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**IS THERE PROOF
SMOKING CAUSES
CANCER?**

—EXCLUSIVE INTERVIEW

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IS THERE PROOF THAT SMOKING CAUSES CANCER?

Are statements that cigarette smoking and lung cancer go hand in hand really true? Just what evidence is there and what does it prove? Are there any other things involved besides cigarettes? And what progress is being made in the search for a final solution to the problem of rising lung-cancer rates?

To get the facts on the subject, *U. S. News & World Report* interviewed Dr. E. Cuyler

Hammond, who heads one of the most extensive research projects in all medical history. Through this research a scientific effort is being made to determine the truth about whether smoking causes lung cancer.

Dr. Hammond at present is director of statistical research for the American Cancer Society and is also professor of biometrics at Yale University.

Q Does smoking really cause lung cancer, Dr. Hammond? People are saying all sorts of things about cigarette smoking—

A That's just what we are trying to find out. There is some evidence that it may be so. For example, material collected from cigarette smoke will produce cancer on the skin of a susceptible mouse if you keep up the experiment long enough. That's an important piece of information, but taken alone it doesn't prove a thing about the occurrence of lung cancer in human beings. It has to be weighed together with other evidence and we are still collecting information.

Q In other fields of research in this country—on other forms of cancer—are you doing this same type of statistical detective work?

A Some. Lung cancer is the one we are doing the most work on, because it is the only type of cancer which is increasing rapidly in age-adjusted rates.

Let me make something clear—all forms of cancer are increasing, in that more people die of them each year. But that is primarily because cancer is a disease largely of later life, and our population is aging—we are getting a larger number of old people in the population. For that reason, and that reason alone, most forms of cancer are increasing in number of deaths each year. But lung cancer is the only form of cancer in which there is a very great rise in the death rate after correcting for age. There are a few others that are rising slightly, and a few that are going down slightly.

Q Is lung cancer always fatal?

A Not always. It is more highly fatal than some of the other forms of cancer. It is one of the most fatal. By and large, the cancers that are internal and in vital organs are more apt to cause death than those, such as skin cancer, which are on the surface. One reason is that those on the surface are more easily diagnosed—you can see them and get to them. Another reason is that cancers in vital organs are more difficult

to treat. The over-all survival rate for those who get lung cancer is around 5 per cent at the present time.

If we can persuade everybody—particularly men over 45—to take an X-ray screening test every year, we think we will raise the survival rate considerably; at least we hope so.

Q How many cases are there in a year now?

A About 22,000, but it is on the increase.

Here we are speaking of cancer that originates in the lungs. A considerable number of cancers in other parts of the body spread, and the terminal cause of death is sometimes a cancer growing in the lung that didn't originate there. Ordinarily, the term "lung cancer" refers only to cancer which originates in the lungs.

Q Oh, you don't call it lung cancer if—

A No, not unless it originates in the lungs. Cancer spreads throughout the body, but we name the type according to where it originates.

Q What is the lung-cancer rate among women as compared to men?

A Oh, there is no question that the lung-cancer death rate is much higher in men than in women, very much higher. I could give you the actual figures on it—it is about 5 to 1.

Q And yet women have become smokers in greater numbers in recent years than men—

A But too recently for the full effect to become apparent. If smoking causes lung cancer, and if, furthermore, it takes about 20 years of heavy smoking to do it, then what is known about the smoking habits of men and women over the past 20 years would pretty well account for the difference, because women didn't start smoking heavily as early as men did.

Q You are the head of a research project that is going to try to find the answer to the question of whether smoking causes lung cancer?

A Right. At least we think that it will provide important evidence leading to an answer.

A Multiplicity of Suspects . . . How the Research Is Being Handled . . . What's Been Found Up to Now

Q Is that the largest project of its kind at present in the country?

A As far as I know, it's the largest project of that general type that's ever been attempted on any disease. About three weeks ago the U. S. Public Health Service started a somewhat similar study which may be about as large. We began our own study more than two years ago.

Q Is your project large because of the number of people involved in it or because of the money being spent?

A Because of the number of people. We are doing the project largely with volunteers—we have 22,000 volunteers working for us. They interviewed 204,000 men, all between the ages of 50 and 69.

Q Who are the people doing this work?

A The volunteers of the American Cancer Society.

Q When did this take place?

A The actual interviewing started on Jan. 1, 1952, and most of the men were interviewed within six weeks, but we continued interviewing until June, 1952.

Q And this is a project to find out what you can about whether lung cancer is caused by smoking or not—

A Well, it's actually a little more than that. We are undertaking the project because there is reason to suspect that smoking may cause lung cancer—we don't know it, but there is good reason to suspect it. Now, what we have actually done is get the smoking history from a very large number of men. We selected white men in order to avoid bringing in the confusion with race, because the death rate is different in the different races.

We took the age group 50 to 69 only because the lung-cancer death rate is highest in that age group. If we had chosen younger people, the study would have taken at least 20 years. Having taken the case histories while the men were still well, we think they are unbiased—that is, their answers were not influenced by emotion. Then we are following them up for the next several years, and about 3,000 of them die each year—the number is going up because they're getting older. The first and most important question is whether smoking affects the death rate.

Q That is, whether people who smoke die faster than people who don't smoke—

A Yes, that is the first and most important question. There is some reason to suspect that the death rate may be twice as high among heavy smokers as among non-smokers. This is based on past evidence, but we don't know yet, and we want to find out on a large sample.

Then the second thing: If smoking has such an effect, we



DR. HAMMOND

want to analyze it by causes of death—and, of course, the major cause we are interested in is lung cancer.

Q How do you choose the people to be interviewed?

A In the first place, we limited the study to nine States—New Jersey, Pennsylvania, New York, Michigan, Illinois, Wisconsin, Minnesota, Iowa, and California. All of those States have reasonably good diagnostic facilities. We didn't go anywhere where the diagnostic facilities are very bad.

Second, we had to go to places where there were a lot of men in the age group 50 to 69. Within those States we then selected 394 counties on the same basis, being sure to include both rural counties and urban counties. We questioned people in Pittsburgh, Detroit, Minneapolis, Chicago and several other large cities. We also got them from rural counties such as in the upper peninsula of Michigan, which is

about as far removed from any industry as anyplace you can think of. We then had our volunteers question men that they knew reasonably well and would be able to follow—that is, they wouldn't lose track of them. They just didn't go out and question people in the street.

In rural counties and small towns there was virtually no selection on the basis of social-economic conditions, or that type of thing, because in a small town everybody knows everybody else and they can all be followed.

Furthermore, in some States the local radio and press were of tremendous help to us when we were questioning the men. In a few counties of Wisconsin, for example, they broadcast every 15 minutes, asking men to come in and give their smoking history. In some of the counties we obtained very nearly a 100 per cent coverage on all the men in that age group from the area. So that in those places there was no selection, practically speaking. Now, it is true that there was some selection in the cities.

Our volunteers for the most part are of the middle or upper-middle social-economic group. So there was some selection in the social-economic classes among their friends. But it's also true that fraternal orders helped us and church groups helped us with the lower economic level. Some labor unions and some plants helped us. Well, we know all those facts, and so for each group we know what sort of people we are dealing with.

Q When you have a selection like that—selection of State, selection of county, selection among the people themselves—how do you know that you have a representative and statistically valid sample?

(Continued on next page)

... "It is possible that smoking has some beneficial effects"

A In the first place, we don't need a representative sample. What we do need to know is the facts about the people we question.

Q There is no need to have a group composed half of smokers and half of nonsmokers?

A I suppose, if there had been any feasible way of doing so, we might possibly have only taken people who smoke very heavily and people who don't smoke at all, in order to get a quick general answer to the question. But in order to ascertain people's smoking habits, you have to question them. Once having questioned them, there is no good reason to eliminate moderate smokers from the sample. The real confusion is going to be among people who have mixed smoking habits—for example, those who smoke a pipe for a while, then cigars, then stop smoking, and then start cigarettes.

Q Now that you have this, what happens next?

A Once a year, in November, we have each of our volunteers give us a report on all the men she questioned. She merely tells us whether the man is living or dead as of November 1. If he died, she tells us the date and place of his death. We then get the death certificate from the Health Department. If the death certificate mentions cancer of any type, or a respiratory disease of any type, then we go back and get additional information from the doctor who signed the death certificate. When possible, we also look into the hospital record and pathological reports to get the most accurate information on the cause of death.

Q How much does it cost to do all of this?

A I don't think you can put a dollar figure on it. The major work is done by volunteers, and the work they have done for us would have cost several million dollars if we had had to pay for it. The main cash expenditure has been for traveling; that is, getting in touch with the volunteers. But we have a staff that travels to get in touch with the volunteers anyway, and I don't think that any great amount of traveling was done on account of this study that wouldn't have been done anyway. We have meetings of volunteers to teach them about cancer.

AN ANSWER, SOON?—

Q How long do you think it will take before you get a result from your research?

A We may have enough information from the follow-up that was started last November—it takes several months to complete the work—to get an answer to the general question of whether death rates are higher among smokers or nonsmokers. It will probably take one or two more follow-ups before we will be able to make an analysis by cause of death.

But I'll say this: If, practically speaking, only heavy smokers get lung cancer, we'll know that in a lot shorter time than if the effect is not that dramatic. It is easier to distinguish between black and white than it is to distinguish between shades of gray.

Q What is your study's criterion of a heavy smoker?

A We don't have a criterion of a heavy smoker at this time. We simply have the facts as to how much smoking the men have done. We are going to divide it up quantitatively all the way from the heaviest smoking down to the lightest.

Now, as a practical matter we will have to group the men by categories to get an appreciable number of people in each group. We'll probably have about eight or ten groups. But

that's a detail of analysis. There is no criterion of a heavy smoker—they go all the way from people who smoke over four packs a day down to people who smoke none, and there is no clear-cut dividing line.

Q Supposing that it is true that the death rate is high among smokers versus nonsmokers, but those people didn't die of lung ailments—what did they die of that might possibly have a relation to smoking?

A That's the problem—to find out.

Q Might you not find that the death rate among any group that's set off from another group is higher than the other group?

A Quite so, yes. For example, if we find that there is a higher death rate from stomach ulcers among smokers as opposed to nonsmokers—stomach ulcers being related to people's nervous dispositions under pressure, and that sort of thing—then it might be due to a mutual cause rather than a cause-and-effect relationship. That is, the nervousness might both produce stomach ulcers and cause people to smoke heavily. On the other hand, the harmful effect of being nervous may be that nervousness causes you to smoke a lot and smoking in turn produces stomach ulcers—you can't tell without more evidence.

However, if we find that smokers have high death rates from certain diseases, where in animal experiments and in short-term human experiments we can see that tobacco smoke has an effect, then we would be more likely to believe that a cause-and-effect relationship exists. It depends upon what other evidence there is. It may be a mere association, not cause and effect, or it may be cause and effect—and we'll need outside evidence to get that settled.

Q How many people in America know anything about this subject professionally?

A I'd say it's a handful of people who have personally done any real work on it. In addition, a number of doctors have gained impressions based upon clinical experience.

Q Do you think this whole thing may lead to the discovery of some way of treating the cigarette so as to eliminate these dangers?

A I hope so. My personal guess right now is that there is a cause-and-effect relationship between smoking and lung cancer, but I have no idea at the present time whether that relationship is trivial—no more dangerous than crossing the street; for, after all, you may get run over in crossing the street—or whether it is so important that making cigarettes ought to stop until we find what's in them that is bad and remove it. But as to whether or not all the harmful ingredients can be removed and still have a cigarette that is pleasant to smoke remains to be seen. I am interested not only in lung cancer, but also other possibly harmful effects of smoking.

It may be that the nicotine is increasing the death rate from heart disease and that the tar is increasing the death rate from lung cancer and that something else is increasing the death rate from cerebral hemorrhage. If so, you will probably have to eliminate the cigarette. We don't know yet. It is also conceivable that smoking has some beneficial effects.

SPOTLIGHT ON CIGARETTES—

Q You say you are studying cigarettes. How about cigars and pipes?

A Oh, we are studying all types of smoking. The reason I have emphasized cigarettes is that it is the sale of cigarettes

... "Cancer death rates are higher in city areas"

which has increased. The sale of cigars and pipes has increased very little in comparison.

Q Is lung cancer greater, then, among cigarette smokers than among pipe smokers?

A There is some evidence that that may be so. Just how valid the evidence is I'm not sure. We are studying all types of smoking.

Q And cigars—there isn't any evidence on that either, recently?

A The evidence from studies of hospital patients seems to indicate that cigars and pipes are relatively harmless so far as lung cancer is concerned, but are harmful as to lip, tongue and mouth cancer, whereas cigarettes are harmful for lung cancer—at least that's the indication. It has face validity, as we say, because the tongue, lips and mouth are subjected to the tar and other material that comes out of the end of a pipe and a cigar in heavy concentration, and pipe and cigar smokers seldom inhale. Very little condensed tar comes out of the end of a cigarette, but people do inhale the smoke and it comes into contact with the lungs. So the evidence sounds reasonable—not absolute proof, but reasonable.

Q Are you particularly worried about it—I notice you are smoking?

A Well, I feel this way about it: If I get altogether too nervous personally about every problem I am working on, I would be one miserable man. I am not going to let it have any effect on my personal habits until all the facts are known. Fear is an occupational hazard which must be guarded against by people who are doing research on fatal diseases.

Q If you read in the paper that a lot of people were hurt crossing the street, you might get scared and never cross the street—

A That's right. Most people I know who have worked on the subject, including those who think as I do—that smoking very likely does increase lung cancer—most of them are still smoking, if they ever smoked. Some of them have cut down, however.

Q How do you know that a person who died of lung cancer or cerebral hemorrhage wouldn't have died of lung cancer or cerebral hemorrhage even if he hadn't smoked all his life?

A That's why I say you have to tie in all the other information on your subject to come to a reasonable conclusion. The only way absolutely to prove it would be to take a large group of people and force half of them to smoke heavily and not let the other half smoke at all; and then put them into the same occupation and same environment and follow them for 70 years. Well, we can't do that. So we have to get all the evidence we can bearing on the subject from such sources as animal experiments, studies of the immediate effects of smoking on human beings, and studies of death rates in relation to smoking.

HOW USE OF MICE HELPS—

Q What about the evidence that has been obtained through mice experiments? Is that very valuable?

A Yes, I'd say it's very valuable. But it is not conclusive in itself.

Q What have mice experiments shown about smoking?

A They have shown that if cigarette smoke is condensed in a very highly concentrated form and smeared on the skin of mice for a good many months, then a large proportion of the mice will get cancer of the skin.

Q Suppose you smear orange juice or grease or something else on them, wouldn't they get cancer of the skin?

A Well, there are a certain number of substances, called carcinogenic agents, which will produce cancer. They're a limited number.

Q What kind of substances are they?

A Most of them are coal-tar products.

Q And if they are rubbed on the skin regularly, they will produce cancer?

A Yes. But it takes a long time. Usually it takes about a third or more of the normal life span of the animal.

Care Needed in Drawing Conclusions

Q Can you jump to the conclusion that, just because coal-tar products can produce cancer on the skin of an animal, it will also do the same thing internally?

A No, you cannot. At least, that's my opinion. Various parts of the body differ in their susceptibility to cancer. Furthermore, something which affects a mouse does not necessarily have the same effect on a man. For this reason, it is necessary to study the human population. But such studies are by no means easy.

For example, try studying cancer death rates versus urbanization, and you find that by and large the cancer death rates are considerably higher as recorded in city areas than in the country. Furthermore, by and large, they are higher in the richer sections of the country than they are in the poorer sections, and putting it on a world-wide basis, you find that the most backward countries have the lowest cancer death rate reported. That may be due to mere difference in diagnosis, because in the rich areas there are more doctors and so you get more correct diagnoses. Therefore, that evidence in itself doesn't show necessarily that city living, with exposure to coal-tar products, causes the higher cancer death rates.

Q How much higher is it in the city than it is in the country?

A If we're talking about lung cancer, it's over 2 to 1 among males.

Q Would you say there are lots of differences between people who smoke and those who don't smoke?

A Probably. Therefore, once you establish that there is a difference in the death rate between smokers and nonsmokers, in either direction, then you have to look at other evidence to determine whether it's a cause-and-effect relationship or whether it is due to association with other factors. But, at least, you have a lead to work on.

Now, the importance of animal experiments is this: Suppose we find that heavy smokers have a much higher lung-cancer death rate than nonsmokers. If you could not produce cancer by smoke, or anything from tobacco, then you would suspect that you were dealing not with a cause-and-effect relationship in the human population between smoking and lung cancer, but some other associated factor. Maybe smokers are more apt to go to a doctor to get diagnosed for lung cancer, for example. But since you can produce cancer experimentally in animals by something from a cigarette, then you would be more inclined to think that a cause-and-effect relationship exists.

Where something has to be operating for a very long time to produce results, either favorable or unfavorable, it is very, very difficult to ascertain the true facts, because too many things have happened in the world in the last 20 years.

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... "Tobacco smoke contains a lot of poisonous agents"

The factors in the environment which produce cancer probably have to operate for—oh, maybe, 10, 15, 20 or 30 years before cancer occurs. But, now, if we think back over the last 30 years, look at all the things that have happened in that time, and many of these things are correlated with each other.

Q What things are you referring to?

A Oh, a tremendous number of things have changed which could conceivably be related to cancer. For example, dietary habits have changed. People now get more vitamins, which promote normal growth, and it is conceivable that this promotes abnormal growth also. Men in this generation are usually taller than their parents. Air pollution has increased. Deaths from infectious diseases have decreased and perhaps people who die of cancer today tend to be the sort of people who would have died of an infectious disease in an earlier period. More people have desk jobs than previously, and there has been a population shift from the farm to the factory.

Innumerable other examples could be given—and it is difficult to separate the wheat from the chaff in trying to ascertain what factors are primarily responsible for changes in death rates from various diseases. Then, too, certain environmental factors are associated with each other. For example, some years ago only rich people could afford to smoke cigars but this was only one of many ways in which the rich tended to differ from the poor.

Q In what age group is a rise showing?

A Well, in all age groups—for lung cancer, that is. This graph I am showing you here does not reflect the rise which took place merely due to the aging of the population. If I showed you that, the rise would appear to be much greater.

Q If you took the general population as a whole, and charted the lung-cancer increase, it would go up to one level, whereas if you took only the age group who would be more subject to lung cancer and chart the rise in that age group, you would get a different and more correct answer?

A That is right. In most forms of cancer, if you plot the trends, showing each five-year age group separately, there is little or no rise, but if you throw all age groups together, and simply calculate the over-all death rate, there is a rise. This is so because the death rate is much higher in old people than in young people, and there are proportionately more old people in the population these days.

This particular graph is corrected for that factor. It shows that the death rate for lung cancer is rising even after correcting for the aging of the population. Something must be causing this increase. There is no change in heredity. Therefore, changes in heredity cannot account for the rise. We are guessing it is something in the environment—therefore we have more clues to work on than in the case of other forms of cancer.

Now, with reference to a previous question, we are doing more statistical research on lung cancer than any other form of the disease because, since the death rate is rising, it is a fair guess that there is something in the environment that is causing it, and this environmental factor is probably also on the increase.

HEREDITY'S PART IN CANCER—

Q It hasn't been proven, has it, that cancer is hereditary?

A There is some evidence which seems to indicate that heredity plays a part.

Q But not in all cases?

A Well, there is probably a hereditary factor in virtually

every case to some degree. But human cancer is probably not inherited in the ordinary sense of the word.

Q Is there a hereditary factor in every disease?

A Yes, to some degree. As a generalization, it may be said that every disease is the manifestation of a reaction between an individual and his environment (the environment containing such factors as bacteria, viruses, and chemical agents). Therefore, the nature of the individual as influenced by heredity is always a matter of importance. You can breed a strain of animals in which cancer cannot be produced by any known process. And there are other strains of animals that have a high number of spontaneous cancers, and are very susceptible to carcinogenic agents. I'd guess that human beings vary from one extreme to the other. But human beings do not intermarry in their own families in such a way as to produce pure strains of high or low susceptibility.

Q Are there animal experiments showing any ill effects from smoking, besides those involving putting coal tars on the skin? You've had some inhaling experiments, haven't you?

A Yes, but the difficulty is that if you try to expose them to a very high concentration of smoke, many of the animals die before cancer has a chance to develop. One experimenter has reported an increased incidence of lung cancer among animals which survived the acute effects of a high concentration of tobacco smoke, but the type of cancer was not the same as the common type of lung cancer seen in human beings.

Q They choke to death?

A I suspect that the people doing the experiment gave the animals a good deal higher concentration of smoke than a person would ordinarily get. I suspect that the animals were killed by carbon monoxide, but I'm not sure. You see, tobacco smoke contains a lot of very poisonous agents, and the most poisonous of the lot is carbon monoxide. Now, there is no evidence whatsoever that carbon monoxide causes lung cancer, but carbon monoxide in high concentration is a deadly poison, as you know.

Q Isn't that largely what happens if you take too much of anything—for example, mashed potatoes? Or if you take too much aspirin?

A That is one of the difficulties. If you depend just upon animal experiments, you have to argue from extremes. An argument will run something like this—I'll deliberately use a ridiculous example—if you hold somebody's head under water, he'll drown. Therefore, using the type of argument some people use, drinking any water is bad for you.

So that type of argument—to use a pun—doesn't hold water. In a problem of this sort, you have to collect information from every source you can think of. I think the most important is to see what happens to the human population.

Now, if the death rate from cancer is no higher among smokers than among nonsmokers in the human population, you can forget the whole business. But if there is a difference, then you should look to other evidence, such as animal experiments, to determine whether you are dealing with a cause-and-effect relationship or whether you are dealing with associated causes.

EFFECTS OF JOB, DIET—

Q By "associated causes," do you mean that the thing that causes the person to take up smoking might be the real cause of his death?

A Yes, it might be that. Or it might be that heavy smokers,

... "For some cancers, pipes are worse than cigarettes"

because they cough, are more apt to go to the doctor for diagnosis and therefore more lung cancer is diagnosed among heavy smokers. That would be the sort of thing I am talking about. Or it may be something like this: People in certain occupations cannot smoke because of their occupations. Maybe they are very safe occupations. All sorts of correlations of that type are possible.

Therefore, you have to look at laboratory evidence, and that is the importance of the laboratory experiment. Nothing done on the mouse is going to prove that the same thing happens to a man, but, at the same time, if the animal experiments tie in with your observations on man, and all other evidence ties in, then you can be reasonably sure of your conclusions. If they go in opposite directions, then you are not at all sure how to interpret it.

If the Appetite Is Poor—

Q Isn't it also true that among these associated factors in smokers is the fact that they may not be eating properly because of the way smoking affects the appetite?

A Yes. But that, then, would be a direct effect of smoking. We are not talking about the mechanism here. Let us suppose that people who smoke heavily don't eat properly and are therefore more apt to die.

Q Then the responsibility would be smoking, but not the cigarette. The cigarette itself wouldn't produce the death—

A That's right. But, nevertheless, smoking would be bad for you in that case. For example, probably one of the worst things about heavy drinking is that people who drink very heavily—the real chronic alcoholics—are practically on starvation diets. They stop eating and they get serious vitamin deficiencies. But still the drinking is responsible.

Q Isn't it true that a lot of women feel that smoking keeps them from overeating?

A Yes, and then their diet is just awful. They starve themselves and eat the worst sort of food in many instances.

Q So that the cause of their troubles would be an improper diet rather than the cigarette?

A A combination of the two. You couldn't distinguish—unless you had outside evidence that smoking per se in an experimental animal had resulted in death. Now, in heart disease there are some immediate effects of smoking. Smoking causes an immediate contraction of the blood vessels. It also causes the speeding up of the heart rate.

Now, that doesn't kill you immediately. But whether having your heart rate continually stimulated over a matter of 30 years and having a continual abnormal contraction of the vessels will eventually have the cumulative effect of causing death from heart disease is anybody's guess.

If we do find a larger death rate from heart disease, arteriosclerosis, cerebral hemorrhage, or something like that, among heavy smokers, what we know of the immediate effect of smoking would make me think we were dealing with a cause-and-effect relationship and not merely an association of the type we were speaking of a few minutes ago.

Q What we know is of a short-range effect, but we don't know about the long-range effects—

A Right. We can study the long-range effects in animals experimentally where the animal does not have too long a life span. There we can eliminate the association. We can make one animal inhale smoke and keep another animal from doing

it. You can't do that with a human being. The animal experiment can be carried out in two or three years, while a comparable study on human beings would take a generation.

IS TENSION A CAUSE?—

Q In all the studies of cancer, is there anything that indicates statistically whether people with tension, what they call the nervous types, are more prone to cancer of any kind?

A I don't know of any specific study that would answer the question with certainty one way or the other. Some of the studies have included all types of cancer, not just lung cancer, and there is no evidence whatsoever that heavy smoking increases the death rate from any sort of cancer, except of the lung, lip, tongue, and mouth.

Now, it is known that tobacco smoke contains something which can cause cancer—at least in mice—and it only causes cancer in that part of the body with which it comes in contact. Smoke comes in contact with the lung.

If we should find that the death rate from lung cancer is much higher among heavy smokers and the death rate from other forms of cancer is not one bit higher among heavy smokers, then I'd say that the evidence would be extremely strong that there is a cause-and-effect relation.

You see, the other forms of cancer act as a control. Cancer is something that happens to an individual cell. Nervous tension might cause a change in hormone secretion, or something of the sort, and if that alone would increase cancer in one part of the body, it would probably increase cancer in any part of the body. It would be a general phenomenon. There'd be no reason whatsoever to suppose that it would affect the lungs and no other part of the body.

Q If you establish that there is some relationship between lung cancer and smoking, why wouldn't you also have an increase in mouth cancer or cancer of the larynx where the smoke comes in contact?

A There is some evidence that smoking increases the incidence of cancer of the lip, tongue and mouth.

Q But this is the same type of evidence that you've been talking about—

A Yes, the same type of evidence. There is also some evidence that for those types of cancers, cigars and pipes are worse than cigarettes, whereas for lungs the cigarette is worse. Mind you, this evidence isn't all perfect. But it is reasonable enough, because in the pipe and cigar you have a great amount of juice coming in direct contact with the tongue and the lip. And very few people inhale cigars and pipes.

HOPE TO PROVE SOMETHING—

Q As a smoker yourself, are you trying to prove anything one way or the other?

A I am not trying to prove anything. I am just trying to ascertain the facts. I hope I am disinterested. There's one thing, however—every research worker is probably prejudiced to a slight degree, in that he hopes that he is going to get definite results of some sort. He may not care which way they go, but he does hope he gets something. And to that extent I guess I'd have to admit that I am not completely disinterested. Of course, I hope to prove something by all of this—I wouldn't have gone to all the work otherwise.

(Continued on next page)

... "I hope to find some cause of lung cancer"

Q What do you hope to prove?

A My only real hope is that we will be able to find a definite answer to the question one way or another. What would make me very unhappy would be to come out with inconclusive results.

Q Do you hope that you will be able to disprove that it is injurious?

A No. I hope to find some cause of lung cancer which we could then eliminate in order to prevent the disease. It may well be cigarette smoking. Lung cancer is going up. So, the hope is that we will find the cause. I will be very disappointed if we don't find a cause which is removable one way or another.

Personally, I don't care if it's something from an automobile engine which could be altered, or whether it's soot which could be controlled, or whether it's smoking, in which case you can either advise people not to smoke or take the active ingredient out of cigarettes.

CHARTING DEATHS SINCE 1910—

Q You were speaking of carbon monoxide being so poisonous. A lot of carbon monoxide is being given off in our garages and in using our automobiles, and people are inhaling it. If we had some statistics to show that people died as much of lung cancer before the automobile was invented as they do now, would we have a cause-and-effect relationship there?

A I can show you some graphs on that. Here are the death

rates from about 1910 on. Figures back of that are unreliable. In the earlier period influenza and pneumonia—you have to lump them together—were among the principal causes of death, along with tuberculosis. In the 1918 epidemic it goes right up there off the paper. That's 200 per 100,000 white males per year.

Q Then it comes down to where it's scarcely 30 per 100,000 white males per year—

A Right. Tuberculosis death rates went from 150 per 100,000 in 1910 down to 20.

Q And lung cancer?

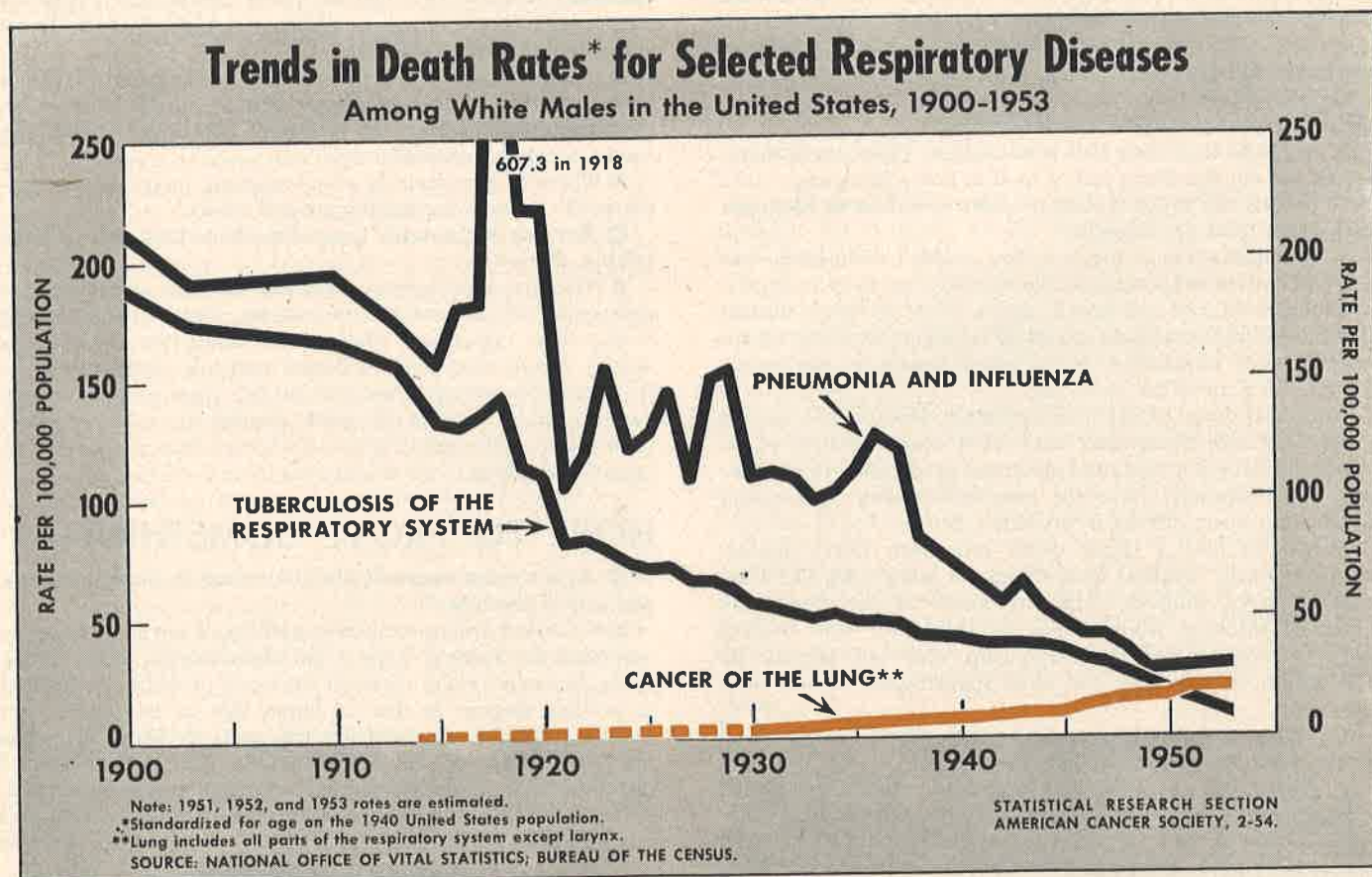
A In 1910 it was just above the zero mark on the graph, and has gone up to about 24.

Lung Cancer—22,000 Deaths a Year

Q Then lung cancer in relation to total diseases and total death rates is negligible, isn't it?

A In a sense, yes. But I wouldn't call 22,000 deaths a year negligible. Today lung cancer is somewhat more important as a cause of death, among white males, than tuberculosis, pneumonia or influenza.

Let's follow this step by step. Remember, you should have a look at the evidence from a great many different sources before drawing conclusions. Since we are talking about diseases of the lung, let us consider some of the things that people inhale. Time trends in some of them are shown on this graph. Asphalt roads produce dust that people inhale. Look how that's gone up. There has been about a fourfold increase in



... Another suspect: "Air pollution from auto fumes"

State asphalt roads since 1930. Likewise, there has been a tremendous increase in the use of motor fuel, fuel oil and cigarettes, as you can see by looking at the graph.

TAR, SOOT, DUST—HARMFUL?—

Q What ingredients do we find in each of these things you have on this chart? For instance, in the asphalt you say there are tar products—

A Asphalt dust has not been studied as much as some of the other things, but it is definitely one of the suspects. It is very likely that some of the tars, oils and asphalt used in road surfacing contain carcinogenic chemicals.

Q What about fuel oil?

A Fuel oil and soot from coal—well, soot from coal was the first thing ever discovered that produces cancer in man as well as in experimental animals. There's no question that soot can produce cancer.

Q Aren't there studies that show that people living around factories where a lot of soot comes out have more lung cancer than people in other areas?

A The trouble with such studies is that the American population moves too much and things change too much. It probably takes 20 years for a low concentration of something like coal soot to cause cancer in man, and these studies in America just don't mean much.

Q What do the English studies show?

A Those studies have just been started. There are higher death rates in places where they have a lot of factories—there's no question about that. But, again, it may be a spurious correlation.

Q What is the evidence on the soot?

A It was noted, many years ago in England, that there was a lot of cancer of the scrotum among chimney sweeps, whereas cancer of this part of the body is a rare disease in the general population. The scrotum tends to be moist, and that is perhaps the reason that it was affected by soot more than other parts of the body. It was rightly concluded that the soot caused the cancer.

Q It was because they were perspiring?

A Possibly. Chimney sweeps may also have had more skin cancer, but the actual observation was cancer of the scrotum. The reason it was noticed is that cancer of this part of the body was an extremely rare disease among other people. Then, following that, laboratory workers took soot from coal and oil and smeared it on the skin of animals and it produced cancer. Practically all we know about cancer-producing agents originated with that observation on chimney sweeps. That is why anybody ever worked with soot in the laboratory.

Later, chemists separated soot into a number of different chemical factors, and it was found that certain specific chemicals caused cancer when smeared on the skin of an animal.

Q What about the smog we hear about now?

A That is composed partly of coal tar and oil products, but also of other products from industrial plants.

Q Have you any evidence as to whether smog is producing cancer?

A Not direct evidence. But then, who's been exposed to heavy smog for 20 years? Look at the increase in motor vehicles as shown on the graph. Not only has the number of motor vehicles increased, but traffic has become more jammed up. About one milligram of a specific, known carcinogenic

agent is produced every minute that an automobile motor is idling.

Q If you have proven carcinogenic agents in cigarette smoke and also have them in what people breathe every day, how can you tell whether it is the cigarette smoke or the pollution in the air that is causing lung cancer?

A There would be no way of telling if all the information you had was what is shown on those two charts. In the absence of other information, you might very likely conclude that the inhalants have caused an increase in lung cancer, but have also caused an even greater decrease in death rates from pneumonia, influenza and pulmonary tuberculosis. Therefore, you must gather other pertinent information, as I have said before.

We know that treatment has lowered the death rates from the infectious diseases of the lung, although it is conceivable that smoking has played some part in the decline. At least this cannot be ruled out as a possibility without more evidence than we have at present. Laboratory evidence indicates that all of the inhalants named could possibly cause lung cancer. But the laboratory evidence in itself does not establish what actually occurred in the human population.

In the case of cigarettes, we have additional evidence from studies on the smoking habits of lung-cancer patients. We are now checking the validity of this evidence. If it turns out to be accurate, then there would be little doubt that cigarette smoking causes lung cancer. This does not rule out the possibility that other inhalants also produce lung cancer. Since air pollution from automobile fumes only became heavy in the last few years, the full effects may not become apparent until 10 to 20 years from now.

I mentioned the decline in death rates from the infectious diseases of the lung primarily to show how cautious one has to be in interpreting parallel trends. From about 1940 on we would have no difficulty explaining why the death rate from pneumonia has gone down. The antibiotics and sulpha drugs have had a great effect. In the period just back of that, we'd have said it was the serum treatments. The decline, however, started before the wonder drugs and serum came in. We have something to account for here.

Q You have something to account for, but you're not certain what?

A We are not certain that this whole trend for this length of time can be accounted for fully on the basis of more effective treatment—most of it, yes, but not necessarily all of it. For example, there may have been a change in the virulence of the disease-producing organisms. Conceivably smoking was a contributory factor, but more evidence would be needed before one could possibly draw the conclusion. This merely illustrates the difficulty in determining all the factors responsible for changing death rates from specific diseases.

CIGARETTE: PNEUMONIA FOE?—

Q Is there any laboratory evidence that cigarette smoking may be related to the decrease in death rates from pneumonia?

A Yes, some evidence. If you bubble the smoke from three cigarettes through a solution containing millions of the bacteria which cause Type I pneumonia, all of the bacteria are killed. This does not prove that the same thing would happen in the human lung. Nevertheless it is interesting and more work should be done on the subject.

(Continued on next page)

... "Lung cancer was a rare disease before 1920"

Q You spoke of poisonous agents—of toxic agents. Would an individual build up a tolerance to those over a period of years, or would they be cumulative and be more poisonous?

A As a generalization, the body builds up a tolerance for toxic agents, if administered in small doses over a long period of time. In some instances the opposite occurs. Cancer-producing agents tend to be cumulative in their effect.

Q Could the carbon particles in a cigarette cause cancer?

A No. My guess is that they would be protective. Carbon particles have the property of adsorbing various chemicals on their surface. You can make very effective gas masks that way. If there are a lot of toxic agents in tobacco smoke, a considerable portion of them may be adsorbed by the carbon particles and deactivated on that account. The carbon might neutralize, as it were, some of the harmful agents. However, there is not enough evidence to give a definite answer on this point.

Q If you prove that there is a definite relationship between tobacco and cancer, would it be likely that you would also be able to find the agent that causes it, and if you find it, can you remove it?

A I hope so. I'm not too optimistic. We have no idea what it is, and there is this possibility—it may not be a single specific chemical. There are a good many benign tumors in people's lungs, and also it seems likely that some lung cancers can go on for a great many years without causing death or serious difficulties. And if a person gets such a thing at the time he is, say, 60, he is apt to die of some other disease before the tumor causes trouble.

Perhaps the chronic irritation of smoking causes a dormant cancer to start growing. If this is the mechanism, then cigarettes probably could not be made safe. This is a pessimistic view. I hope that a substance will be found after the removal of which cigarettes will be safe.

Filters? "We Don't Yet Know"

Q How effective are filters in removing harmful materials from cigarette smoke?

A Nobody will be able to give a complete answer to that question until all the harmful materials in cigarette smoke are identified by chemists and tested on animals and human beings. Some filters remove a considerable proportion of the nicotine, and nicotine is probably quite harmful. Filters now in use probably do not remove carbon monoxide and it may be that this is the most harmful factor in tobacco smoke. Some filters remove a portion of the tar and perhaps they remove the cancer-causing fraction but this is by no means certain. Filters may or may not turn out to be the solution to our problem; we don't yet know.

Q Let's assume you had statistics which show that smokers get lung cancer in greater proportion than nonsmokers. Would you have figures to show how many of the parents of nonsmokers died of cancer, so that the factor of heredity could be taken into account?

A Well, if you are talking about lung cancer specifically rather than cancer in general, then it is practically certain that not many of the parents could have had lung cancer in either group, because lung cancer was a rare disease before about 1920.

Q Yes, but again, if we assume that there were cases of cancer, would your figures show the hereditary cancers among those smokers and nonsmokers?

A Well, now, I would be extraordinarily surprised if there is only one factor operating. I think it much more likely that

there is a combination of factors, and that susceptibility varies. Not everybody that smokes heavily gets lung cancer, remember. And, for that matter, not everybody who is exposed to contagious diseases gets those diseases. There are differences in susceptibility. I think heredity undoubtedly is important, but it is not that easy to get the answer on it.

Q Are you giving weight to the fact that there are other things in a cigarette besides tobacco?

A Well, to my mind the first question to answer is, what does the cigarette, as now made, do? The cancer-causing factor could perhaps be something in the paper, or it may be the arsenic sprays that are used on tobacco, or it may come from tobacco itself. We are trying to find that. Work is now going on at New York University, in which they are fractionating the material condensed from tobacco smoke, and trying to determine which fraction causes cancer when applied to the skin of a mouse. I understand that they hope to have the answer in a year or two from now. I certainly hope that they succeed.

HOW X RAYS CAN HELP—

Q How would it be if people got X-rayed in the mobile units that test for tuberculosis—would X rays show up lung cancer?

A They usually do, but not invariably.

Q What can you do when signs of cancer do show up?

A Operate.

Q Operate for what?

A Operate to remove the lung that has the cancer. An early cancer of the lung is quite curable. However, the difficulty is that it is seldom found early. Until we find a way to prevent lung cancer, we are doing the best we can to get earlier diagnosis through X-ray screening, and persuading people to see their doctor as soon as they have symptoms, so they will have the best possible chance of being cured.

Q Do you think that smokers should have X rays oftener than nonsmokers?

A That's a leading question if there ever was one. My answer is yes. So long as there is even a strong suspicion that smoking causes lung cancer, a heavy smoker is very foolish if he does not have a chest X ray taken twice a year.

But everybody should get them—smoker or nonsmoker. You should have an X ray at least once a year, if you are over 45, or particularly if you are over 50. If you are a timid soul, then you should also give up smoking at least until the facts are known.

Q Is it conceivable that persons who live in the city and who inhale soot of various kinds and are heavy smokers are more likely to die of cancer than those who live in the country and are heavy smokers?

A I think it is more likely than not. Soot and fumes in addition to cigarette smoke would probably have more effect than either one alone.

Q In other words, a factor might be added in the city? For instance, if you had the same statistics for heavy smokers, it might show different results?

A Yes, it is quite possible that no one of the three things—smoking, automobile fumes or soot—alone has a sufficient quantity of carcinogenic agents to produce lung cancer, but all of them added together might be sufficient to cause lung cancer. Even so, one of these factors might be far more important than the others.

... "We can't do anything about heredity—only environment"

Q In other words, you would have to, for statistical purposes, go out on a farm, find some of these farmers that never leave the farm, and never ride a tractor, and never get any carbon-monoxide fumes, and never get any soot, and yet heavy smokers, and compare them with heavy smokers somewhere else in order to get an answer?

A That is what we will have to do.

Q You will have that?

A Practically speaking, yes. Statistically we will have it, though we don't have the whole life history of the people we are studying. In America people move around so much that if you question them they will tell you—

Q Then it is an oversimplification to say that results among heavy smokers show one thing, and among non-smokers show something different?

A You have to analyze the evidence in detail.

Q And you have to take all the surrounding factors into consideration?

A Yes, in so far as possible. I think you will agree with this: Let us say that two things must be present in order to produce lung cancer, and let us say those two things are an inherited susceptibility and very heavy cigarette smoking over a long period of time. Now if you eliminate either one of these, either the inherited susceptibility or the exposure to tobacco, then you wouldn't get lung cancer. But we can't do anything about heredity—the only thing we can control is the environment. So, although you could say on a technical basis that

it wasn't smoking alone that caused it, from a practical standpoint you would say that cigarette smoking caused it.

Now suppose that you have to have exposure to fumes from an automobile, plus cigarettes, plus coal soot in order to get lung cancer—in that event, removing any one of these factors would solve the problem. Or maybe smoking four packs of cigarettes a day, without exposure to automobile fumes would be the same as smoking one pack of cigarettes plus exposure to automobile fumes. Some people seem to think this is a simple problem to answer. They look at it in terms of a very simple cause-and-effect relationship, with only one factor involved.

I am afraid we have a multiplicity of causes, and the question is: Is there one cause so much more important than the rest of them that removing that one will practically solve the problem? That's the thing we have to find out.

Q Do you think your studies will show that there is one big cause, or will they show that there is a multiplicity?

A If smoking is the principal factor in the causation of lung cancer, our study will certainly show it. We do not know yet.

People ask us if we are making progress. How do we know? For example, if it turns out that smoking causes lung cancer, then our present activities may be called "making progress." But if the results are negative, then it will be said that it was another false lead we tried. You can't tell whether you are making progress until you get the final answer. In other words, you can only tell in retrospect.

What Britons Are Told About Smoking

Here's what Britain's Minister of Health, Iain Macleod, told the House of Commons on Feb. 12, 1954, when asked about the relationship between smoking and lung cancer:

Mr. Iain Macleod: The Standing Advisory Committee on Cancer and Radiotherapy have had this matter under consideration for three years. As a result of preliminary investigations, a panel under the chairmanship of the Government Actuary was set up in 1953 to inquire and report. I have now been advised by the Committee in the following terms:

"Having considered the report of the panel under the chairmanship of the Government Actuary on the statistical evidence of an association between smoking and cancer of the lung, and having reviewed the other evidence available to them, the Committee are of opinion:—

"(1) It must be regarded as established that there is a relationship between smoking and cancer of the lung.

"(2) Though there is a strong presumption that the relationship is casual, there is evidence that the relationship is not a simple one, since:—

"(a) the evidence in support of the presence in tobacco smoke of a carcinogenic agent causing cancer of the lung is not yet certain;

"(b) the statistical evidence indicates that it is unlikely that the increase in the incidence of cancer of the lung is due entirely to increases in smoking;

"(c) the difference in incidence between urban and rural areas and between different towns, suggests that other factors may be operating, e.g., atmospheric pollution, occupational risks.

"(3) Although no immediate dramatic fall in death rates could be expected if smoking ceased, since the development of lung cancer may be the result of factors operating over many years, and although no reliable quantitative estimates can be made of the effect of smoking on the incidence of cancer of the lung, it is

desirable that young people should be warned of the risks apparently attendant on excessive smoking. It would appear that the risk increases with the amount smoked, particularly of cigarettes."

I accept the Committee's view that the statistical evidence points to smoking as a factor in lung cancer, but I would draw attention to the fact that there is so far no firm evidence of the way in which smoking may cause lung cancer or of the extent to which it does so. Research into the causes of lung cancer has been pressed forward by the Government and by other agencies in view of the increase in the incidence of this disease and we must look to the results of its vigorous pursuit to determine future action.

I should also tell the House that before these recommendations were considered by Her Majesty's Government the tobacco companies had offered to give £250,000 [\$700,000] for research. They have, on my advice, agreed to offer this money to the Medical Research Council.