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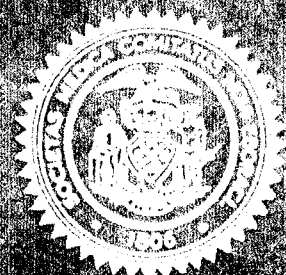
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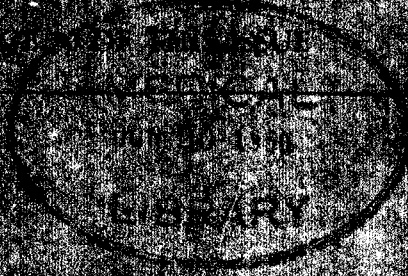
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Medical Progress

CANCER OF THE LUNG: CONSIDERATION OF INCIDENCE AND ETIOLOGY*

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Introduction: Every specialist naturally considers his professional work to be valuable and important. There seems, however, to be valid reason for giving serious consideration to the problem of lung cancer. Perhaps the subject warrants considered attention because it has so recently (1933) been brought from the ranks of hopeless new growth into the family of curable cancers. Its very newness, in this respect, suggests the need for searching discussion of the problem, which in turn may well lead to a method of diagnosis for this disease while it is yet in its beginning phase. The need for prompt diagnosis becomes more compelling when we are made aware that acceptable, almost routine, surgical management of the disease is already at hand, and an insignificant operative mortality and an appreciable five year salvage rate can reasonably be assured the patient and his physician.

Besides the fresh concept of lung cancer brought about by Dr. Graham's pioneer pneumonectomy in 1933, cancer of the lung warrants attention at this time because the incidence of this highly fatal form of cancer is most certainly increasing at a startling rate. The time has arrived, perhaps, when we should not mince words with the public, or our colleagues, internes, and students because the facts seem to indicate clearly that cancer of the lung is a much more common disease today than it was twenty-five years ago.

Incidence: There are numerous possible explanations for the increased incidence of this deadly disease. First of all, there is an increased awareness of cancer in general on the part of the public and the medical profession. Also, the prominent symptomatology of cancer of the lung has been well publicized. The antibiotics, penicillin and aureomycin, undoubtedly have played an important role in more frequent and more accurate diagnosis of cancer of the lung. In the past pneumonia in elderly males was a

* Presented at the March 27, 1950 meeting of the Medical Society of the County of New York.

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common cause of death, and undoubtedly many of those so-called pneumonias were cases of pneumonitis secondary to bronchogenic cancer. Nevertheless, the death certificate classed the death as one due to pneumonia.

Nowadays, the antibiotics do a great deal to relieve this pneumonitis. Fewer patients die of the inflammatory complications of cancer of the lung in its early stages at least, and therefore many of them receive further clinical investigation which leads to an accurate diagnosis of cancer of the lung. I should estimate that better than 75 per cent of the patients now coming to us with cancer of the lung have had a previous clinical diagnosis of virus pneumonia. This error in diagnosis has often been substantiated by competent radiographic studies of the chest. Of course, a so-called atypical pneumonia in a patient over forty years of age which recurs, or fails to resolve, should be viewed with considerable suspicion.

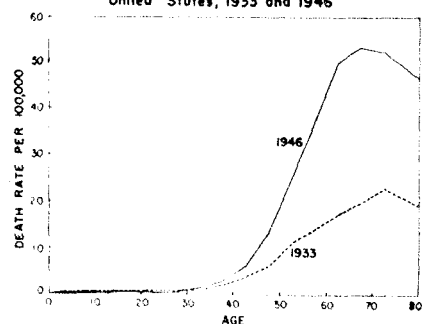
Perhaps the increase in life expectancy brings into the lung cancer age a considerable number of patients susceptible to this disease, and one should therefore expect an actual increase in the number of its victims. Prolonged exposure to factors of chronic irritation, such as smoking, dust, city gas fumes and industrial factors also may play a part in the increased incidence of this disease.

Improved methods of diagnosis due to routine chest x-ray studies, extension of hospitalization, easily available bronchoscopy, the recognition of specialists trained in thoracic diseases, routine bronchial cytology studies, together with public knowledge of the possible significance of chronic cough, blood spitting, and so forth, all may prove to be factors in explaining the rapid increase in the number of patients coming to us with cancer of the lung. Coupled with the foregoing generalizations is the important factor of better cancer teaching at the medical school level. Fig. I, compiled from the mortality statistics of 1933 and the vital statistics of the United States of 1946, reveals a very sharp rise in respiratory system cancer in the thirteen year period following the first surgical cure of cancer of the lung.

Table I, compiled by the Statistical Research

Section of the American Cancer Society, reveals a summary of the lung cancer deaths in the United States during the year 1947. There were 14,666 deaths due to cancer of the lung and this represents a death rate per hundred thousand of 10.2. More than twelve per cent of all male cancer deaths, and 3.2 per cent of all female cancer deaths can be charged to cancer of the lung—or 7.7 per cent of all cancer deaths (1947).

FIGURE I
RESPIRATORY SYSTEM CANCER DEATH RATES BY AGE
United States, 1933 and 1946



Source: Mortality Statistics, 1933, Vital Statistics of the United States, 1946: 10-49

TABLE I
CANCER DEATHS AND DEATH RATES BY AGE, SEX, AND SITE
United States—1947

21. Cancer of Lung and Bronchus (International List Nos. 47 c and 47 d)

	BOTH SEXES			MALE			FEMALE		
	Number of Deaths	Percent of all Cancer Deaths*	Death Rate**	Number of Deaths	Percent of all Male Cancer Deaths*	Death Rate**	Number of Deaths	Percent of all Female Cancer Deaths*	Death Rate**
ALL AGES	14,666	7.7	10.2	11,546	12.3	16.1	3,120	3.2	4.3

* Percent cancer deaths of the lung and bronchus in a specified group of all cancer deaths in that group.

** Rates are the number of deaths in a specified group per 100,000 estimated midyear population of that group, including the armed forces overseas.

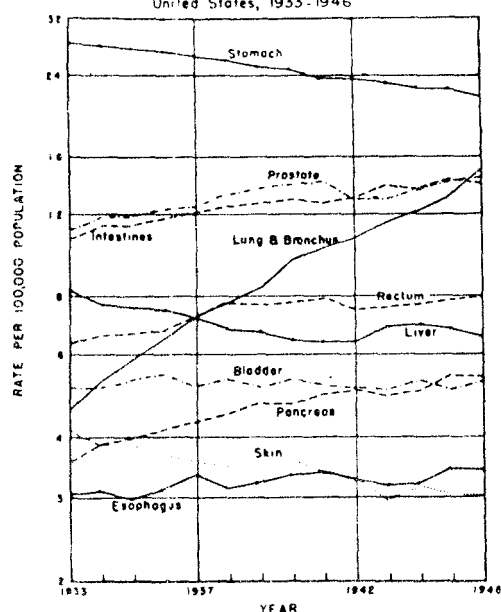
Source: Vital Statistics of the United States, 1947

Statistical Research Section, Medical and Scientific Dept. American Cancer Soc.

Now, if the foregoing reasons are used to explain the increased incidence of cancer of the lung, it should be equally valid to use these data to show an increase in the other common types of cancer. But, from fig. II, we see that from 1933 to 1946 the incidence of cancer of the lung in males has shown a sharp increase in rate without a corresponding increase in the number of cancers of the stomach, prostate, bladder, skin, esophagus, and so forth. Fig. III illustrates the fact that cancer of the lung in females has increased in relation to

malignant disease of the ovary, breast, uterus, and stomach.

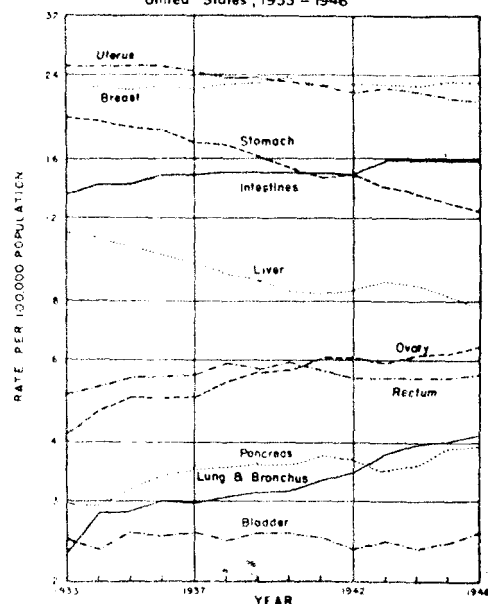
FIGURE II
WHITE MALE CANCER DEATH RATES* BY SITE
United States, 1933-1946



* Standardized for age on the 1940 United States population

FIGURE III

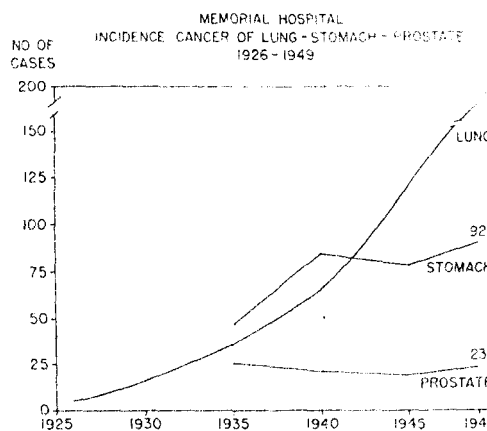
WHITE FEMALE CANCER DEATH RATES* BY SITE
United States, 1933-1946



* Standardized for age on the 1940 United States population

In at least two large medical centers in the United States, it is now reported that cancer of the lung is a more common disease than cancer of the stomach, so that in these two institutions, at least, a relative increase in the frequency of cancer of the lung seems to have taken place. The figures at Memorial Hospital clearly substantiate these reports as shown in fig. IV, indicating the relative incidence of cancer of the lung cases admitted to Memorial Hospital in relation to cancer of the stomach and cancer of the prostate. From 1926 to 1933,

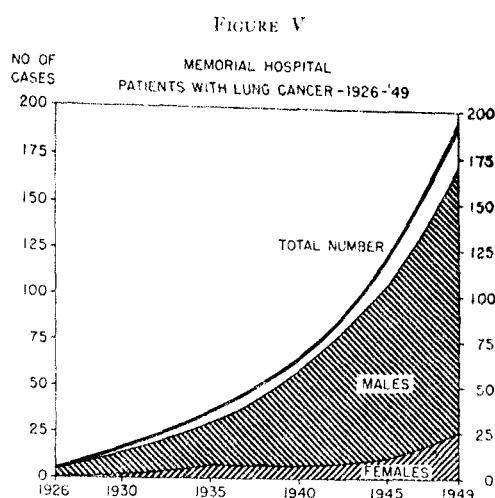
FIGURE IV



a very small number of lung cancer patients were seen at Memorial Hospital, but from 1935 to 1940 there was a sharp rise in the incidence, and shortly after 1940 the admissions for cancer of the lung crossed the line for cancer of the stomach and went on to a precipitous rise in 1945, and continued through 1949, when a total of 193 patients with cancer of the lung were seen at Memorial Hospital. It may be of significance that the increase starting in 1935 was more or less coincidental with Dr. Graham's report of the first successful pneumonectomy for cancer of the lung, and the almost vertical rise from 1945 on coincides with the general introduction of the antibiotics, penicillin, streptomycin and aureomycin.

Etiology: Macklin, in his monograph on this subject, "What Causes Primary Cancer of the Lung?," makes the statement that his data indicate the thesis that primary carcinoma of the

lung is due to chronic inflammatory changes in the lung is unproved. He further states that the role of chronic bronchitis as a causative agent in the production of pulmonary cancer has not been demonstrated. He also believes that emphysema, bronchiectasis, asthma, pulmonary abscess, and so forth, when found associated with cancer of the lung are probably of coincidental interest only. Tuberculosis, pneumonia, and war-gassing have not been proved to be unequivocal factors in the inception of cancer of the lung.



Occupational relation to primary cancer of the lung is difficult to prove, and efforts along this line have for the most part been unsuccessful. The sole exception to this rule being the pulmonary cancer which occurs in the miners of Schneeberg and Joachimstal in Bohemia, the incidence of which is so high in comparison with that of cancer of the lung in other localities, and so high in comparison with the incidence among the neighbors of the victims who are not working in the mines, that there seems to be little doubt that this occupation is strongly productive of cancer of the lung. But even the effect of close inbreeding and heredity have not been exonerated as possible factors.

Chromium dust, iron oxide in silica dust, exposure to coal gas in the air or coal tar on the skin, and the preparation and sale of tobacco have all been brought forward as possible causes of cancer of the lung. A few cases of asbestosis associated with primary cancer of the

lung have been reported. Pneumoconiosis has been said to cause cancer of the lung, and yet South African miners have a high incidence of pneumoconiosis, but a comparatively low incidence of cancer of the lung. I have two brothers as patients, each of whom worked thirty years or more in the anthracite coal mines; one has cancer of the lung, and the other has anthracosis and no cancer. Tarred roads, roentgen rays, motor exhaust fumes, and so forth, have all been suggested as possible causes.

When we review all the theories on the cause of pulmonary cancer, we find that not one supposed cause has been proved to be a real cause, and that none of the alleged causes have been investigated with sufficient statistical accuracy to enable the observer to pass an opinion carrying any great weight. Perhaps there is good reason to believe that there is no one cause for cancer of the lung, but certainly there are additive factors which lead to the inception of cancer of the lung; that is, a number of etiological factors working together over a period of years probably result in the eventual inception of cancer in sensitive tissues which have become altered due to the degenerative changes of age.

In this regard, considerable interest has been evidenced in the recent past regarding the significance of prolonged cigarette smoking as a possible factor in the inception of cancer of the lung. Schrek, in the January, 1950, issue of *Cancer Research*, discusses tobacco smoking as an etiological factor in cancer and concludes: "A relatively high percentage of cigarette smokers was found among the patients with cancer of the respiratory tract as compared to the control. This positive correlation between the incidence of cigarette smoking and incidence of cancer of the respiratory tract appeared to be both statistically and biologically significant. There is strong circumstantial evidence that cigarette smoking was an etiological factor in cancer of the respiratory tract."

In the United States some recent publicity was given to this subject of smoking and cancer by Dr. Graham's group at St. Louis, and, although it was not mentioned, one hundred, or one-half of the cases studied, came from Me-

(Continued on page 40)

(Continued from page 18)

morial Hospital, and the figure as first reported seemed to indicate that 97.5 per cent of our cases were heavy smokers and none of our patients with cancer were non-smokers. These figures were widely quoted, but unfortunately they are inaccurate. Tables II, III and IV show our figures on that series of 100 cases of cancer of the lung in relation to smoking. Table II is, of course, open to criticism, but it is the classification which we finally selected. We decided to use three groups: The first group, the non-smokers; the second group, the moderate smokers, or patients who smoked up to 20 cigarettes per day for twenty years or more with inhalation; and the third group, the heavy smokers (chain smokers), or the patients who smoked from 20 to 60 cigarettes per day for twenty or more years with inhalation. We arbitrarily decided, for purposes of comparison, that one pipe was the equivalent of two and a half cigarettes and one cigar the equivalent of five cigarettes.

TABLE II
MEMORIAL HOSPITAL
SMOKING AND LUNG CANCER
CLASSIFICATION

- I. Non smokers.
- II. Moderate smokers: Up to 20 cigarettes per day for 20 years or more with inhalation.
- III. Heavy smokers: 20 to 60 cigarettes per day for 20 or more years with inhalation.
(1 pipe=2½ cigarettes; 1 cigar= 5 cigarettes)

In Table III, for the Males, we see that in Class I (non-smokers) in the Control Series eleven per cent of men did not smoke, and in the Cancer Series five per cent of men did not smoke; in Class II (moderate smokers) in the Control Series 70 per cent and in the Cancer Series 58 per cent. But in Class III (heavy smokers) 19 per cent in the Control Series and 37 per cent, or nearly twice the previous figure, in the Cancer Series. We think this latter figure is of considerable significance. And, as can be seen in Table IV, for the Females, 60 per cent did not smoke in the Control Series and 58 per cent in the Cancer Series. In Class II (moderate smokers) 37 per cent in the Control

Series and 25 per cent in the Cancer Series. But, when we come to Class III (heavy smokers), only three per cent of the Control Series of women were classed as heavy smokers, but in the Cancer Series 17 per cent were heavy smokers.

TABLE III
SMOKING AND LUNG CANCER
MEMORIAL HOSPITAL
MALES

	Control	Cancer
Class I—Non Smoker . . .	11%	5%
Class II—Moderate Smoker	70%	58%
Class III—Heavy Smoker . .	19%	37%

TABLE IV
MEMORIAL HOSPITAL
SMOKING AND LUNG CANCER
FEMALES

	Control	Cancer
Class I—Non Smoker . . .	60%	58%
Class II—Moderate Smoker	37%	25%
Class III—Heavy Smoker . .	3%	17%

SUMMARY

It has been concluded from statistical studies that comparison of the smoking habits of victims of lung cancer with those of control cases obtained by careful questionnaire affords strong grounds for suspecting the carcinogenic possibilities of heavy, chronic smoking. But, however, strongly suggestive, they cannot afford incontrovertible proof, especially in the eyes of smokers themselves. Chronic, heavy cigarette smoking may very well be an additive factor in the causation of lung cancer in sensitive individuals. However, the individual irritant itself may not be as significant as the chronicity of the patient's exposure to that irritant. In this respect, I suppose we are witnessing a vast human experiment never before carried out by man; namely, what will be the long range result on the human tissues and structures which come in contact with that chronic smoke stream. But, whether we indict cigarette smoking as a cause for cancer of the lung, or whether we admit that we do not know the actual inciting cause of cancer of the lung, the fact remains that the incidence of cancer of the lung has risen sharply since 1926.

