

TOBACCO SMOKING AND CANCER OF THE LUNG

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THE average clinician is slow in appreciating and applying, in clinical practice, the great advances made during the last half century in the basic sciences of chemistry, physics and biology. This approach becomes most important when we consider the increasing number of cancer cases which involve the respiratory tract, and examine, at the same time, the possible bearing which excessive smoking may have on this pathologic condition.

A comprehensive review of the literature on this subject has brought to light many interesting reports, but the experimental studies of Roffo,¹ conducted in Buenos Aires, demand, in my opinion, some comment, because of the great influence they might have upon an important phase of medical science, namely, that of preventive medicine.

After having had an opportunity to observe, over a period of ten years, an unusually large series of patients with cancer of the lung, in two of the large municipal hospitals in New York City, two very distinct elements were noted in these patients: First, the patients were almost always men; second, they were heavy cigarette smokers and almost always inhalers. There is no experimental proof at hand to demonstrate that the smoking of many cigarettes was the cause of lung cancer, however, some aspects of this problem should be carefully evaluated.

Roffo has shown, what seems extremely logical to me, namely, that a carcinogenic compound (benzpyrene) can be isolated from tobacco tar. This investigator has studied the action of tar, particularly tobacco tar, upon the human organism. He found that the latter is more active and malignant than coal tar, and that 95 per cent of all cancers of the lung, larynx

and pharynx occur in smokers. Mortality among smoking patients afflicted with cancer mounted from 148, in 1926, to 513, in 1937. These observations and chemical investigations indicated that the carcinogenic agent is not contained in the nicotine but is a component of the products of combustion of tobacco while smoking. He finally isolated the actual carcinogenic component (benzpyrene) from tobacco tar by fractional distillation at a temperature of more than 380°C. Experiments with this substance revealed that it is highly carcinogenic, and causes invasive, expanding and destructive proliferations. The primary lesions appear earlier than those caused by the use of total tobacco tar. On the basis of these observations, Roffo concludes that tobacco benzpyrene is responsible for the carcinogenic action found in tobacco tar.

It is obvious, therefore, that this product of combustion deeply inhaled into the lungs of cigarette smokers—for cigarette smokers usually inhale—is deposited in the lung along the entire bronchial system, and most of the biologic principles are present, I believe, to produce bronchogenic carcinoma in accordance with well known animal experiments.

The three cases which were studied at this Clinic were all heavy smokers, and all had inhaled over a period of at least fifteen years. All three had a very active and inoperable cancer, with metastases, and died as a result of this disease.

CASE REPORTS

CASE 1. W. D., a male, age forty, came to the Clinic, March 24, 1937, with a history of numerous head colds, developing during short intervals, combined with sore throat, and followed by a dry, hacking cough. There was a small amount of thick, blood-streaked sputum.

This patient had been gassed during World War I, and at that time had been ill for four months. His father had died of a brain tumor.

and, microscopically, it was a Grade IV tumor, probably a bronchogenic metastasis.

The general condition seemed fair during

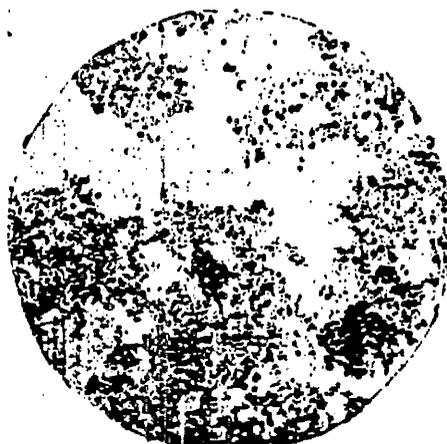


FIG. 1. Case I. Microphotograph taken at operation.



FIG. 2. Case II. Microphotograph taken at operation.

The patient had been losing weight. There was no fever or night sweats and no chest pain. Sinus trouble had been present for some time, and it became worse on March 26, 1937. Roentgenograms taken shortly before this time revealed a possible tuberculous lesion at both apices, which was of minimal extent, of fibrotic appearance, and apparently arrested. However, a mass-like infiltration was noted extending from the upper part of the left cardiac border into the first and second left intercostal spaces. No tubercle bacilli were demonstrable. Fluoroscopy of the esophagus showed that the latter was pushed over to the right of the level of the pulmonary lesion.

On September 14, 1937, exploration of the left thoracic cavity was made by an anterior approach between the second and third ribs. The upper mediastinal area was entered and a tumor mass found which was fixed and obviously inoperable. The tumor occupied the entire three-fourths of the upper part of this cavity, and was confluent with an adherent mass in the upper left lobe. In view of the inoperability of the tumor, fifteen seeds of radium emanation were implanted into the mediastinum. There was no gross evidence of metastases on the surface of the left lung, but the primary tumor was probably in the periphery of the left upper lobe.

A biopsy of the mediastinal mass was taken

repeated check-ups, the radon seeds having apparently helped the mediastinal obstruction. In August, 1938, he complained of pain in the left forearm, with numbness in the fifth finger. His cough was becoming worse, and was accompanied by nausea and vomiting. He subsequently developed a classical Horner's syndrome. The patient continued to lose weight, and all symptoms grew progressively worse. Death ensued shortly afterward.

CASE II. F. R. P., a male, age fifty-four, reported to the Clinic, in March, 1940, with a history of having had a slight cough for two or three years. During the past three months there had been some pain in the left shoulder, radiating to the hand. The patient was losing weight and had moderate hemoptyses. Roentgenograms, taken elsewhere, showed marked infiltration in the left upper lobe, with a large cavity just below the level of the clavicle, strongly suggestive of pulmonary tuberculosis. One positive sputum was obtained. The best method of treating the condition appeared to be an upper-stage thorocoplasty. At operation, there was found, between the third and fourth ribs, a protrusion about the size of a small egg, grossly, suggestive of a neoplasm.

Pathologic examination revealed bronchogenic carcinoma, Grade II. No tuberculosis was found at any time in the many tissues involved.

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Shortly before his death a classical Horner's syndrome developed, probably as a result of the spreading neoplasm. The patient died three months postoperatively.

CASE III. A. H., a male, age thirty-nine, complained of pain in the chest, chronic cough, and loss of weight during the six months preceding his visit to the Clinic (October, 1941). Roentgenograms revealed atelectasis and fluid in the left side. Bronchoscopic examination demonstrated a neoplasm involving the left main bronchus. Operative exploration was undertaken through an anterior approach. Adhesions were found throughout most of the pleural space, which were unusually dense over the left lower lobe, where they were firmly adherent to the chest wall and diaphragm with numerous metastatic implants. Surgical removal was not possible.

A biopsy of the lung showed bronchogenic carcinoma, Grade III.

The patient died, January 2, 1942, with generalized metastases involving the pericardium, pleura, pancreas and stomach, with the primary site in the left lung.

I believe the three cases discussed here bear out the theory of Rolfo, that possibly the carcinogenic irritants from tobacco tar are deposited in the lung, and the end result of this irritation, in a biologically susceptible individual, is the production of a bronchogenic carcinoma.

In spite of all the technical improvements of dealing with cancer, we, at present, cannot successfully cope with high grade neoplasms of the lung, and the low grade tumors which give a better prognosis surgically, represent a badly handicapped group of individuals.

In attempting to analyze these cases of cancer of the lung using tobacco smoking as the causative agent, we note data that might be productive of important preventative measures. Cramer, in discussing the many causes of cancer, and from experimental evidence at present available, when applied to man, established four distinct groups: (1) Carcinogenic agents, (2) precancerous conditions, (3) susceptibility, and (4) time factor.

In applying Cramer's grouping to the

three cases herewith reported, in Group I (carcinogenic agents), we find a very potent carcinogenic compound (Benzpyrene) in



FIG. 3. Case III. Microphotograph taken at operation.

the tar of smoking tobacco that all these patients deposited in their lungs.

Regarding Group II (precancerous conditions), Dr. Cramer reports that "during the prolonged period of induction necessary for a carcinogenic agent to elicit cancer, the tissue on which these agents act undergoes a pathologic change, and it is in this altered tissue that eventually a malignant condition develops in a sharply circumscribed area." We believe that in our three cases this etiologic factor was probably produced by tissue alteration from the constant inhalation of the tar with its carcinogenic agent.

Group III (susceptibility) cannot be directly applied to any of these cases with certainty, except possibly in Case I, where the history states that his father died from brain tumor. However, the mere fact that a tumor did develop shows that some degree of susceptibility may have existed, which might have been stimulated by a

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carcinogenic agent. In genetically susceptible individuals. In spite of these apparent imponderables, in attempting to establish scientific facts, Cramer states: "The relationship between the two factors susceptibility and carcinogenic agent can be expressed crudely by a simple equation of two variables A and S , and a constant, C : $A \times S = C$. In such an equation the one variable increases as the other diminishes. If A represents the carcinogenic agents, S the susceptibility, and the constant C the carcinogenic effect, the equation expresses the fact that cancer can arise in an organism either with a high susceptibility and a weak carcinogenic stimulus or with a low susceptibility and a strong carcinogenic stimulus. The equation reads therefore: Carcinogenic agent \times susceptibility = carcinogenic effect." It is believed that the three cases reported partly fulfill these requirements.

In Group iv (time factor) all these cases more than fulfill this time requirement. Their ages being forty, fifty-four and fifty-nine, respectively, the period of smoking with the induction of tar, with its carcinogenic compound, into the lung was a minimum of twenty years. The significance of this time factor is obvious because the production of cancer by coal tar requires on the average six months in a mouse and fifteen years in a man. With a life span of

two years for a mouse and seventy years for a man, six mouse-months represent one-fourth of the life span of a man. During this long period of induction the tissue on which the carcinogen acts undergoes a series of pathologic changes involving among other things increased cell division. Eventually this altered tissue passes into a condition in which a few cells within this altered tissue undergo, sooner or later, an irreversible intracellular change which transforms them into malignant cells. When this happens the scene changes from the exterior to the interior of the cell."

CONCLUSIONS

In three proved cases of cancer of the lung, it would seem logical to assume that possibly in some biologically susceptible individuals, the carcinogenic agent in the tar of smoking tobacco might be the causative factor. Using clinical data, and coordinating it with studies in the basic science of chemistry and biology, further evidence is suggested to confirm our opinion that the gravity of this habit of smoking should be clinically emphasized.

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