

CARCINOMA OF THE LUNG

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I am very happy to talk to you about a favorite subject of mine, namely, bronchogenic cancer.

(slide) Bronchogenic cancer is the most frequent cancer in the human body today. These are figures from the State of Massachusetts, and are valid statistics, and you can see that since 1950, bronchogenic cancer exceeds cancer of the breast. Prior to 1950, breast carcinoma was more frequent than bronchogenic cancer.



Alton Ochsner

Bronchogenic cancer has increased from 1930, at which time it was 3.08 per 100,000 population, to 42 per 100,000 population in 1955.

(slide) It is a disease primarily of men, but it has been a disease of men for a relatively short time. As seen in this graph, until the mid-thirties the incidence involved both men and women with about equal frequency, and by the mid-thirties it began to increase tremendously in men and now is by far more frequent in men. The reason this began in the mid-thirties was that in 1914, during the First World War, men began to smoke heavily and the 20 year period between 1914 and 1934 is just about the time necessary for the carcinogenic effect of the cigarette smoke to exert itself.

(slide) In New York State, from 1931 to 1950, it increased in men 385%, during which time all other cancers increased only 2%. In women during the same period it increased 68% and during this time all cancers had decreased 15%.

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Slides were used in the presentation.

(slide) It has increased in other countries as well. In Holland there has been a ten-fold increase in women from 1914 to 1951, and a 21-fold increase in men.

(slide) In England also, from 1920 to 1954, there has been a 38-fold increase in the British Isles. In 1953, of all the men who died between the ages of 45 and 55, the most productive years of a man's life, 10% died of cancer of the lung.

(slide) We all know that cancer is a disease primarily of advancing age. Of all the persons 90 years of age, a greater percentage will have cancer than those aged 80, and of those aged 80 a greater percentage will have cancer than those 70. This is true of every cancer except one. The only exception is cancer of the lung. Bronchogenic cancer increases very sharply to reach a peak at the age of 55, decreasing with advancing years. This is the only cancer that reaches a peak and then decreases. Why does this occur? It occurs for one reason and one reason only, I believe, and that is that the individual who has been a heavy smoker, has subjected his heart and blood vessels to the deleterious effects of tobacco and as a result develops coronary thrombosis and does not live long enough to develop his bronchogenic cancer. The dubious advantage of smoking, therefore, is that one can prevent a cancer of the lung death by smoking heavily and dying earlier of coronary disease. One might carry this absurd analogy further and say that you might spare yourself death from both these causes by shooting yourself at the age of 40.

(slide) In England Doll and Hill did a prospective study because one criticism that has been made of the various statistical studies is that a retrospective study which consists of totalling the number of heavy smokers among patients with bronchogenic cancer, is a study of a selected group and therefore of not much value. Dr. Cuyler Hammond, the chief statistician of the American Cancer Society used to say that one cannot say there is a causal relationship between smoking and cancer sim-

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ply because 98.5% of patients with cancer of the lung are heavy smokers. Until one knows what the incidence of cancer of the lung is among smokers as contrasted with non-smokers, one cannot say that there is or is not a causal relationship. I have to admit that from a purely statistical standpoint this is probably true. The prospective study by Doll and Hill in England was made among the medical profession. Each physician filled out a questionnaire concerning his smoking habits, and then they were followed for a period of six years. This shows the incidence of cancer of the lung among British doctors. In the non-smokers, 7 per 100,000 population died of cancer of the lung; pipe smokers, 38, pipe and cigarette smokers 68, and cigarette smokers 125.

(slide) Not only did the incidence of bronchogenic cancer vary according to smoking habits, but it varied according to the amount smoked. As you see, this slide demonstrates the deaths were: non-smokers, 7, up to 15 cigarettes a day 47, from 15 to 25 a day 86, and 25 or more 166. It is almost like a mileage ticket; you can determine how soon one is going to develop cancer of the lung by the amount one smokes.

(slide) A similar study was done here as you know, by the American Cancer Society. Two hundred thousand men between the ages of 50 and 70 were interviewed by 22,000 volunteer workers. These men were asked to fill out an elaborate questionnaire. They too were followed for a period of six years. The result of that study showed that here too, as in England, there was a relationship in incidence of cancer of the lung according to whether the men smoked or not. Here is seen the non-smoking group; this is the group that smoked occasionally; here is the group who smoked a pack or more of cigarettes a day; the group who smoked only pipes and the group who smoked only cigars. The same mileage ticket that the British showed was shown here in the American Cancer Society study.

(slide) This is a recapitulation of the American Cancer Society study. The overall death rate was 105% higher among cigarette smokers than among non-smokers. The death rate from coronary disease was 115% higher among cigarette smokers than among non-smokers, and the death rate from bronchogenic cancer was 800% higher among cigarette smokers than among non-smokers! There are some who say it has not been proved. One wonders what proof it is going to take.

(slide) Several years ago I attended a Cancer of the Lung Committee meeting, and someone said there can be no causal relationship between smoking and cancer because if there is, why do we not see precancerous lesions. I asked Dr. Dunlap, our Professor of Pathology at Tulane University, if precancerous lesions are seen in the lung. He thought for a moment and said—"We don't look for them." He then started a Senior Medical Student on this project, the project consisting of taking blocks from the tracheobronchial tree of men coming to autopsy, men aged 50 and above. The next three slides are of men of the same age, 50, the only difference being their smoking habits.

(slides) The first is the mucous membrane of a man who had never smoked. One sees a perfectly normal mucous membrane, one can see the cilia, and it is about as normal as anyone's mucous membrane could be—it is the way mine would look because I do not smoke.

(slide) This is the mucous membrane of a man who had smoked moderately. One sees that there is definite piling up of the mucous membrane, it is beginning to look somewhat like a skin.

(slide) This is the mucous membrane of a man of the same age who had smoked heavily. There is a precancerous lesion. This work has subsequently been corroborated much more conclusively than we did it, by Auerbach in New York and by Chang in St. Louis. These gentlemen have shown that there are changes in the bronchial mucous membrane which are metaplasia, precancerous changes, carcinoma in situ and invasive cancer, depending upon the amount one smokes.

(slide) This shows that we have become a nation of cigarette smokers, a fact known to all of you: the total tobacco consumption in the United States has increased tremendously since 1896. The consumption of cigars and pipe tobacco and snuff have remained about the same—actually pipe and snuff have decreased—the tremendous increase has been in the consumption of cigarettes.

(slide) This shows the annual per capita consumption in all persons aged 15 and older in the United States from 1880 to 1956. In 1880 it was 16 per capita, whereas in 1953 it was 3,556, and the only thing that seems good to me was that in 1956 it was less than in 1953.

(slide) Also there is a parallelism between the consumption of cigarettes and the incidence of cancer of the lung.

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(slide) This I got from our local paper and to me it is very significant. It is a poll of teenagers, and it shows in teenagers from 13 to 15 years that 37% are smoking, and from 16 to 19 years inclusive, 67% are smoking cigarettes at the present time. So we may expect to have a much greater incidence of cancer of the lung later on.

(slide) This is the work Dr. Graham and Dr. Wynder did on the experimental production of cancer. This machine, which looks like a giant candelabra, smokes 64 cigarettes at a time, just as a human would. Every 60 seconds a drag of two seconds is taken, the smoke is collected and cooled and the tar residue is obtained. This tar residue is added to a solvent, acetone, and the combination of acetone and the tar residue is applied to the skin of animals three times a week.

(slide) This shows the result of that study. At the end of 8 months, one benign tumor developed. At the end of a year one cancer developed, which behaved as a human cancer does in that it metastasized and killed the animal. In the control group, and I am emphasizing that because there are critics of this work who said that the work should be disregarded because cancer-susceptible animals were used. They were not, because in the control group only the solvent was used, and not one animal at the end of two years developed either a benign or malignant tumor. The statement is frequently made that one cannot compare animal cancer with human cancer. In this investigation no attempt was made to do so. It simply shows, without question or doubt, that there is in the smoke from cigarettes a cancer-producing agent—that's all. Since we know that cancer of the lung is increasing more than any other cancer, a disease which was extremely rare 10 years ago and is now the most frequent cancer in the human body, and since we know that there is a parallelism between the consumption of cigarettes and the incidence of cancer of the lung, and since this work shows that there is a carcinogen in the smoke of cigarettes, the only logical conclusion is that there must be a causative relationship.

(slide) I am frequently asked if filters help, and I always answer in the affirmative—they do. They help sell more cigarettes. These are five top popular brands, four with filters and one without, presumably the one without ought to have the greatest amount of tar. Actually there is no difference at all, the filters do not

take anything out except the shekels out of your pocket.

(slide) In 1954 we spent per capita in the United States eight cents for the control of heart disease, we spent 14 cents per capita for the control of cancer—in other words we spent 22 cents per capita in the control of the two principal killers. During the same period we spent \$30 per capita for cigarettes; that is, we spent 136 times as much to cause the two principal killers as we did to prevent them.

(slide) The British have more courage than we have. This is an official poster of the British Government, which is posted in all public places: "To all smokers: There are now the strongest reasons to believe that smokers, particularly of cigarettes, run a greater risk of lung cancer than non-smokers. The more cigarettes consumed the greater the risk." Our Government has not seen fit to take this step even though the Surgeon-General of the Public Health Service went on record as saying that he thought there was a causal relationship between smoking and cancer. Why have we been reluctant? The reason is of economic significance. Far be it from me to want to interfere with the economy of our nation, but what is our economy worth if we destroy the health of the nation?

(slide) This is apparently the Board of Directors meeting of one of the tobacco companies. He said—"All right, then, we just have to convince the public that cancer is good for them."

(slide) We have had now something more than 1500 cases of cancer of the lung. Unfortunately it is a disease that is hard to diagnose, or the diagnosis is usually late. It is primarily a disease of the white race; 83% were in whites and 17% were in the non-white.

(slide) It is a disease primarily of men, because men have been the smokers. I have broken this down into several groups. This is a group of 17 five-year survivals, and I would like to call attention to the fact that in the overall group the ratio of male to female was 8.2 to one, whereas in the five-year survival group the ratio was 4.8 to one. In other words, although carcinoma of the lung is relatively infrequent in women, when it does occur in women it offers a better prognosis.

(slide) The age incidence is primarily in the group from 50 to 70, but again I would like to call attention to the fact that in the younger age group, those under 50, we have a relatively high incidence of survivals. Where-

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as in the overall group a little more than 20% were less than 50, of the survivors 18% were less than 50. We have no five-year survivals beyond the age of 70.

(slide) The histologic type—most of them are epidermoid, 28% are undifferentiated. These are caused by cigarettes. Adenocarcinomas have no relationship to cigarette smoking. It is interesting to see the incidence of adenocarcinoma does not vary from year to year but the percentage is going down. The number of cases remains about the same. Of the five-year survivals a much larger per cent are epidermoid than undifferentiated and adenocarcinoma, both of which give a poorer prognosis.

(slide) The clinical manifestations of bronchogenic cancer unfortunately begin so insidiously that diagnosis is difficult at the time it should be made. There is not infrequently a history of a previous respiratory tract infection. At the present time we often get a story of "viral pneumonitis." Unfortunately the diagnosis most frequently is a viral pneumonitis. This is due to the fact that about 10 or 12 years ago there was a good deal in medical literature about viral pneumonitis, and it was called atypical pneumonitis, which it is. But unfortunately the profession has come to think of an atypical pneumonitis as being synonymous with a viral pneumonitis and, although I realize that a man past the age of 40 who has been a heavy smoker, who develops an atypical pneumonitis, can have a viral pneumonitis, I think his chance of having a bronchogenic cancer with an associated atypical pneumonitis is much greater. So I would warn you not to treat an atypical pneumonitis over too long a period and, if the patient does not get well within a relatively short period, think of the possibility of bronchogenic cancer and take steps to prove or disprove it. Cough is the most frequent manifestation but every cigarette smoker has a cough so that is likely to be disregarded. Hemoptysis means ulceration and always demands investigation. Thoracic discomfort is something that should be investigated. Most of us are not aware of the fact that we have a chest and, if we do become aware of it, that should not be disregarded.

Finally, wheezing: Wheezing means bronchial obstruction. It is probably less important in an individual who has been an asthmatic all his life, but in an individual who has previously not had asthma, who develops wheezing for the first time, it means bronchial

obstruction and if he has been a heavy smoker it is very likely to be a bronchogenic neoplasm.

(slide) The late manifestations are those of advanced disease; fever, due to the pneumonitis caused by blocking of the bronchus or the breakdown of the tumor with production of an abscess; pain, involving the parietes; digestive disturbances due to involvement of the vagi; and emaciation due to the extent of the disease.

(slide) The diagnosis is not difficult if one will only think of the possibility of the existence of the disease. Roentgenography is the best method of diagnosis largely because of the ease with which it can be done. One can usually see a shadow, rarely the tumor may produce incomplete obstruction of the bronchus, and since the bronchus is not a rigid tube but dilates during inspiration and contracts during expiration, air can get beyond during inspiration but cannot get out during expiration because of the contraction of the bronchus on the tumor, thus trapping the air and causing obstructive emphysema. Unfortunately it does not occur very commonly. Atelectasis may occur due to absorption of air beyond an obstructive bronchus. Bronchography is of value in those tumors which are around the corner and cannot be seen. Bronchoscopy should be done in all instances, but unfortunately failed in two-thirds of our cases, and in only a third of our cases were we able to make a diagnosis by bronchoscopy. Cytologic examination of bronchial secretions, either obtained by bronchoscopy or sputum, is the best method of making a positive diagnosis; in about 60% of cases diagnosis can be made by this means. Thoroscopy is more of prognostic than of diagnostic value. Aspiration biopsy I mention only to condemn; because of the danger of implanting tumor cells along the aspiration site, it should be done only in patients who are obviously inoperable. Finally, thoracic exploration is of diagnostic value; in 20% of our cases it was necessary to resort to exploration in order to make a positive diagnosis.

In treatment of bronchogenic cancer I believe there is only one curative measure and that is a radical pneumonectomy, i.e., removal of the lung with an en bloc excision of the regional lymph nodes. We do not feel that lobectomy is a good cancer operation. I do not mean to imply that we don't do lobectomy. We do lobectomies only in those patients in whom previously performed pulmonary func-

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tion studies indicate that the patient cannot tolerate pneumonectomy. Obviously if this is so we will not do a pneumonectomy, but we have never been able to cure a patient by lobectomy. That is not quite fair to lobectomy, because we use it only in patients whose pulmonary function studies indicate that they would not tolerate pneumonectomy.

(slide) In the 1453 cases the results are not good, as you can see. Almost half of them were so far advanced when we first saw them that nothing could be done except palliative procedures such as nitrogen mustard or x-ray or a combination of both. There were 818 that were considered operable, of which 7% refused surgery. There were 759 that were explored, of which 37% were found to be non-resectible, and almost 20% of that group died in the hospital not of the exploration but because of the extent of the disease. There were 477 in which resection was done with a mortality rate of 20%—and that is high. I do not apologize for it because we believe that palliative resection, removal of a lung even though there is massive extension to the lymph nodes, even though it involves the chest wall or the pericardium, is justifiable. These people remain more comfortable and I will show you that we have been able to cure some of these patients.

(slide) This shows the resectibility in our series. It was at an all time low in 1913, it reached an all time high ten years ago, and then became markedly less due to the mistaken diagnosis of viral pneumonitis, and now is increasing again. This is the resectability according to age, and you can see that it is a little better in the younger age group as one would expect.

(slide) All patients in the survival group had pneumonectomy. We did not cure a patient by lobectomy.

(slide) I would like to show that in the five-year survivals there were 12% in which the lesion had extended beyond the lung; to the mediastinal nodes, the chest wall or the diaphragm. The resection in these cases we have

designated as a clinical palliative procedure. Actually not all were palliative because some were cured.

(slide) This shows the type of involvement; 34% of our survivors had nodal involvement; 8.5% had pleural involvement.

(slide) These are the results in the overall group; 5.2% of the entire group are alive within five years. These include the extensive cases for which nothing could be done.

(slide) These are the 177 that were resected; 15% are alive at the end of five years.

(slide) This is the group of cases in which the lesion was apparently limited to the lung at the time of operation and 32% of those are alive at the end of five years.

(slide) This is a comparison of the group in which the lesion was apparently limited to the lung, and those that had extensive involvement of the lymph nodes or the chest wall or diaphragm or pericardium. Almost 20% of those are alive at the end of five years.

(slide) This simply shows again that the younger age group offered a better prognosis.

(slide) This shows that 67% have no nodal involvement in the five-year survivals; 38% had nodal involvement.

(slide) This is a recapitulation—85% of the population of this age—only 85% are alive whether they had cancer or not; the curative group, 32%, all resected, 15%, and the palliative resections 8.6%.

(slide) The final slide shows the overall group. There were 52% that were explored, 33% resected; 26% survived resection, and about 6% were alive at the end of five years.

How are we going to improve this? We are going to improve it by physicians thinking about bronchogenic cancer in an individual who has been a heavy smoker who develops an atypical pneumonic condition. And, finally, I urge those of you who smoke that you get an x-ray of your chest at least every six months so that when you do develop a cancer—and you will if you don't die of something else—it can be diagnosed in time, while it can still be resected.

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