London, 1928, p. 318, Bristol, John Wright & Sons, Ltd. The Occupational Incidence of Cancer. Newark, N.J., Prudential Press, 1931.

HOFFMAN, W. J., Prevent. Med. 6: 7, 1936.

International Labour Office Reports, Tumours of Occupational Origin and Occupational Cancer, No. 171, Geneva, 1921.

JACOBS, E., Ztschr. f. Krebsforsch. 32: 469, 1930.

JEPHCOTT, C. M., Canad. Pub. Health J. 28: 391, 1937.

JOHNSTONE, R. T., J.A.M.A. 111: 1741, 1938.

KENNAWAY, E. L., The Occupational Incidence of Cancer of the Penis and of the Scrotum in the General Population. Report International Conference on Cancer, London, 1928, p. 303. Bristol, John Wright & Sons, Ltd.

KOELSCH, FR., Jahresb. f. ärztl. Forthild. 15: No. 9, 1924.

KOINUMA, B., Gann 24: 416, 1930.

LOTH, R., in Weyl, Th., Handbuch der Arbeiterkrankheiten, Gustav Fischer, Jena, 1908.

MCCONNELL, W. J., J.A.M.A. 109: 762, 1937.

MARTLAND, H. S., J.A.M.A., 103: 643, 1934.

MEYERS, J., Am. J. Pub. Health 20: 581, 1930.

NAGAYO, M., and KINOSITA, R., Yale J. Biol. & Med. 12: 301, 1940.

NEWSHOLME, A., Brit. M. J. 1: 74, 1898; 1: 161, 1894.

OLIVER, TH., Dangerous Trades, London, John Murray, 1902, p. 138.

PERROTT, G. St. J., and HOLLAND, D. F., J.A.M.A. 108: 1876, 1937.

RECTOR, F. L., J.A.M.A. 101: 672, 1933.

RUF, H. W., and FLUCK, W. Z., Am. J. Pub. Health 29: 1149, 1939.

SAPPINGTON, C. O., Indust. Med. 6: 85, 1937.

STAEMMLER, M., München. med. Wchnschr. 85: 121, 1938.

STEPHENS, G. A., Med. Press 187: 283, 1933.

STOCKS, P., Brit. Emp. Cancer Campaign Annual Report 13: 257, 1936.

STÖRRING, E., Klin. Wchnschr. 18: 794, 1939.

TEUTSCHLAENDER, O., J.A.M.A. 95: 1278, 1930.

UYEHOSHOTI, Arch. méd. soc. et d'hyg. 2: 830, 1939.

VOSS, H., Arch. f. Gewerbepath. 9: 453, 1939.

YOUNG, M., and RUSSELL, W. T., An Investigation into the Statistics of Cancer in Different Trades and Professions. H. M. Stationery Office, London, 1926, Special Report Series No. 99.

ZANGGER, H., Arch. f. Gewerbepath. 1: 1, 1930.

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/28

that certain general environmental factors or some occupational hazards of chemical or physico-chemical character played a significant role in the production and increased frequency of pulmonary tumors (Haintz; Rice; Koelsch; Bonser; Fischer-Wasels; and Shennan). Other workers suspected or directly blamed one or several extraneous agents as being prominently involved in this respect.

I. ILL-DEFINED OCCUPATIONAL AND NON-OCCUPATIONAL CHEMICAL AGENTS

Prolonged environmental and occupational exposure to dust without regard to its chemical nature, but with emphasis on the quantity inhaled, is considered by many as a cause of the chronic inflammatory conditions of the bronchial and pulmonary epithelium, which may lead to cancerous processes of these tissues. The chronic bronchitis, chronic interstitial pneumonia, and fibrosis (pneumoconiosis) set up in the lung, by the inhalation and deposition of dust particles, give rise to the development of regenerative, metaplastic, epithelial proliferations; or they may activate preformed metaplastic lesions (post-influenza) and prepare the soil for a subsequent malignant transformation of these epithelial changes (Ssipowsky; Tuttle and Womack; Katz; and Hampeln). In the opinion of Hampeln, bronchiogenic carcinoma is a dust inhalation disease. An augmented production of dust, resulting from the rapid expansion of industrial activities and the marked rise of vehicular traffic during recent years (affecting, especially, the thickly populated industrial districts and big cities), is implicated in the increase of pulmonary malignancy among the general population during the same period, according to Dissmann; Schmidt; Ewing; Brandt; Ferenszy and Matolscy; Maternia; Heilmann; Ménétrier; Ribbert; Moise; Rostoski; Rostoski, Saupe and Schmorl. This conception was supported by the observation that lung cancer is found more often in domesticated animals exposed extensively to the inhalation of street dust (horses, cattle, sheep, and dogs) than in those living in rural areas (Joannović; and Sticker); while wild animals were supposed to suffer only from benign pulmonary adenomas (Fox).

A similar reasoning has been applied by many workers to connect the genesis of lung cancers and their recent rise in incidence with the more generalized occupational exposure to industrial dust. A relatively higher frequency of pulmonary malignancy among persons exposed occupationally to the inhalation of solid particles (street dust, stone dust, metal dust, coal dust, and glass dust) was recorded by Seyfarth. The late increase of pulmonary malignancy among inhabitants of the Dresden district was related by Schmorl to the production of chalicosis among workers of the sandstone industry, and of anthracosis among coal miners there. Workers employed in the following dusty industries: manufacture of pottery, metallurgy, building trades, and tobacco plants, have an increased liability to lung cancer, according to Simpson. Harvey reported from Australia that 38 per cent of the cases with

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/29

lung cancer had been exposed to noxious types of dust during their work (quartz, gold ores, copper ores, tin ores, and coal). The greatest susceptibility to lung cancer was displayed by workers exposed to house dust. Among men engaged in dusty occupations, an especially high incidence of lung cancer exists in grooms (Hudson). In the series reported by Duguid, there were 72 outdoor workers against 71 indoor workers. Since three-fourths of the population is represented by indoor workers, the incidence of lung cancer is three times higher in outdoor workers than in indoor ones, who are exposed to the inhalation of dust to a lesser degree than the former, in the opinion of Duguid. This investigator believed that this evidence supports the causative significance of dust in the development of pulmonary malignancy. Schachter emphasized the etiological importance of a dusty occupation for the production of lung cancer. Among 898 cases of lung cancer, collected by Brochbank, 61 cases had occupational exposure to some kind of dust (18 metal workers, 15 cigar makers, and 28 carpenters); while in Brockbank's own series of 62 cases, 9 or 14.5 per cent were associated intimately with dust and 18 or 29 per cent were exposed to fumes. Among the cases, reported by Ferenszy and Matolscy, 43 per cent came from professions with a dust or fume hazard. Occupational exposure to tobacco dust has figured prominently in the studies of several investigators concerning a carcinogenic dust hazard. Rottman listed cigar makers, metal workers, and spinners among professions most often affected by pulmonary malignancy. Similar claims have been made by Wacker and Schmincke; Krompecher; Langbein; Behla; Heilmann; Benda; Borst; Ferenszy and Matolscy; Enger; Brinkmann; and Seyfarth. Cigar makers, sorters, dealers, and other tobacco workers have been cited as showing an increased liability in this respect and Jaeger and Kolbe considered cancer of the lung as an occupational disease of tobacconists. Cancer of the respiratory tract was found to be especially frequent among male workers of certain Sheffield trades connected with metallurgic industries (machinists, foundry workers, and metal grinders) (Turner and Grace). An occupational exposure to dust was present in 20 per cent of the cases reported by Ask-Upmark, and in 75.4 per cent of those recorded by Rosedale and McKay. From death certificates of England and Wales for the years 1920 to 1932, Kennaway and Kennaway obtained the following correlations between dusty occupations and incidence of lung and larynx cancer. A rather high excess of these neoplasms was statistically found in workers exposed to road dust [paviours, street cleaners, dustmen, and drivers of horse drawn vehicles and automobiles (chauffeurs had a normal rate of larynx cancers)], masons, concretors, council workers, workers exposed to producer coal gas and tar products, pottery makers, French polishers, tobacconists, and metal grinders (silica exposure); while a low lung cancer death rate was found among workers of the agricultural and mining industries, and cotton mule spinners (crude oil exposure), a normal liability existed among carpenters and grooms of horses. As no special occupation

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/30

seemed to account for the total increase of lung cancers, Kennaway and Kennaway concluded that industrial hazards did not play any important role in this connection.

A similar opinion was expressed by Harris, who observed in a series of 117 cases of laryngeal carcinoma (age, 39 to 53 years), 6 cases of laryngeal cancer and two lung cancers in coal miners after an occupational exposure to coal dust for 15 years or longer. The actual incidence of laryngeal cancer is not as high in miners as in occupational groups not exposed to a dust hazard. Occupational exposure to wood dust was blamed by Sekoulitsch for the increased occurrence of cancer of the larynx, tonsil, and base of the tongue in carpenters and cabinet makers. Benign laryngeal tumors have been related etiologically to an excessive, occupational, mechanical stress of this organ, such as existing in singers, teachers, officers, and professional speakers (Kahler); consequently, significant excess of laryngeal cancer exists among musicians and a doubtful one among teachers (Young and Russell).

The negative attitude of Kennaway and Kennaway toward the causative role of dust in connection with pulmonary malignancy is shared by Fischer-Wasels; and Landis. The fundamental contention that there has been an increase in street dust in late years was challenged by Teleky, who pointed out that in spite of greatly increased traffic, the production of dust had decreased in comparison to former years because of better road conditions. Street dust does not possess any carcinogenic significance in the opinion of Berblinger; Kikuth; and Schmidtmann. The absence of an excessive incidence of lung cancer among persons especially exposed to street dust (policemen, trolleymen, teamsters, chauffeurs, street workers, and street venders) was cited by Probst in refutation of the theory of a carcinogenic action of this substance. A similar conclusion was reached by Pancoast and Pendergrass, who observed three cases in which a lung cancer occurred in association with pneumoconiosis. These investigators felt that the report of isolated cases of bronchiogenic cancer among coal miners, stone cutters, cigar makers, and men engaged in many other dusty occupations did not render conclusive evidence to warrant any definite decision. A concurring opinion on this subject was expressed by Saupe, who added that the physical examinations, conducted by Krüger, and Rostoski and Thiele, on workers of various dusty industries (stone masons, workers in pottery factories, cigarette plants, bronze works, and asbestos plants, and bakers) did not yield any evidence of a causal relationship between pneumoconiosis and pulmonary carcinoma. Observations made by Feil in France caused him to state that lung cancer is not frequent in workers exposed to dust (coal and iron miners).

The etiological significance of tobacco dust was questioned by Lehmann, who pointed out that persons engaged in the tobacco trade are, in general, heavy smokers, and that this habit is more likely to be of causative importance than the exposure to the tobacco dust. The presence of pneumoconiosis in

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/31

only 2.9 per cent of Olson's series of pulmonary malignancy does not support the conception of a significant causative role of dust in the genesis of this type of neoplasia. It was pointed out by Duguid that the smoke abatement campaign, which was conducted in England some time ago and which resulted in a considerable decrease of the solid particles in the air, was not followed by a decrease in the incidence of lung cancer. The dust theory of lung cancer does not explain, in the opinion of Assmann, the marked regional differences in the incidence of lung cancer existing among certain industrialized districts in Germany (Saxony: high lung cancer rate; Ruhr district: low lung cancer rate). The evidence favouring the dust factor is not too convincing in the opinion of Stout, who refers to a statement of Huguenin. This author remarked that there was no increased incidence of lung cancer among miners of England, France, Germany, and Belgium.

From an evaluation of these contradictory data it is quite apparent that dust as such, irrespective of its chemical character, is not conducive to lung cancer (Kennaway; Kikuth; and Assmann). The evidence cited presents, perhaps, the most striking illustration of an error repeatedly committed in connection with statistical investigations on the cause of environmental and occupational tumors. It must be considered a fundamental fallacy, if an attempt is made to find the extraneous carcinogenic agent of a certain neoplasm by determining statistically its incidence among members of large occupational groups (chemical workers, miners, and metallurgical workers), comprising an indefinite and multifarious conglomeration of smaller and larger groups of workers exposed to environmental influences of the most diversified nature. Even in smaller occupational groups a certain hazard may vary greatly in intensity and duration, and in effect, as far as the various members are concerned and depends upon the type of work in which they are engaged. Therefore, it becomes clear beyond any doubt, that no reliable or conclusive information can be obtained when large occupational groups are evaluated. This consideration applies to an even greater degree when general classes of individuals, such as outdoor and indoor workers, are analyzed. The result of such an approach usually causes not a clarification but an increased confusion of an already complex situation. The concept of the "chronic irritation" theory of carcinogenesis, still considered by many workers as a plausible explanation of this biological phenomenon, has furnished the "scientific" basis for such a mistaken and futile approach.

The recent developments of experimental and occupational cancer research have demonstrated rather definitely that chemically specific agents rather than non-specific irritative factors, such as dust in general, play an important and essential role in the production of malignant neoplasms. Moreover an outstanding histologic feature of the development of experimentally induced pulmonary tumors in mice was the absence of any inflammatory changes in the precancerous and early cancerous lesions (Andervont). The investigations deal-

ing with the potential carcinogenic action of certain well-defined, abnormal, atmospheric ingredients are of greater scientific significance and have produced more reliable and definite information.

II. CHEMICAL AGENTS OF DEFINED TYPE

The exposure to the inhalation of chemically well-defined substances is to a large extent restricted to industrial hazards. The industrial exposures consist of contact of the respiratory organs with abnormal atmospheric ingredients present in the form of dust, fumes, vapors, and gases of the most varied types. Non-occupational contact with atmospheric contaminants is limited to the inhalation of coal dust, soot, carbon monoxide, sulfur dioxide, and, in some mining regions, arsenicals [smelting of arsenic containing ores (copper, iron, and silver)].

Silicosis

Silicosis, which is second only to anthracosis the most frequent type of industrial pneumoconiosis, has been incriminated by Fine and Jaso; Dible; and Charr as direct or indirect cause of pulmonary cancer. There are approximately 40 to 50 verified cases on record in which these two pulmonary conditions coexisted (Dible; Fine and Jaso; Klotz and Simpson; Klotz; Maxwell; Sladden; Middleton; Sweany; Porsche and Douglass; Vorwald and Karr; Allen; Sokoloff; Pancoast and Pendergrass; Simons; Schnurer; and Charr), when combinations of asbestosis and lung cancer are excluded from this list. Silica belongs to the biologically active types of dust (in contrast to the inert types, such as carbon), which are capable of exciting a characteristic tissue response of fibrotic nature in the lung (Gardner) by causing foci of chronic inflammatory irritation. Silicotic pneumoconiosis fulfills all the requirements which may be asked from a nonspecific carcinogenic agent acting on the basis of the chronic irritation theory of carcinogenesis.

A recent analysis of the pulmonary cancer incidence in 50 cases of silicosis observed from 1925 to 1936 by Klotz led this author to believe, that the liability to pulmonary malignancy was excessive in silicotics compared with that of the general population. There were four cases of lung cancer in this group, whereas 53 lung tumors were found among 4,500 necropsies performed during the same period. Only one of the silicotic cases with lung cancer was employed as a miner, while the others belonged to different occupational groups, such as metal workers, laborers, and gas company employees. A marked pulmonary fibrosis was present in only one case; this condition was of minimal or slight degree in the rest of the cases. The type of evidence, advanced in support of the conclusion drawn, cannot be admitted as adequate. In view of the great practical and scientific importance of this potential interrelation, it is fortunate that a number of very comprehensive, reliable, and thorough clinico-statistical studies have been made and have led to a definite decision concerning this question.

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/33

Important autopsy observations made on South African gold miners, in whom silicosis is of frequent occurrence, were used in a study of the alleged causative interrelation of lung cancer in silicotic individuals (Reports of the Miner's Phthisis Medical Bureau of South Africa, 1932 and 1935). Among 3,215 autopsies performed on European males employed in the mines or members of the white population of Johannesburg (deaths in the Johannesburg General Hospital), there were 16 cases of lung cancer during a period of eight and a half and eleven years, respectively (report of 1932). The relative percentage of lung cancer of these groups was as follows:

	European Non-Miners	*Miners without Silicosis*	*Miners with Silicosis*
Autopsies	1023	1109	1083
Per cent of Lung Cancer	0.58	0.54	0.37

Similar relations were stated in the report of the year 1935

Autopsies	1393	1679	1438
Lung cancers	13	12	10
Per cent	0.93	0.71	0.70

These data, obtained through post-mortem examinations, indicate clearly that the presence of a silicosis does not predispose or favor the development of a pulmonary malignancy. Similar extensive studies of the question, based on the roentgenological and clinical examinations of persons exposed to dust, were reported by Vorwald and Karr, using evidence collected from the literature and their own observations. The following tables are taken from the paper of these two investigators:

Incidence of Pulmonary Tumors in Clinical and Roentgenological Examinations of Individuals Exposed to Dust, as Reported in the Literature

Number of Cases	*Non-Silicotics*	*Silicotics*	*Pulmonary Tumor*
57,362	45,156	12,206	3(0.005%)

Incidence of Pulmonary Tumors as Revealed by Serial Chest Roentgenograms in Individuals Exposed to Dust and Examined in the Saranac Laboratory

Occupation	*Number Examined*	*Pulmonary Tumor*
Iron Mines	7,324	3
Foundries	6,613	0
Cement plants	823	0
Gypsum plants and mills	762	0
Copper mines	65	0
Silicotics	1,357	1 (0.074%)
Non-Silicotics	14,230	2 (0.014%)
Total	15,587	3 (0.019%)

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/34

Incidence of Carcinoma Seen at Autopsy in Individuals Exposed to Dust and Examined in the Saranac Laboratory

Number Examined	*Years Exposed*	*Silicotics*	*Carcinoma*	
			Pulmonary	*Non-Pulmonary*
178	1-46	136	2 (1.12%)	4

"In the remaining 176 cases without pulmonary carcinoma, proliferation of the respiratory epithelial elements was not observed. This obtained even though pulmonary dust fibrosis was often massive and had compressed many epithelial-lined air passages" (Vorwald and Karr).

The conclusion reached by these two investigators is that the inhalation of silica dust cannot be considered as an etiological factor in the development of primary pulmonary carcinoma.

This decision is corroborated by studies, conducted by Schulte and Schulz, on miners employed in the Ruhr district, where silicosis is frequently observed. Schulte even expressed the opinion that silicotic lungs provide a poor soil for the growth of a malignant tumor. Allen, who agreed with this opinion, stated, in connection with a report of two cases of anthracosilicosis associated with pulmonary carcinoma in coal miners of Pennsylvania, that pulmonary carcinoma was rare among coal miners of that part of the country, according to evidence supplied by roentgenological examinations.

There do not exist any experimental observations which support the existence of causal interrelation between the inhalation of silica dust and lung cancer. Guinea pigs, exposed to the inhalation of dust containing 98 per cent silicon carbide three to four days a week, 50 hours per month for 18 to 31 months, did not develop any pulmonary cancers (Willis; and Willis and Brutsaert); but seven animals showed adenomatoid formations in the lung at autopsy. Since similar lesions occur spontaneously in the lungs of guinea pigs (Sternberg; and Leitch) without leading to malignancy, the interpretation of these nodes under experimental conditions remains doubtful. Similarly negative results were obtained by Vorwald and Karr in a series of 3,338 animals of various species (guinea pigs, rabbits, rats, mice, cats, and chickens) exposed to the inhalation of varying types of dust for periods extending up to 749 days. The majority of substances used in these experiments were silicates (chalcedony, quartz, granite, chert, asbestos, and carborundum). The table appearing on page 399 prepared by Vorwald and Karr summarizes these studies.

Clinical as well as experimental evidence indicates that the common types of silica dusts do not possess any direct or indirect carcinogenic properties in connection with the development of pulmonary malignancy. This statement may not apply in regard to the inhalation of the special types of silicates contained in asbestos. Clinical observations, made during recent years, arouse the suspicion that the occupational inhalation of asbestos dust has a certain causal relationship to the production of bronchiogenic carcinomas.

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/35

Type of Dust	Guinea Pigs	Rabbits	Rats	Chickens	Mice	Cats	Pulmonary Tumors
Chalcedony	242	28			40		0
Quartz	894	41	201	12	24	4	0
Marble and quartz	25						0
Hematite and quartz	28						0
Quartz and gypsum	88		27		6		0
Granite	298						0
Chert	196	3	52		10		1
Hematite	106		31				0
Asbestos	235						0
Soft coal	37						1
Fluorspar-crude			15				0
Carborundum	213						0
Marble	172		12				0
Gypsum	200		12				0
Total	2832	72	338 3338	12	80	4	2 0.06%

Asbestosis

Chemical and Technological Aspects. Asbestos, designating a group of silicate minerals of crystalline fibrillar structure, was known to the ancient world. At that time and during the following centuries it was used occasionally in the production of perpetual lamp wicks, shrouds for cremation, and other purposes partly of curiosity character. It was only since the latter third of the last century that this material has attained a major industrial importance, and has become of serious significance from the standpoint of industrial hygiene.

Asbestos is distributed widely in the world but occurs in relatively few places in sufficient quality and quantity to make mining profitable. The chemical nature of commercial asbestos varies with the site of its occurrence.

1. Amphiboles, found in Italy, South Africa, and Australia, occurs in five varieties: a) tremolite is a white, brittle, calcium-magnesium silicate; b) actinolite is a mineral consisting of fibrillar or radiating crystals; c) hornblende-asbestos or amphibole-asbestos is a flexible, greenish, fibrillar matter containing much calcium and a high amount of silicic acid; d) mountain leather, mountain cork, or mountain wood is of a greyish or brownish color occurring in the form of sheets of interlacing fibrils; e) crocidolite, which is mined mainly in Australia and South Africa, has a bluish color, a silky lustre, and elastic fibers of considerable length and tensile strength, and is a soda-iron silicate. These types are usually very acid resistant, but less fire resistant.

2. Serpentine and its subvarieties, picrolite and chrysolite, are hydrated magnesium silicates in which the magnesium may be replaced by iron in

some types. The serpentine has a bandy or slate texture and may contain traces of nickel and copper. It is mined in Canada, Russia (Ural Mountains), Germany, Corsica, France (Pyrenees), Siberia, and South Africa.

The Canadian asbestos, mined at Thetford near Quebec, where approximately 78 per cent of the world production is obtained, consists of 33 parts of magnesium, 41 parts of silicic acid, and 5.75 parts of iron oxide (Oliver); while South African asbestos is composed of 2 parts of magnesium, 50 parts of silicic acid, and 40 parts of iron oxide. Italian asbestos contains 42 parts of silicic acid, 38 parts of magnesium, and 3 parts of iron oxide. None of the various types possesses any free silicic acid.

The production of asbestos has risen enormously in recent years. It received this great impetus from its use in the automobile industry. The total production in 1868 was two hundred tons; in 1880, five hundred tons; in 1925, 330,000 tons; and in 1929, 430,000 tons. The United States is the principal consumer of this product. More than 12,000 persons are employed in the chief asbestos plants of this country. Occupational contact with asbestos is present in many industries using asbestos products. Asbestos is employed for a great variety of purposes, such as the manufacture of incombustible and insulating materials (fire resistant clothes, blankets, theater curtains, sheets, ropes, cords, twine, and threads), filter cloths, mill-board, wall board, shingles, tiles, mortar (together with cement and plaster of Paris for providing a fireproof wall lining), clinkers, gaskets, packing material of pumps, insulating material of steam pipes, water pipes, boilers, and electric wires, brake lining, paper, mattresses, adsorbent of dyes (for manufacture of fire proof and acid proof stains), ingredient of rubber products, and artificial wood (mixed with wood powder) (Lanza; Lynch; Stewart, Bucher and Coleman; Ullmann; Encyclopedia Britannica; Dewirtz; Nordmann; Alwens; and Cooke). The fibrillar types are spun, twined, and woven, while the brittle varieties and the dusty waste are compressed and molded into the desired shapes.

Conditions and Types of Exposure. The chief health hazard consists in the inhalation of asbestos dust, which is produced abundantly during the preparation of the mineral for the spinning process (purification and removal of stony impurities) and during various other phases of the production and manufacturing processes of asbestos and asbestos containing goods. Direct contact of the skin with asbestos is of minor importance. The number of actually exposed persons is rather large in the industries manufacturing asbestos products. Of the 12,000 workers employed in the major asbestos plants of the United States, Lanza estimates that 10,000 are exposed appreciably to the asbestos dust; while in Germany, where several thousand asbestos workers are present, only a fraction are said to be actually exposed.

Symptomatology: Cutaneous Lesions. The direct skin contact with mined asbestos is responsible for the production of painful warts formed around the asbestos needles, which penetrate the skin of the palms of the hands. The

majority of asbestos miners in the Ural Mountains are said to have on the inner surfaces of the right hand three to five or more papular, non-inflammatory, wart-like formations of round or polygonal shape reaching the size of a pea (Dewirtz). They consist of hyperkeratoses sometimes associated with acanthosis and prolongation of epithelial cell pegs. There is some lymphocytic infiltration in the cutis. Between the cornified masses asbestos needles are found. Many mitoses may be present in the thickened malpighian layer, and large giant cells with centrally located multiple nuclei may be present in this stratum. These lesions will persist unless the asbestos needles are removed. The warts do not exhibit any appreciable proliferative tendencies.

Pulmonary Lesions (Asbestosis). The asbestotic pneumoconiosis, resulting from a prolonged occupational inhalation of asbestos dusts and fibrils, is a condition more serious than the cutaneous manifestations. The first fatality of asbestosis was reported by Murray in 1899. It was not until 1914 that a record of an asbestosis death was published in Germany (Fahr). Fatalities from asbestosis as the main or contributory cause of death were published in the United States by Lynch; Stewart, Bucher and Coleman; and Shull. The Metropolitan Life Insurance Company recorded, between 1924 and 1936, seventeen cases in which asbestosis contributed to the lethal outcome of the main disease.

In Germany there was no appreciable interrelation between asbestosis and tuberculosis of the lung, such as exists regarding silicosis. In England there were 30 cases of asbestosis complicated by tuberculosis in a series of 100 cases of this type of pneumoconiosis reviewed by Wood. Similarly, in the United States a certain relation to tuberculosis was apparent, but the coexistence of the two diseases was not as frequent as in the case of silicosis (Stewart, Bucher and Coleman; Shull; and Lanza, McConnell and Fehnel). The development of a pulmonary asbestosis depends, according to Bauer, upon the duration and degree of exposure to asbestos dust, and on a certain personal disposition. A similar observation was made by Sweany, who remarked that some people develop an asbestosis rapidly, while others may be exposed to the same conditions for years without detriment. Individual differences in the filtering qualities of the nasal passages are mentioned by Lehman as possible reasons for such discrepancies in susceptibility.

Asbestosis usually develops after an exposure of three to fifteen years (Martz), but may not produce subjective symptoms until many years after the cessation of exposure to asbestos material. The first symptoms are dyspnea and a cough with expectoration. Later there is pallor, cyanosis, palpitation of the heart, loss of appetite and weight, and piercing pains in the chest during breathing. The shortness of breath becomes aggravated during physical exertion. In the beginning the physical examination reveals scarcely any pulmonary changes; but later there appears a diminution of resonance, especially over the lower parts of the lung (particularly the right side), where dry and

MEDICAL LIBRARY

crackling sounds are perceptible in auscultation. The respiratory capacity is decreased, and there is a diminution of the respiratory shift of the pulmonary borders during respiratory movements of the lung. The heart is often enlarged due to the increased functional demand placed on it, because of the decreased respiratory surface and impaired circulation in the lung caused by the pulmonary fibrosis. The enlargement of the right side of the heart becomes accentuated as a cardiac insufficiency ensues. The roentgen-examination of the chest shows an early, diffuse, interstitial fibrosis having reticular honeycomb-like outlines and showing progressive tendencies, which later cause a filmy-hazy appearance of the lung. This condition has been termed "ground glass" appearance. The hilum shadows are enlarged in the more advanced stages. The movements of the diaphragm are reduced. The microscopic examination of the sputum executed with proper methods and thoroughness reveals the presence of golden brown asbestos bodies.

Pathology. The observations made at necropsy reveal a shrunken, blue-black lung of firm consistency containing little air, especially in the lower lobes which often are covered by a thickened pleura. The cut surface shows a widened, thickened, and prominent, interstitial, connective tissue. There are bronchiectases and small abscesses together with pleural adhesions and bronchopneumonic foci. The hilum nodes are enlarged, hard, and brownish.

Upon histological examination asbestos bodies are found in the interstitial connective tissue, and the peribronchial and hilum lymph nodes. These characteristic formations consist of a central translucent fiber or needle-like crystal (asbestos crystal) measuring 10 to 100 microns in length and 1 to 12 microns in thickness. The central fiber is ensheathed in a shiny golden or brown substance with varying architectural figuration. The whole body may have the shape of a rod with smooth blunt ends, or with one or both ends forming a single knob or a conglomeration of knobs. The shaft is often a series of rounded beads or discs strung closely along the central filament (Lynch). In other instances the asbestos body has the shape of a hoe or a club, or represents a long slender filament. The bodies give a characteristic Prussian blue reaction, which is attributed to their iron content. The iron content of the asbestos bodies is higher than that of the asbestos needles. The assumption has been made that the additional iron originates from decomposed erythrocytes. The nature and chemical composition of the asbestos body is still uncertain. McDonald advanced the theory that the central part of the body is represented by a particle of an asbestos fiber in the process of alteration and absorption by hydrolysis, while the enveloping matter was supposed to consist of silica in a colloidal or gel-like state. This latter conception was proposed, also, by Koppenhofer.

Beger contended that the sheath was composed of proteinic matter. The asbestosis bodies are found within the bronchioli, in the alveoli, and in the interlobular, peribronchial and subpleural tissues among the lymphatic routes.

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/39

They occur, moreover, in the peribronchial lymph nodes, within the walls of the sinuses, and embedded in fibrous areas. In the alveoli they are surrounded by phagocytic, mononuclear cells and foreign body giant cells massed especially around the larger bodies. The interstitial tissue shows a diffuse fibrous thickening and scarring. The asbestosis is, thus, an indurative, interstitial, diffuse fibrosis of the lung increasing in degree from the apex to the base.

Asbestosis and Carcinoma of the Lung. It is only in very recent years that serious consideration has been given to the possibility of a cancerigenic action of asbestosis upon the lungs. In an analysis of 18,280 death certificates for cancer of the lung and larynx in males from England and Wales from 1921 to 1932, Kennaway and Kennaway did not find any cases of lung cancer in asbestos workers. Since 1935, an appreciable number of cases of asbestosis associated with carcinoma of the lung, have been reported from England, Germany, and the United States (Lynch and Smith; Lynch; Gloyne; Wood; Horning; Nordmann; and Egbert and Geiger). The incidence of lung cancer among workers in whom an asbestosis was found at autopsy is relatively high, ranging from 17 per cent (Nordmann: 2 out of 17 cases) to 20 per cent (Wood: 2 or possibly 3 out of 12 cases). Teleky noted that there exists a minimum of 99 and a maximum of 78 autopsies in fatalities from asbestosis, the records not being clear in this respect. Teleky only knows of 6 cases of pulmonary cancer with asbestosis, and feels that this ratio is high in comparison to the number of necropsies. Koelsch mentioned the occurrence of 12 cases [Lynch (3); Egbert and Geiger (1); Gloyne (2); Dominici (2); Baader (1); Nordmann (2); Wood (3); and Horning (1)]. Lynch and Smith found among 35 autopsies with asbestosis 2 cases of pulmonary malignancy (six per cent), whereas there was an incidence of only 0.3 per cent of this type of neoplasia among approximately 2,300 autopsies of the general population. The period of occupational exposure to asbestos dust ranged for five cases from 7 to 21 years, but in an additional case only a year and a half. In several instances the lung tumor became manifest several years (10 to 12) after cessation of the work in asbestos. Fifteen to twenty-one years elapsed (average, 18 years) between the first exposure to asbestos and the death from asbestosis with carcinoma of the lung. The age at death depended upon the age of the individual at the time of the first exposure. The workers dying in the more advanced age groups entered an occupation with an asbestos hazard later in life, while those who died at an early age started to work in asbestos plants when still young. There was no evidence of a so-called old age predisposition, as two of these cases died at the age of 35 years and a third was 41 years old.

The majority of neoplasms were cornified squamous-cell carcinomas. Only one case was an adenocarcinoma, and a second was an anaplastic, round-cell carcinoma. The latest case reported by Lynch and Smith showed squamous cellular and glandular carcinomatous structures. This numerical distribution between the different histologic types of carcinomas varies distinctly from

that usually observed (Nordmann), but agrees with the shift toward a more frequent occurrence of the cancroids noted in recent years by Probst in pulmonary malignancies of unknown genesis. A multicentric development of malignant growths in asbestos lungs was found by Nordmann and Gloyne, and it is considered by Nordmann as a characteristic feature of this type of lung cancer. A multifocal sprouting of squamous cells lining the bronchial walls was seen by Nordmann, who regards these changes as precancerous in nature. A diffuse, proliferative thickening of the bronchial epithelium was recorded by Gloyne, who believed that this constituted a continuous prolongation of epithelial growth from some unknown starting point rather than a series of isolated proliferative units. These epithelial prolongations were hollow in places, showing a degenerating layer of cells surrounding a central empty space, and, in turn, being enveloped by rings of keratinized squamous cells. The carcinomas of three cases were very small [Gloyne (2); and Nordmann (1)], and had not produced any metastases. For this reason two of these cases (Gloyne) represented coincidental observations made during the post-mortem examination. The other cases were large tumors with extensive metastatic deposits in remote organs.

An evaluation of the evidence presented reveals certain features connected with these cases, which are suggestive of an occupational causation. There is an incidence of lung cancer in asbestosis of the lung which is definitely excessive. The relatively small number of necropsies on which this conclusion is based represents an urgent indication for more extensive post-mortem examinations in cases of asbestosis; especially considering that pulmonary malignancies seen in previously reported cases were, in several instances, very small and were coincidental observations. A second point favoring an industrial origin is the young age of an appreciable portion of the cases thus far recorded, and the relationship existing between the time of exposure to asbestos dust and the manifestation of the neoplasms throughout the entire series. The third factor consists in the shift of the histological types observed in the direction of a predominance of cancroids, and in the multicentric development of two (Nordmann; and Gloyne) and possibly even three (Lynch and Smith) of these pulmonary neoplasms. The existence of the cutaneous warty lesions suggests that asbestos needles embedded in epithelial tissue are apparently capable of eliciting non-inflammatory, epithelial proliferations. Nothing is known about the actual causative mechanism through which asbestosis may produce such epithelial lesions, and may transform them subsequently into malignant growths. The assumption of a chronic irritation of nonspecific nature or of specific silicotic character, such as proposed by Lynch, is scarcely acceptable and satisfactory in view of the negative evidence available in this respect. One of the cases reported by Nordmann in association with Horning showed symptoms of a marked and generalized, allergic disposition (bronchial asthma, and hematic eosinophilia), which may have played a

contributory role in the development of the neoplastic response. Asbestos bodies contain a considerable amount of iron, and there exists some evidence that points to a possible causative interrelation of pulmonary siderosis and carcinoma. The relatively small number of asbestosis carcinomas of the lung reported does not disprove an occupational origin of this condition. Previous experience with other industrial neoplasms (lung cancer of the Joachimsthal miners; and lung cancer of the chromate workers) has shown that such isolated cases may represent the first warning of a subsequent appearance of large numbers of similar tumors of undeniable occupational derivation.

Medico-Legal and Social Aspects. Asbestosis carcinoma of the lung is not included in any group of occupational tumors recognized by any country. The evidence presented is sufficiently serious, and the number of persons exposed to the suspected causative agent large enough to indicate a thorough and extensive clinical, statistical, and experimental investigation of the incidence and causative interrelation of asbestosis and pulmonary carcinoma. In view of the fact that several of the states with many large asbestos plants do not include asbestosis among compensatory occupational diseases, this study is even more urgent. Such a condition militates against an effective hygienic control of an important industrial hazard, and impedes the collection of pertinent and essential information in regard to the incidence, nature, and potentialities of an occupational disease growing steadily in general significance. Workers dying from asbestosis should be subjected to a post-mortem examination including a histological study of the pulmonary lesions, as multiple neoplastic manifestations in asbestosis may be mistaken for tuberculosis (Lynch).

Sanitary Measures. The following measures may be taken to eliminate or reduce the existing hazard caused by the inhalation of asbestos dust: humidification of the asbestos matter and the air to decrease the production of dust; introduction of a closed production system, wherever possible; establishment of an extensive and efficient exhaust ventilation; frequent cleaning of the workrooms to remove the accumulated dust; prevention of air currents caused by moving machinery parts; construction of rooms, machinery, and pipelines offering little opportunity for deposition and accumulation of dust; separation of operations in which the production of dust can be eliminated entirely from those in which this is not possible; wearing of respirators by workers engaged in dusty operations; and mechanization of operations under elimination of human labor to reduce the number of workers exposed. The dust hazard is most pronounced in store rooms for raw material, in rooms in which the raw fibers are handled, and in spinning, weaving, mixing, and filling rooms.

Siderosis

Occupational siderosis of the lung is of the black type, which is caused

by the deposition of metallic iron in the lung, or of the red type, which is the result of the inhalation of iron oxide (hematite) dust (Hart). The black type of siderosis is associated as a rule with a silicosis, as the metallic iron dust is produced during the polishing or grinding process of iron parts in which sand blasting is used. The red type of pulmonary siderosis occurs mainly in hematite miners, especially those engaged in pneumatic drilling. Other miners, also, are exposed, as large amounts of dust are produced in the mines by frequent blasting. The hematite ores contain, in addition to ferric oxide, approximately 12 to 13 per cent silica (Bohrod; and Stewart and Faulds). Ferric oxide is used for the polishing of metal parts, such as screws, in the watch industry in Switzerland (Dreyfuss). Iron dust is not a biologically inert dust (Gardner), as a considerable number of fatalities have been placed on record as the result of occupational pulmonary siderosis, which is characterized by interstitial fibrosis and pulmonary arteriosclerosis.

The existence of a causal interrelation between pulmonary siderosis and primary carcinoma of the lung is suggested by several observations. Metal grinders have an excessive incidence of pulmonary malignancy (2.25 fold of that of the general population), according to Kennaway and Kennaway. The same conclusion was reached by Turner and Grace as well as Campbell. The three cases of lung cancer discovered by Vorwald and Karr among 15,587 workers roentgenologically examined at the Saranac Laboratory were iron miners, one having a silicosis, while the other two were negative for silica. Their ages were 59, 64, and 68 years, respectively, and the period of occupational exposure to hematite dust was 27, 35, and 43 years, respectively. The occurrence of a carcinoma of the lung in a boy, 19 years old, who had been engaged in sand blasting metal parts in an automobile factory was reported by Simons. Two similar cases were recorded by Dreyfuss. This investigator observed a pulmonary carcinoma in two members of a family (brother and sister), which developed twenty-four years after their exposure for twelve years to the inhalation of iron oxide (Fe_2O_3) dust, which was used by their mother at home for the polishing of screws. While the number of lung carcinomas after an occupational inhalation of iron dust is at the present time still small, the evidence presented is considered of sufficient significance to warrant further study as to the actuality of causal interrelations. Some experimental support of the existence of such a relationship was recently provided by Campbell, who found an increase in the lung tumor incidence of mice dusted with iron oxide ($Fe_2O_3 \cdot H_2O$).

Arsenic

In view of the notoriety arsenic has attained as a carcinogenic agent the studies of Saupe, in regard to pulmonary cancer in arsenic workers, are of interest and importance. This investigator examined workers employed in an arsenic ore smelter at Freiberg in Saxony. These men were exposed to

Published by AsbestosClaims.Law
asbestosclaims.law/library/25352/43