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PATHOLOGY
OF
TUMOURS

BY

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is apt to be so dubbed until its progress demands a more precise diagnosis. In many cases in which "bronchitis" has appeared to precede the appearance of lung cancer by some months or years, the symptoms were caused by the cancer from the beginning. There is no clinical evidence that bronchiectasis predisposes to carcinoma; but Womack and Graham, and Stewart and Allison found minute cancerous foci in bronchiectatic lungs.

(*iv*) *Pneumonia.*—There is no evidence that pneumonia is ever a significant precursor of cancer. Attacks of "pneumonia" due to bronchial obstruction, or of "pleurisy" due to the same cause or to tumour invasion of the pleura, are common inaugural symptoms of bronchial carcinoma.

(2) Pneumoconiosis

Hueper gives a full discussion of the contradictory opinions held regarding the possible importance of the several kinds of pneumoconiosis in the causation of lung cancer. *Silicosis* is, of course, sometimes seen in association with cancer, and has been thought by some workers (e.g. Klotz) to predispose to this disease; but the evidence is inconclusive, and study of occupational groups exposed to silicosis does not suggest any special predisposition (Vorwald and Karr, Kennaway and Kennaway, and other references by Hueper). Experimental results also have been inconclusive. Vorwald and Karr failed to demonstrate any carcinogenic effect of inhaled silicates of various kinds in laboratory animals; but Campbell's experiments (described in Chapter 4) showed an increased incidence of lung tumours in mice following inhalation of inorganic dusts containing silica. *Asbestosis* has been reported in association with carcinoma in a few cases (Holleb and Angrist); and a causative relationship has been suggested because of the youth of several of the patients, predominance of carcinomas of the squamous type, and multicentric origin apparently related to precancerous squamous metaplasia in some of them. However, the number of cases is yet too small to permit any definite conclusion to be drawn. *Siderosis* accompanying lung cancer has been described in only a few cases; but the apparently excessive liability of metal grinders to pulmonary carcinoma, and the results of Campbell's experiments with dusts containing iron oxide, suggest a possible causative relationship. *Anthracosis* has not been proved to be a causative factor. According to Kennaway and Kennaway, the registered deaths from lung cancer are fewer in coal miners than in the population generally. It has been suggested, however, that inhaled atmospheric soot, the main source of the common anthracosis of city dwellers, may be carcinogenic, not because of its carbon content, but because it may contain carcinogenic hydrocarbons, a possibility now to be briefly discussed.

(3) Carcinogenic hydrocarbons

Experimental investigation, outlined in Chapter 4, has shown that the incidence of lung tumours in mice can be markedly increased by the administration of carcinogenic hydrocarbons by inhalation or by subcutaneous, intraperitoneal or intravenous injections. The possibility must, then, be conceded that exposure of human beings to such substances may be a factor in the causation of lung cancer; and that, while inhalation is clearly the most likely mode of introduction

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of such agents, absorption by other routes must also be considered. Tar, oil, soots, tobacco smoke and other smokes, must all be arraigned; but clearly, proof of either the culpability or innocence of any particular material will not be easy to establish. Such proof will entail (a) demonstration of the presence of carcinogenic substances in the suspected material, (b) evidence that the material is inhaled or otherwise absorbed by exposed persons, and (c) evidence that habitually exposed persons do show an excessive incidence of lung cancer, and that this excessive incidence is reduced by eliminating the suspected risk. While the first step (a) has already been accomplished for many of the suspect materials, scarcely any of the evidence (b) or (c) has been obtained, and it will be very difficult to obtain.

For example, suppose that tobacco smoking *is* an important cause of lung cancer and that it acts by producing chemical carcinogens which are inhaled. It may be easy to identify the carcinogens in tobacco smoke or tar, but it may be difficult to prove that they are effectively inhaled, even more difficult to group patients correctly according to their present and past tobacco consumption, and probably impossible to prevail on any large group of men of homogeneous occupation to renounce smoking for life so that the ultimate incidence of lung cancer in them (proved by necropsy) may be compared with that of their smoking fellows. Comparisons of the smoking habits of victims of lung cancer with those of control cases obtained by careful questionnaires, like Müller's, afford strong grounds for suspecting the carcinogenic results of smoking; but, however strongly suggestive, they cannot afford incontrovertible proof—especially in the eyes of smokers themselves! Proof of the harmfulness of inhaled domestic and industrial soots and smokes or of dust from tarred roads, to which all persons in urban populations are almost equally exposed, will be even more difficult to secure.

(4) Schneeberg and Joachimsthal: and radio-active substances

The frequent occurrence of fatal lung disease in the miners of the Erzgebirge has been recognized for over four centuries, but only within recent years has this disease been clearly identified as bronchial carcinoma. Hueper (p. 435) gives a full outline of the subject, and Pirchan and Sikl's paper (1932) is a valuable source of information. The frequency of lung cancer in workers in the offending mines is very high; about three-quarters of the Schneeberg miners and nearly one-half of the Joachimsthal miners die of this disease. There is then no doubt of the operation of some highly potent occupational factor, probably an inhaled substance.

The air in the mines contains not only iron, cobalt, nickel and silica dusts, but also arsenic and radio-active substances, especially radon. Each of these has been incriminated as the carcinogenic agent by one writer or another; but the weight of the evidence, fully outlined by Hueper, points to radon as the main factor. This is supported also by the fact that cancer of the lung has occurred in a number of laboratory workers handling radio-active material. However, experimental work has not yet verified the efficacy of inhaled radio-active substances as a cause of lung cancer; and until this has been done, a final decision must be deferred.

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