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Occupational Health

HAZARDS OF THE WORK ENVIRONMENT

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findings, a history of exposure, and appropriate cardiorespiratory function tests.

As previously indicated, early and progressive dyspnea, at rest as well as on exertion, is an outstanding feature of asbestosis, and, as in the case of berylliosis, it is attributed primarily to alveolar capillary block. Cough, which is usually unproductive, loss of weight, anoxia, weakness and chest pains, or pains between the shoulders, are characteristic features of the clinical picture. On physical examination one finds reduced chest expansion, with diminished breath sounds and resonance. There may be rales and pleural friction sounds.

A high incidence of lung cancer associated with asbestosis, reported by Merewether the Chief Factory Inspector of Great Britain in 1955, attracted considerable attention. Since then studies in New York, South Africa (*12*), Wales and elsewhere have clearly shown that a high risk of bronchogenic carcinoma is not confined to persons suffering from asbestosis, but that such tumors may also develop in the absence of the disease asbestosis. Mesotheliomata, which are rare tumors, have been found in the pleura and peritoneum. Smoking appears to increase susceptibility of workers to bronchogenic carcinoma when exposed to asbestos (*13*). This is discussed further in Chapter 24, under Medical Perspectives.

"Neighborhood cases," analagous to those associated with beryllium exposure, have been found associated with exposure to asbestos dust. Here, also, host differences in response are striking.

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Occupational Cancer

In view of how little is known, at the present time, with reference to the causes of cancer, it is of some interest that a few specific chemical and physical agents in the occupational environment have been found capable of producing cancer, under certain circumstances, and at specific primary sites of predilection. These sites are primarily the skin, the urinary bladder, the nasal sinuses, the larynx, the lungs, and the bones. While the biological mechanisms are by no means clear, the mere presence of known, or suspected, carcinogenic agents in the work environment provides an unusual opportunity to study these mechanisms, under known conditions of exposure. Most of the chemical agents which produce cancer in laboratory animals are not carcinogenic to man; and here, as elsewhere, species differences make it impossible to extrapolate such laboratory data to man. In general, occupational cancers cannot be distinguished pathologically from similar types of cancer, which are non-occupational in origin, and which develop at similar primary sites. Nevertheless, occupational cancers have a few distinguishing characteristics. They appear to develop, and prove fatal, at an earlier age than similar tumors which are non-occupational in origin; they appear to develop as a result of repeated, though not necessarily continuous, exposures; and they often appear long after the initial exposure, even years after cessation of exposure. Time-dosage relationships are still obscure.

It is obviously essential to identify potential carcinogenic agents in any particular work environment, for purposes of control and prevention. However, it is also important to obtain precise epidemiological data, insofar as possible, as to the distribution of carcinogenic agents in occupational environments generally, in order to obtain precise information as to the nature of the exposures involved, preferably in time-dosage relationships. Of vital importance also is the medical recognition

of pre-cancerous lesions, such as early signs of skin atrophy, alopecia, hyperkeratoses, leukaderma, melanoderma, papillomata; changes in the fingernails characteristic of radiodermatitis, and early blood dyscrasias suggestive of leukemia. These precancerous lesions are not all necessarily occupational in origin. Their early recognition, therefore, is a challenge not only to industrial physicians, but to every medical practitioner (*1*).

In the field of occupational cancer, the practicing physician is often unaware of the vital contributions he can make, in the course of his regular work, to the scant data now available. The opportunity is unique in that much of the data required cannot be developed in a research laboratory, or in a university. It must come from physicians who actually see cancer cases, or cases of suspected cancer, either in their private offices, in cancer-screening clinics, in the hospital or plant medical offices. It is, actually, a research problem of extraordinary importance, practically made to order for the medical practitioner who is willing to devote the few extra minutes necessary to take a careful occupational history, and report, *for further investigation,* patients suspected of having been exposed to carcinogenic agents in the course of their work. Subsequent investigation of the work environment of his patient may, or may not, confirm his suspicions. When they are confirmed, however, he has contributed not only to control and prevention in a particular plant or occupation, but also to basic research in the field as a whole.

In plants having well organized medical departments, research data with reference to known, or suspected, carcinogenic agents can be developed in the course of preplacement and successive follow-up medical examinations. This is being done in some plants, at the present time, with a view to identifying the occupational causes of cancer in specific plant operations, for purposes of control and prevention. In the final analysis, definitive data with reference not only to occupational cancer, but all other occupational diseases, must come from such studies of workers on the job.

EPIDEMIOLOGICAL STUDIES

In epidemiological studies of diseases which develop slowly, such as cancer or emphysema, for example, and which are common to the community as a whole, one encounters unusual difficulties in acquiring precise environmental data, particularly in terms of time-dosage relationships. Account must be taken of persons exposed to carcinogenic agents who do not develop cancer, as well as those who do. Both the occupational and non-occupational environments present a great number of variables which are difficult to deal with; and, in large measure the data are not suffi-

ciently precise. Moreover, when one attempts to distribute the data obtained from large numbers of individuals, among the different variables, one tends to come out with too few cases in any one category to be definitive. The numbers of cases must always be large enough to be statistically significant. Otherwise, the conclusions are necessarily suspect.

In studying occupational causes of cancer, one is limited not only by the technological complexities of occupational environments, but also by the dearth of information which can be obtained from the records now available. Even job classification data provide inadequate information as to a worker's precise occupational exposures. Social security records are equally uninformative even when made available. Death certificates provide only the last occupation, which probably has no relation to the patient's previous exposures over the years. Moreover, many of the diagnoses on death certificates are never confirmed by autopsy. In hospital records, occupational histories tend to be casual or nonexistent; and many workers are loosely classified as "laborers," without regard to the type of plant in which they had been working. Such designations have been found, even in cancer hospitals, on the records of patients who had been admitted from neighboring plants, which, on later investigation, were found to use carcinogenic agents.

That workers, when interviewed, can provide very little precise data as to the chemical agents to which they have been exposed is not surprising. Information as to dosage can never be obtained in this way. A visit to a plant, years after the event, is usually futile because during the long interval which had elapsed, the materials used and the processes employed may have changed completely from what they had been when the cancer patient was employed there; or the plant may no longer be in business. A prospective, rather than a retrospective approach, is preferable, therefore, in epidemiological studies of occupational cancer. This was amply demonstrated by the research work carried out by the New York State Occupational Cancer Committee (1).

As one reviews workers' exposures to factors in their work environments which are potentially inimical to health, one is impressed with how seldom they seem to be associated with cancer. A great many substances highly irritating to the skin, for example, which are capable of causing many types of dermatoses, do not necessarily cause skin cancer. A great many sensitizing agents are not potentially carcinogenic, although some chemical carcinogens are also sensitizing agents. Air contaminants capable of causing acute and chronic irritation, and other types of serious pathology of the upper respiratory passages and the lungs, are not necessarily carcinogenic (*2*). While asbestos dust is carcinogenic, as we have seen, silica dust and many other fibrogenic dusts are not. Beryllium causes lung cancer in animals, but apparently not

in man. Many substances in the chemical and dye industries, which are capable of producing a hemorrhagic cystitis or methemoglobinemia, do not cause bladder cancer. The occupational diseases, with relatively few exceptions are not characteristically associated with occupational cancer.

CHARACTERISTIC SITES FOR OCCUPATIONAL CANCER

Skin Cancer

Skin cancer is by far the commonest type of occupational cancer; and because precancerous lesions on the skin are readily visible, they are susceptible of early detection, and effective removal. Soot (which caused the early scrotal cancers in chimney sweeps), coal tar, shale oil, pitch, creosote, asphalt, fuel oils, crude mineral oil, and carbon black are all potentially carcinogenic to the skin. In the petroleum industry, wax pressmen and other workers exposed to petroleum fractions, with a boiling point above 700°F, can develop scrotal cancer, particularly when their trousers become saturated with the oil (*3*). Among other agents suspected of causing skin cancer are arsenic, and ultraviolet light. Skin cancer is not uncommon among farmers with heavy exposures to the sun. Workers exposed to external radiation, including X-ray and fluoroscopic equipment, can develop skin cancer unless adequately protected by proper shielding and other control measures discussed elsewhere (see Chapters 7 and 17, under Industry and Laboratories).

Skin cancers are usually squamous cell carcinomas, which develop slowly and cannot be differentiated, pathologically, from similar skin cancers, of non-occupational origin. A careful history of significant exposure is indispensable, therefore, for a differential diagnosis.

Lung Cancer

The incidence of lung cancer is sufficiently great, in the general population, to be a matter of major concern, particularly because it has been steadily increasing in the last two or three decades. This increase has occurred during a period of tremendous technological development; when workers were being exposed to an increasing variety of chemical and physical agents, some of which are present, as irritant and toxic air contaminants, in the form of dusts, gases, fumes, mists, etc.; when community air pollution has gradually increased; and when smoking has become a universal habit. It is natural enough to speculate that these factors have been important in the increasing incidence of lung cancer. On the other hand, it is difficult to determine the respective contributions of each of these factors (*4*). Among the chemical carcinogens known to be capable of causing lung cancer, are certain of the

chromates, nickel carbonyl, asbestos and arsenic. Whenever one is dealing with carcinogenic air contaminants, one must bear in mind that the eyes, nose and upper respiratory passages may also be involved under certain circumstances. Occupational lung cancers are characteristically bronchogenic carcinomas, of the squamous cell type. Metaplasia of the bronchial epithelium appears to precede the appearance of the tumor. These tumors develop slowly, and may not be diagnosed for many years after cessation of exposure to the etiological carcinogenic agent.

Chromates

Both American and European experience has confirmed the etiological role of certain of the chromates in the production of lung cancer. As a result of the independent studies of Machle and Gregorius (*5*) and Baetjer (*6*), the chemical compounds believed to be responsible are the hexavalent chromium compounds, Na and K monochromate or dichromate, and zinc chromate, inhaled as dust. Most of these cases were found to be bronchogenic carcinoma. An exposure of 4 years appeared to have been sufficient in some cases. In most cases, however, there were a great many more years of exposure. A characteristic latent period, of varying duration, between cessation of exposure and the development of the lung cancer has been observed.

Asbestos

Bronchogenic carcinoma, originally thought to be associated solely with the disease, asbestosis, has now come to be accepted as due to the inhalation of asbestos dust, even in the absence of asbestosis. The tumor is usually found in one of the lower lobes, where asbestos fibers are most numerous (*7*). In other types of bronchogenic carcinoma, the upper lobes appear to be more characteristically involved (*8*). Tumors have also been found to develop elsewhere in the body, particularly in the pleura and peritoneum. These pleural and peritoneal tumors are mesotheliomata, a very rare type of cancer at the present time. The fact that they develop at sites remote from the initial sites of deposition of the asbestos fibers in the lungs, has raised interesting questions of transport and migration. All of these tumors, found in persons exposed to asbestos dust, usually develop after very long latent periods, but they may apparently also develop following a relatively limited exposure. Some are not diagnosed until many years had elapsed since the last exposure. The precise type of asbestos fiber appears to be of some importance as an etiological factor (see Chapter 4).

Reviewing the changing medical picture over the years, resulting from exposure to asbestos dust, Gilson (*9*) suggests that, in the early

ays, exposures were high and workers died young, perhaps from com-lications such as pneumonia or pulmonary tuberculosis. As living nd working conditions improved, however, and tuberculosis became less revalent in the community, workers lived long enough to develop progres-ive pulmonary fibrosis, and other features of asbestosis, often ending ı cor pulmonali. Under modern conditions of exposure, on the other hand, orkers develop only moderate degrees of asbestosis, and live long enough ɔ develop bronchogenic carcinoma. He suggests that, in the mesothelioma, e are witnessing the very long-range effects of low-grade exposure ɔ asbestos dust. This is an interesting historical perspective. The athogenesis of this disease is quite obscure at the present time, and ıany conjectural model constructs are under intensive investigation.

Environmental exposures to asbestos dust are apparently not con-ned to the workers exposed. Here we find so-called "neighborhood ases," analogous to those found in relation to beryllium exposure—ıe development of the disease in persons who had never worked with ıese substances; and even those who live within a considerable radius f the plants. Contact with the dust on workers' clothing, when they re brought home to be laundered, is believed to be a possible ex-lanation in some cases, but not all. It has been suggested that other ɔexisting sources of community air pollution, which go unrecognized t the present time, may play contributing roles. There are apparently reat differences in individual susceptibility not only among workers cposed to asbestos dust, but among persons living in the neighboring ɔmmunities.

Ionizing Radiation

The lung cancers which develop in miners exposed to radioactive es are believed to be caused primarily by the radon gas given off and s degradation daughters. This has been discussed in Chapter 14, under lining.

Bladder Cancer

As in the case of lung cancer, bladder cancer has been on the increase ıroughout the world during recent decades, and this has stimulated in-nsive research as to the etiological factors involved. In industry, the ırcinogenic aromatic amines include beta-naphthylamine, para-amino phenyl, auramine and magenta. Benzidine is still controversial. Alpha-ıphthylamine which had long been suspected of being carcinogenic is no nger suspect. It is now believed that because it is a contaminant of beta-ıphthylamine, it was improperly included among the bladder carcino-ms. Aniline, which had also been suspect, is not carcinogenic. There are number of chemical agents which can produce cancer of the bladder animals, but not in man.

Beta-Naphthylamine

Beta-naphthylamine is an intermediate in the manufacture of the aniline dyes, to which workers have been exposed since the early development of the dye industry, in Germany, prior to World War I. Subsequent manufacture of these dyes in the United States carried this potential hazard with it. In the early days, alpha- and beta-naphthylamine, benzidine and aniline were all suspect. Gehrmann (*10*) studied the problem intensively in both countries for purposes of prevention.

Beta-naphthylamine can be absorbed through the skin, the respiratory and the gastrointestinal tracts. The metabolic mechanisms involved are not completely understood, but is believed that it is not the beta-naphthylamine, per se, which is responsible for bladder carcinogenesis, but rather the presence of its metabolites in the urine (*11*). Experimentally, it has been shown that extracts made from the urine of animals with beta-naphthylamine-induced bladder cancer, are carcinogenic. And certain fractions, made from these extracts, are individually capable of producing bladder tumors in animals. There is great species specificity here as elsewhere, in susceptibility to the induction of bladder cancer by beta-naphthylamine. Such cancers can be produced in dogs, for example, but not in rabbits.

Once induced, the bladder tumors progress in the absence of further exposure. They start as small, apparently benign papillomata, near the trigone of the bladder, or around its ureteral orifices, and go on to develop into epitheliomata. Bladder cancer has been known to develop after only a few years of exposure, but may not develop for 48 years. On an average, 10 or more years have been found to elapse between the beginning of exposure, and the development of the bladder tumor.

This time-lag creates serious difficulties in differential diagnosis. A history of exposure is vitally important, because these bladder cancers are indistinguishable clinically, cystoscopically, and histologically, from epitheliomata of the bladder which are non-occupational in origin. They are similar, also, in the fact that they metastasize slowly. When removed by fulguration they tend to recur, and become progressively more malignant as time goes on. Any bladder tumor seen in a worker in an aniline dye plant is always regarded as potentially malignant.

The entire bladder wall may be involved. Submucosal telangiectases make their appearance early with dilatation of capillaries and small arteries. This explains the early and sometimes profuse bleeding, with hematuria. The villous papillomata which follow may be latent for many years. They are more often multiple than single, and may be raised in appearance, or flat. They may or may not ulcerate or infiltrate.

The clinical manifestations are essentially the same as those as-

sociated with non-occupational bladder cancer: frequency of urination, urgency, dysuria, nocturia and hematuria. Gehrmann (*10*), who first introduced routine cystoscopy as a control measure, has shown that hemorrhagic areas in the bladder, and early tumor formation, can be observed in advance of bladder symptoms, or any other clinical manifestations of their presence. Profuse bleeding, with severe hematuria, may, however, be a very early sign. On the other hand, there may be only a few red blood cells in the urine, and tests for occult blood may be required for the early detection of pathology. Hematuria can also be due to noncarcinogenic chemical agents to which workers in the aniline dye industry may also be exposed. Hematuria is also a common symptom of ordinary cystitis. It cannot, therefore, be solely depended upon for purposes of differential diagnosis.

Prevention is based upon the most rigid engineering and medical control measures. All modalities of control and prevention assume unusual importance, particularly complete enclosure, and mechanization of all processes utilized in the production, or use, of this chemical substance. Frequent periodic reevaluation of all existing control measures is essential to check up on their current efficacy. Protection of each worker, as an individual, involves the utilization of annual cystoscopic examinations to detect early bladder pathology. Although many of the metabolic end products of beta-naphthylene are still obscure, the urine should be examined, whenever possible, for such metabolites as can be chemically identified and interpreted (*12*). The Papanicolaou smear techniques have been particularly useful in reducing the frequency of periodic cystoscopic examinations in workers who are unwilling to submit to cystoscopy. Gehrmann believed that exposures should be limited to as few workers as possible, and that those leaving the industry should be routinely followed up. Because of the long latency period moreover, he has urged workers to return at any future time for treatment, without charge, should any bladder symptoms develop.

OSTEOSARCOMA AND LEUKEMIA

The osteogenic sacromata, which developed in radium dial painters following World War I have been discussed under Radium Poisoning, in Chapter 7. The relatively high incidence of leukemia among radiologists has been discussed in Chapter 17, under X-Ray Laboratories. The question as to whether exposure to benzol can produce leukemia has no definitive answer, as yet.

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