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INDUSTRIAL TOXICOLOGY

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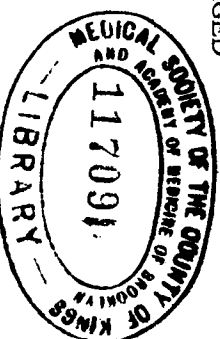
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vi
Preface to Second Edition

field there are almost three times as many bibliographic references as before. However, the authors make no claim to an exhaustive treatment of the voluminous records of animal experiments to test the toxicity of the newer chemicals. For these the inquirer is referred to the Industrial Research Laboratory of the National Institute of Health, Bethesda, Maryland.

Industrial skin diseases have been dealt with only casually. For this class of occupational lesions the reader is referred to *The Dermatoses or Occupational Affections of the Skin* by R. Prosser White, Fourth Edition, H. K. Lewis and Company, London, 1934, and to *Occupational Diseases of the Skin* by Louis Schwartz, Louis Tulpan, and Samuel Peck, Lea and Febiger, Philadelphia, 1947.

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CONTENTS

Preface to Second Edition

Introduction

1. Diagnosis of Industrial Poisoning	21
2. Alkalies, Acids	26
3. Chromium	44
4. Lead	49
5. Mercury	104
6. Arsenic	127
7. Phosphorus	138
8. Cadmium	145
9. Antimony, Metal Fume Fever, Zinc, Manganese	157
10. Beryllium	172
11. Selenium, Tellurium, Vanadium, Aluminum, Copper, Tin	188
12. Nickel and Other Metals	205
13. Asphyxiants: Carbon Monoxide, Carbon Dioxide, The Cyanides, Hydrogen Sulphide	219
14. Aromatic Series: Coal Tar, Benzene, or Benzol	268
15. Aromatic Series (Continued): Benzene Derivatives	284
16. Aromatic Series (Continued): Toluene and Xylene, Derivatives of Toluene and Xylene, Naphthalene and Naphthylamines, Chlorinated Naphthalenes and Diphenyls	303
17. Aromatic Series (Continued): Aniline Dyes	317
18. The Petroleum, Fatty, Aliphatic Series	319
19. Chlorinated Hydrocarbons, Bromine Derivatives of Hydrocarbons, Methyl Iodide	356
20. Carbon Disulphide	398
21. Turpentine, Tobacco	409

older chromate workers the x-ray picture often showed a swelling of the lymphatic glands on one side. Whether this was an inflammatory process or, because it was limited to one side, a cancerous process, could not be determined without following the cases.

Teleky adds what he believes to be the first reported American case. This was in a factory in Baltimore. The man worked from 1945 in a plant producing chromates from chromate ores. He was part of the time in production, part in the shipping department where probably there was a great deal of dust. He died in 1960 at the age of 31 years and the autopsy revealed bronchiogenic carcinoma with metastases in the liver.

Recently Machle and Gregorins (756a) have published the results of the first extensive study so far made to determine the incidence of cancer of the lung in workers exposed to dust in the course of producing chromates, bichromates, and chromic acid. This study was made at the suggestion and with the full cooperation of the five companies in the United States which are now extracting chromates from ore in seven plants employing 1445 men. It was found possible to obtain records of these plants to secure records of 11,019 man-years employment with 156 deaths, among which were 46 from all cancers, and of 32 were cancers of the respiratory system. The seventh plant, with adequate employment records, yielded 20 deaths from cancer, of which 10 were from lung cancer. This means a total of 42 deaths from pulmonary cancer. These figures leave no doubt of the influence of occupation on the occurrence of cancer of the lungs.

Since no less than 28.8 per cent of all deaths in the chromate industry were reported as being due to cancer of the respiratory system, the ratio is 16 times the expected ratio of 1.3 per cent. The overall death rate for cancer of the lung averaged 25 times the normal, rising from eighteen- to fifty-fold. The rate was higher in the group 50 years of age and under (20 to 70 times that for a comparable industrial group) than for the age groups over 50 years (10 to 15 times). The rate for cancers other than of the lung was 12.4 per cent, slightly lower than the 15 per cent for a comparable industrial group. Several other facts of great importance were revealed in the course of this study. The incidence of nasal irritation and perforation de-

not run parallel with that of lung cancer, but may occur in plants with no records of lung cancer. In two plants belonging to the same company there was a marked difference in the occurrence of lung cancer although the plant populations were similar with regard to location, race, color, age groups, length of exposure. But in plant D1 17 per cent of all deaths were from lung cancer while in plant D2 there were no deaths from that cause. The difference apparently lay in the nature of the compounds handled. Plant D1 handled chromite, sodium chromate and sodium bichromate. Plant D2 only sodium bichromate, chromic acid, and basic chromic sulphate, a trivalent chromium compound. This suggests that the monochromates may be the compounds responsible for lung cancer.

Association of Lung Cancer with Silicosis and Asbestosis. Klotz (615) and also Anderson and Dible (13) have demonstrated a possible causal relation between silicosis and lung cancer but in both reports the evidence is presented as tentative only and further study is urged.

Teleky (1165), reviewing the subject in 1939, found that the connection between silicosis and lung cancer is very dubious as shown by statistics. On the other hand, the incidence of cancer of the lungs among asbestos workers is fairly high. Le Coeur (679), discussing lung cancer of occupational origin, says that in a lung with asbestosis it takes some twelve years for a cancer to develop. Islands of cancer cells are deeply embedded in fibrous tissue, which also surrounds the lymph glands, and contain particles of asbestos. The process is a "chronic interstitial indurating pneumonitis with cancerous change." The course is slow, the tendency to metastasis less than in chromate cancer.

Lynch and Smith (See 538) have described 2 cases of pulmonary cancer associated with asbestosis and 1 case of squamous metaplasia of the bronchial epithelium with asbestosis, which they tentatively present as a precancerous condition, since the above-cited cases were of cancer predominantly squamous in type. In their series of 2308 necropsies the rate of primary lung cancer is 0.21 per cent; among 35 cases of asbestosis it was about 6 per cent.

Welz (1235) attributes to the irritating action of asbestos 2 cases of lung cancer which were complicated with asbestosis.

Another case of lung cancer in an asbestos worker was reported in 1941 by Linzbach and Wedler (538). The patient had been followed radiologically from 1934 to his death in 1940. By 1938 there was stage III of asbestosis, in 1940, a tumor. Autopsy revealed changes characteristic of asbestosis and a squamous-cell carcinoma.

The Saranac Laboratory group admits the possibility of asbestos dust, which is mechanically irritating, setting up a squamous cancer, but similar changes in the epithelium occur in other chronic inflammations of the lung, notably tuberculosis, and, in their wide experience, tuberculosis is not attended with an increased incidence of primary cancer of the lung (see Vorwald [1202]).

Association of Lung Cancer with Other Irritants. Hueper has some proof of a connection between pulmonary siderosis and cancer. English statistics show that metal grinders have 2.25 times as many cases of cancer of the lungs as does the general population. He has some 6 scattered cases, but holds that the connection has not yet been proved. Teleky says that in Germany cancer of the lungs is two and one-half times as frequent among metal grinders as in the general population.

Among the many causes that have been suggested to account for the apparent increase in lung tumors in recent years is the dust from asphalt-paved roads, which is undeniably a feature of modern life, and one of constantly increasing importance. Leiter and his colleagues (700) produced sarcoma in mice by subcutaneous injections of tar extracted from dust collected in streets of five cities. Kling (613) tested the various tars used in road-paving and urged the use of those produced at low temperatures, or those with asphalt base, bitumens known to be free from carcinogenic elements, to obviate the possible danger from street dust.

Hueper is skeptical as to such causes as these. It is true that there are more cases of lung cancer in city populations than in rural ones, but diagnosis is more accurate in cities and more post-mortem examinations are made.

That exposure to hot, tarry gases may give rise to lung cancer is claimed by Kawahata and Kuroda (651) who encountered, during a six-year period, 21 cases of lung cancer among men working in a Japanese steel mill where illuminating gas was generated. The

were continually exposed to dust, flames, and hot gases containing tar. The ages of the affected men ran from 35 to 65 years, their exposure from nine to seventeen years. The upper lobe of the right lung was most often involved; metastases occurred with relative frequency in the brain and spinal cord.

Lovelock (744) describes a complicated and difficult case in a Welsh miner, employed for twenty-two years in coal mines. The patient died, apparently from carcinoma of the liver, but the lungs contained over eight times the normal silica content (a guinea pig injected with substance from the lungs died of generalized tuberculosis), and there was carcinoma of the right lower lobe bronchus.

The theory that severe infectious respiratory disease may predispose to pulmonary cancer is apparently refuted by statistics, for the latter has been on the increase while pulmonary tuberculosis has been decreasing, and the influenza epidemic of 1918 had no demonstrable effect.

English statistics (Kennaway and Kennaway [See 538]) show that there has been an increase not only of lung cancer but of cancer of the larynx. Between 1921 and 1932 these tumors increased 1.4-fold in men and 1.75-fold in women. This may possibly be attributed to cigarette smoking; it would hardly be occupational, or men would be affected more than women.