

FILE NAME: Saranac 7th Symposium (SSY)

DATE: 1952

DOC#: SSY021

DOCUMENT DESCRIPTION: Transcript of Presentation by Dr. Merewether
with Discussion

TAKEN FROM PAGE 396.

PHENOCOSIS AND PULMONARY CANCER (Continued) 2:30 to 5:30 P. M.

Chromate Workers

Anthony J. Lanza, M. D.

Discussion

Experimental Pulmonary Cancer - General Review

G. Ransburgh Elder, M. D.

Discussion

Pulmonary Cancer in Experimental Exposures to Chromate

Anna Eastler, Sc.D.

Discussion

Pulmonary Cancer in Experimental Exposures to Beryllium

Arthur J. Vorwald, M. D.

Discussion

BY DOCTOR RHOADS:

Will the meeting please come to order? You will remember that we were forced by the delay starting this morning, to put over Doctor Merewether's paper to the first one on the program this afternoon. It is, therefore, my honor to introduce E. R. A. Merewether, Senior Medical Inspector of Factories, Administrator of Labor and Allied Service, London, England. Doctor Merewether.

BY DOCTOR MEREWETHER:

Doctor Rhoads, Ladies and Gentlemen: I am greatly honored to be invited to attend this erudite meeting which has now, by virtue of the diverse and inspired work of my old friend, the late Doctor LeRoy Gardner, and Doctor Vorwald, become an international event.

Now, only a foolhardy criminal would speak after the most stimulating papers of this morning, but I'll endeavor to do my best, and I shall not detain you long.

All I have been able to do in the short time available is to bring up to date our mortality and pathological data on this matter and lay them before you in the confident hope that if there is an explanation of them, and there are deductions to be drawn from them, I shall obtain them during this conference.

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Frankly, I'm puzzled and disturbed at the possibility which may emerge, not only in connection with the

question of an etiological relationship between cancer of the lung and asbestos, but also between cancer of the lung and other local illness.

In 1948, I made a note of the deaths from asbestosis, asbestosis with tuberculosis and either of these with also cancer of the lung, recorded in the United Kingdom from 1924 to 1947. I placed alongside them for comparison, the corresponding data we have from silicosis and cancer of the lung. These were factual data which speak for themselves insofar as they go, but I attempted to make deductions since I felt the asbestosis deaths were too few for the purpose. I have now brought these figures up to date.

The corresponding figures for silicosis deaths amount to several thousands. They were, I think, sufficiently large to show that there is no etiological relationship between silicosis and cancer of the lung and in this I'm fortified by the data produced by the South African experts. I will not weary you, therefore, with the additions in the last three and a quarter years to our silicosis figures.

Briefly, therefore, our latest figures are recorded deaths from asbestosis, asbestosis with tuberculosis, or either complicated with cancer of the lung, with cancer, are 306. I am excluding ten of these where there is also cancer of sites other than the lungs. Our net figures are,

therefore, 296 deaths and of these forty-eight or 16.2 percent were associated with cancer of the lung. This shows an increase from a 13.2 percent disclosed by our earlier figures. This means that, as more deaths from asbestosis come to hand, the cumulative percentage of deaths with complicating cancer of the lung is rising rather than falling.

Now, where do we go to from here? Are these figures sufficient to indicate a causal relationship between the retention of asbestos dust in the lungs and subsequent cancer of the lung? The small numbers certainly dictate caution. Nevertheless, they represent the great majority of the deaths from asbestosis which have occurred in the United Kingdom during the past quarter of a century.

Nowadays, because of the greatly increased awareness of workers, doctors and others in the neighborhood of asbestos plants, of the disease, because of the duty of Coroners to investigate with autopsy and to report to my department, deaths suspected to be due to occupational disease, whatever it may be, the compensation benefits accruing to cases of pneumoconiosis, the system of factory inspection, our periodical check-up of the death certificates provided by the Registrar General, and for other reasons, it is likely that very few deaths from asbestosis escape notice.

Therefore, with confidence, I think we can say that the figures point to the necessity for the collection of similar data from other communities with an asbestosis hazard, so that by means of statistical examination of the global figures so obtained, we can settle the question of whether cancer of the lung is an additional risk of asbestos exposures.

Now, I should mention here that the figures in United Kingdom, that these figures include all of them, because they come to me, so that we must not add up excess figures and - the X figures and Y figures and Z figures, and think that they're all additional cases of asbestosis, with carcinoma of the lung. One can add up, of course, different countries, but one must be very careful adding up or duplicating the same cases in the same countries.

There is another point that was brought up this morning, that the population risk of asbestos is small relatively to other industries and it fluctuates. A war brings a great increase of people, because obviously, there is a great demand for high class asbestos insulation for use in war ships and other types of work, and then it drops off again, so that one could never really get a population, for instance, to which one could relate a particular case of asbestosis, assuming that asbestos is a factor in this matter.

Now, another thing is the reverse which I think has got to be brought in mind, into mind, that when one is considering a hazard in an industry and one wants, as the statisticians always do want, something like a world population before they give us anything very satisfactory about the matter, that you - you say that, for all purposes, the population of an industry is say two hundred thousand, your very risk may be lost in the mass of the population.

That occurs, for instance, in coal carbon trade, where I tried a number of years ago, a relatively small portion of people exposed to tar or tarry vapors, and they're lost in the whole population of the trade, but when you limit them to the people who are exposed to tar and tarry vapors, you find there is six times the risk of cutaneous cancer. In other words, the risk was lost in the overall numbers assumed to be at risk.

And, it is something like that in the asbestos trade. A lot of people don't have much exposure to asbestos at all. Now, as far as the rate in asbestos, I haven't got into that yet, but following a remark made this morning, I will try and do so.

Then Doctor Lynch did say, what is the degree of asbestosis. Now, all these people have been autopsied and all of them died primarily of asbestosis, whether they had tubercle or cancer later.

Doctor Oppenheimer, has - who has done some experimental work with cellophane wrapped around hinges, which may be a pointer to this factor if it is material. Thank you.

BY DOCTOR RHODES:

Thank you, Doctor Merewether. Is there a comment about the Merewether discussion? (No response).

Doctor Lanza, I think you can make some comment on this.

BY DOCTOR LANZA:

Mr. Chairman, Ladies and Gentlemen, before going into this brief statement of mine on chromates, I would like to make a few comments on Doctor Merewether's observations.

I was very much impressed with what Doctor Merewether said, and there is no question but what a very careful, painstaking job has been done in Great Britain on the subject of trying to determine what the hazard might be in the asbestos industry with respect to cancer.

There are just a couple of comments, I'm not saying one way or the other, that it may or may not influence the incidence of cancer. I would raise a couple of points which I think all of us might keep in mind, and which might possibly have some bearing on the situation in England.

Now, I have visited, somewhat extensively, I think, nearly all the asbestos plants of the United States, and the mines and the mills in Canada and have spent quite a lot of

time there, and have spent a lot of time reviewing films, and not long ago, spent several days with Doctor Kenneth Smith on asbestos, reading his films.

I find it difficult to believe that our cancer incidence among asbestos workers could be anything like as large as it seems to be in England, because while I'm perfectly free to admit that we may have missed cancer cases which we should have not, on the other hand, I don't think we could have missed all of them if they had occurred, into the same extent that apparently they do in England.

Now, that is simply an observation of mine. Of course, it is true that as soon as the business of the harmful effects of asbestos once took hold in the American industry, they did start to clean up their plants and, while I wouldn't say that all the asbestos plants in the country were marvels of industrial hygiene perfection, nevertheless great strides have been made, and particularly, for instance, in the plant in Doctor Kenneth Lynch's town in Charlotte, South Carolina, where they have done a very beautiful job, so that with the small number of people in the industry, it's obvious that we are never going to have the clinical experience with asbestosis that we have, for instance, with silicosis, because there is not going to be the material to work on.

Now, back of that, there is still one more question.

That is the nature of the asbestos itself. Now, when I first used to go to Canada, I used to hear frequently that, up there, that the Canadian asbestos was less damaging than the kind they used in England, I believe, and I have put that comment down to what we might call the national or local patriotism, you know, like the rivalry between towns, so that you so frequently see, but the fact remains the same, that in this country, we do use the asbestos, mostly the asbestos that we get from Canada, and I believe, from what I hear from our English friends, that a great deal, if not the major part of the asbestos used in England, is Rhodesian asbestos, which is quite dissimilar in its construction and in its formation, its physical characteristics, to the kind that comes from Thetford and from asbestos in Canada.

Now, that may have nothing to do with it, and up until two or three years ago, I dismissed that. I thought that was just purile, but since we have in the last few years, learned that different types of silica, for instance, produce entirely distinct pathological effect, I am beginning to wonder if we have not failed to pay sufficient attention to the type of asbestos which varies even, as I am informed, there is a difference between the asbestos that is mined in the town of Asbestos and the kind that is mined not far away in Thetford, and yet both of these, in turn,

are quite different from the asbestos that come from Rhodesia, and possibly from other parts of the world with which I'm not acquainted.

And, having in mind the lesson we've learned in the silica dust, I think that is something perhaps that we should pay more attention to. Now, I simply raise that point, because I think it may have a great deal more significance than we have been inclined to give it.

Now, I have summarized - I have summarized my remarks here very briefly, because the topic of chrome is going to be handled by Doctor Anna Bastjer, who has done the experimental work in chrome, and has a more intimate knowledge of it from that point of view than I do.

The available evidence is that chromate workers do have an incidence of cancer of the lungs in excess of what might be expected. Beyond this, we do not as yet know a great deal.

Interest in chrome as a possible carcinogenic agent, with particular respect to lung cancer, is comparatively recent. The officials of one of the largest chrome producing companies in this country supplied the impetus that started interest in this subject in the United States, their apprehensions to tangible form, in setting on foot the statistical survey conducted by Machle and Gregorius, and published in the Public Health Reports on August 27th, 1948.

Efforts were made to reduce exposure in chromium plants and more intensive medical service was inaugurated with a much more free use of X-ray examination, as I venture Doctor Baetjer will tell you of her work in Baltimore with experimental animals.

Now, Doctor Baetjer published a comprehensive paper on pulmonary carcinoma in chromate workers in the Archives of Industrial History in 1950, and up to now, there is not much more to say that was not said in her paper. In a word, as the saying goes, she covered the subject 'from soup to nuts' and as far as our question stated along that line, goes.

Now, fortunately, during 1952, the Division of Occupational Health of the United States Public Health Service, with the assistance and cooperation of the industry, conducted a survey of the whole chrome industry. Through the courtesy of Doctor Edward E. Miller, in charge of the Division of Occupational Health, I have been given a copy of the medical portion of their admirable report. Doctor Miller was kind enough to make that available to me when I asked him if he was going to present his findings here and he said no.

The report, however, is in the press now, and as it will be presently available, I will only refer to it in a very brief summary. I quote from the Public Health

Service Report: All specific causes of mortality in chrome workers, the chrome workers had frequency rates that were not greatly different from other workers. However, cancer with a rate of 7.1 compared with .7 stands out as markedly in excess for chromate workers. For cancer of all sites, the actual number of deaths of chromate workers was approximately four and a half times the number that would have been expected had the cancer rate for all males in the United States prevailed. When cancer of the respiratory system was observed separately for chromate workers, nearly twenty-nine times as many deaths as were expected were found. All other types of cancer failed to show an excess among chromate workers.

It is obvious -- that's the end of the quote -- it is obvious that much research and experimentation remain to be done before we can talk with more assurance of this situation. In the meantime, the industrial plants are being cleaned up and in some cases re-built with the hope and expectation of steadying this tide of cancer cases.

Before leaving this topic, I again would like to make a plea for the more careful and precise use and association of words. The evidence of the relationship of chrome exposure and pulmonary cancer appears conclusive. This cancer of the lungs in chrome workers does not follow, as far as I can ascertain, does not follow, nor is it dependent

upon a pre-existing pneumoconiosis. I mention this so that there may not be any false conclusions drawn from the association of these two terms as they are used in heading up our program. Thank you.

BY DOCTOR RHOADS:

With very characteristic precision, Doctor Lanza has laid to rest any illusions or questions that might be raised concerning the relation of chrome to pulmonary cancer. Is there a comment on Doctor Lanza's presentation?

BY DOCTOR RICHARDSON:

Who were the workers that were effected in this?

BY DOCTOR LANZA:

As far as I know now, I can't tell you positively until I have had a chance to digest the Public Health Service report, but you know these are small plants and in small plants, men shift around, so that not only do we not know what particular chrome substance or what particular process in the manufacture of chrome is responsible, if it is a cancer, but we do not know or you can't depend on this group of men in this department or that group of men in that department, unfortunately, we can't do it.

BY DOCTOR RICHARDS:

Well, could we say when does the exposure to chrome begin and when does it end in the process of the handling of chrome?

BY DOCTOR LANZA:

Well, you would have to then. We had, I think, the engineering portion of the Public Health Service report, which will give the details of the process, the dust studies, and so forth, at different stages all along the line, from the time they get their ore out until it is shipped out of the plant.

BY DOCTOR RICHARDS:

Well, then, is there any hazard after it is shipped out of the plant?

BY DOCTOR LANZA:

As far as I know, there has been no complaint from any source, but that again is something we don't know.

BY DOCTOR RHOADS:

Doctor Hueper has comment.

BY DOCTOR HUEPER:

You asked the question whether the material shipped out of the plant will become carcinogenic. There have been reports from Germany that zinc pigment workers have developed carcinoma. The zinc chromate, the yellow dye with which we spray our airplanes and with which we spray the oil tanks and oil pipe lines, if you see those beautiful bright yellow colors in the landscape of our refineries, that's zinc chromate. We are quite a bit interested to find out whether the painters who sprayed the zinc

chromate on our airplanes during the last war have increased cancer incidence. We don't know that. They can't be traced, but it seems to be.

BY DOCTOR VICKERS:

In regard to the previous question, I might say that in the chrome industry, workers are exposed to chromate in one way or another all the way through the plant. Some of your workers are exposed to chromium, and some to hexavalent all through the operation.

BY DOCTOR BROAD:

You can't pin down any particular step or form of chromium?

BY DOCTOR VICKERS:

No, some workers will have exposure to chrome in some form or other, but there are mixed exposures in one form or another and definitely to chromium all the way through.

BY DOCTOR BROAD:

Would you care to comment on the zinc chromate observation, Doctor Vickers?

BY DOCTOR VICKERS:

No.

BY DOCTOR BROAD:

Is there further comment? Doctor Baetjer?

BY DOCTOR BAETJER:

In the literature, there have been reported,

already in the literature, a hundred and thirty-four cases that are already on record. Of that number of cases of lung cancer, there were a hundred and twenty-one of those are in the chromate producing industry; ten are in the chrome pigment industry, that is where they are manufacturing the zinc chromate pigments, and the varying, the lead chromate pigments, and only two have I been able to find reported in the literature, among people who use chromium.

We had one case in Baltimore in a chrome plater, but he was also exposed to many other substances, and there is one reported in the literature who sprayed chromium or sprayed with chromium paint. Whether it was spray painting or not was not stated. So that, altogether, of the one hundred and thirty-four cases, there are a hundred and thirty-two or thereabouts that are in the chrome producing or chrome pigment producing industry, and only two, so far, in the chrome users.

There are a few other points, if I may add a few points to this, if Doctor Lanza will forgive me for adding onto his paper. I don't know whether he got over the point to you that we have never had, interestingly enough, any cancer of the skin in chromate workers, nor have we ever had any cancer of the nasal septum, even though a large percentage of these workers have perforation of the nasal septum.

There are some figures that might interest you concerning the duration of the exposure of these people until they get cancer. May I show one slide? This might interest you to show the distribution of these cases by length of exposure. If you just focus your attention, because we don't have much time, on this column and the range, you will see that the average age is fifty-two years, and the range was from thirty-one to seventy-two of these cases that have been reported in the literature.

The duration of exposure is the interesting thing here, and it varies from four to forty-seven years. These men have been exposed to chromium, before they developed their cancer. The interval between initial exposure and the diagnosis of cancer was approximately the same, because once it is - about seventeen, and the range is four to forty-seven.

Then between the end of exposure and the diagnosis of cancer is also interesting. It shows that in some cases, the cancer may develop many years after the end of the exposure. The interval between diagnosis and death is, as in all cases of lung cancer, an average of a very short period of time.

Many of these cases which we have had and which we have studied, have come to our dispensary claiming that their symptoms, their severe symptoms, didn't begin until

two weeks before they came to the clinic, and they could then be diagnosed as having lung cancer. The clinical symptoms and the pathology are no different in the chromate workers, as far as we have been able to determine, than in lung cancer of other origins. I think those are the principal points.

BY DOCTOR READE:

That raises the question, Doctor Baetjer, of asymptomatic or cancer which simply means no symptoms referable to the lungs. What brought these patients to the clinic, symptoms to the lung?

BY DOCTOR BAETJER:

No, some came with lung symptoms, pain in the chest. Some of the patients I have read, came with symptoms referable to the metastases.

BY DOCTOR READE:

Is there further comment on this?

BY DOCTOR SMITH:

Doctor Lanza, again commented on Doctor Herowether's discussion, asbestosis, and then went on to the chromate situation. I wonder if I may call for a little more discussion of the asbestosis problem.

At the end of the morning session, a question was brought up as to association of lung cancer with the degree of asbestosis. Shortly before Doctor Glynn's death, I had

two weeks before they came to the clinic, and they could then be diagnosed as having lung cancer. The clinical symptoms and the pathology are no different in the chromate workers, as far as we have been able to determine, than in lung cancer of other origins. I think these are the principal points.

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BY DOCTOR RHOADS:

Is there further comment on this?

BY DOCTOR SMITH:

~~Doctor Baetjer, I am interested in the question of the association of lung cancer with the degree of asbestosis. I have read that some of the patients who have been operated on for lung cancer have been found to have a little more asbestosis than the average. I am interested in the question of the association of lung cancer with the degree of asbestosis.~~

At the end of the morning session, a question was brought up as to association of lung cancer with the degree of asbestosis. Shortly before Doctor ^{Gray's} death, I had

an opportunity to visit him and learn something of the material that he had assembled. He had seventeen cases in which there had been co-existent carcinoma and asbestosis in the lungs. In his series, there was no relation that could be detected between the degree of asbestosis and the presence or absence of cancer, or the degree of asbestosis and fight of cancer.

Now, his series came from a plant that used the Rhodesian blue asbestos which, as Doctor Lanza has pointed out, has certain characteristics that are different from the Canadian asbestos. It's a more brittle fiber and, therefore, gives rise to more dust. However, it was my understanding that some of the cases described in Great Britain, had had exposure to the Canadian white asbestos.

I wonder if any of our colleagues from overseas who are in the room, might care to comment on that?

I would like also, to make one further point in connection with a matter that both Doctor Devan and Doctor Rhoads brought out, and that is the experiment of nature, where one may vary circumstances and see if that has anything to do with a phenomenon that has been observed. The question of exposure to nickel, which was brought up this morning, is something that I have been asked about by several individuals over the lunch hour.

I recently had an opportunity to visit with Doctor

an opportunity to visit him and learn something of the material that he had assembled. He had seventeen cases in which there had been co-existent carcinoma and asbestosis in the lungs. In his series, there was no relation that could be detected between the degree of asbestosis and the presence or absence of cancer, ~~which suggests that asbestosis is a pre-neoplastic condition.~~

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~~I would like also to raise the further question of connection with asbestos that both Doctor Brown and Doctor Lanza brought out, and that is the experiment of Wilson, where under very, very circumstances and results that has anything to do with the phenomenon that has been observed. The question of exposure to nickel, which was brought up this evening, is something that I have been asked about by several individuals over the lunch hour.~~

I recently had an opportunity to visit with Doctor

Amore who was formerly medical officer for the plant in Wales where these nasal sinus tumors had been observed, and I also visited Doctor Morgan who is the Medical Officer there at the present time.

They both stated that the man who has developed the nasal sinus tumors were not men who had been employed in the part of the plant where there might be exposure to nickel carbonyl, and they were, for that reason, very reluctant to believe that the nickel carbonyl was a factor in the nasal sinus tumors that had been observed.

They further pointed out that the tumors that had occurred were in men who have been exposed to the calciners, that is the ores with the - that since 1924, when the calciners were redesigned, they have not seen cancer of the nasal sinus in men whose employment in the industry has taken place only subsequent to 1924, so that it would seem that there is an instance which fulfills the stipulations that were raised this morning as to whether an experiment of nature might be performed which would have bearing on the question of an occupational hazard in the way of a respiratory tract carcinoma.

BY DOCTOR RHOADE:

Doctor Merewether, would you comment on these remarks?

BY DOCTOR MEREWETHER:

I couldn't comment on some of them, but I think I can partially answer some of these, sir, and I think Doctor Knox can answer conclusively one of them.

First of all, I think Doctor Lanza is misinformed about the proportions of asbestos used and where they are used in England. The original cases of asbestosis, fifty years ago, were all Canadian asbestos. The earliest asbestos work in England was either seventy-eight or eighty-two and there may have been some crystalline fiber then, but very quickly the asbestos trade concentrated on the white Canadian crystalline.

Later on, the Rhodesian asbestos and the Rhodesian - the South African blue, and the third one which is also an iron silica, the amacite, came in. Now, of all of these, the amacite is definitely the most brittle. It has short fibers, it's brown and it's got fibers as long as that (indicating) whereas the best Canadian spinning fibers have only got fibers as long as that (indicating) and the best blue is about that.

Well, there is no doubt about the dustiness of the amacite. That is the brown long fibered stuff, to such an extent that it's very little used today, so it's at the period where some of these cases are concerned, or where the cases of asbestosis occurred - some of my old friend Glynn's cases occurred - there was a good deal of blue and

a good deal of amacite used.

Now, I think Doctor Knox will be able to tell us, in his plant, which is the biggest in the country, what about the types of asbestos they use in that particular factory, and the - whether they have had any carcinoma of the lung.

Now, about the nickel cancer, it is perfectly correct that none of us think that nickel carbon has anything to do with it as such for the very simple reason that - well, one reason is that nickel carbon is so toxic that we should build a factory in order to get the - in order to get the little cancer, and of course, it might act in that proportion, then I should imagine a lot more people would have been effected.

Doctor Amore or Doctor Morgan and myself feel that the - that the re-building of the old calciners was the crucial change in the matter, though there was some operation in the constitution of the materials which are shipped from Fort Home in Canada. The difference, as I know, because I saw it before and afterwards, between the old and extremely dusty calciners and the modern build, is enormous. Therefore, there may be some hope in the fact that perhaps a lot of big dosage is necessary to produce some of these cancers.

BY DOCTOR RADS:

Id Doctor Knox here? Do you care to comment on these remarks? (No response). Apparently not.

BY DOCTOR MEREWETHER:

Well, I can finish it if he won't.

BY DOCTOR RHODES:

Why don't you?

BY DOCTOR MEREWETHER:

Because all of my information on this is derived from him; he's unduly modest. The fact is that it's mainly crysolites used in that factory. I don't think they use any blue at all, and they've had a number of cases of cancer of the lung as one might expect. Of course, not all cases of cancer of the lung, even if it is due or associated with asbestosis, must be included in the list that we have, because there must have been an ordinary occurrence of cancer of the lung quite irrespective of any factor of asbestos.

BY DOCTOR LEVIN:

It just happens that I talked with Doctor Knox about his data at lunch, and he showed me the data which he has. That's the occurrence of cancer of the lung at his plant.

Now, from 1932 to 1951, they have had exactly sixteen cases of lung cancer. Unfortunately, Doctor Knox did not as yet have the information which would enable either him or anyone else to say whether that was an excessive

number of cases. That's the kind of statistics, which we presented to statisticians, that makes them wish that they did have a psychiatrist.

BY DOCTOR RHOADS:

Very proper statement, I'm sure. Is there further comment on our questions of chromate or nickel?

(No response).

We have dismissed these conclusive topics. We will proceed to the paper by G. Burroughs Mider, Director of Cancer Research, National Cancer Institute. Doctor Mider - on Experimental Pulmonary Cancer.

BY DOCTOR MIDER:

(Doctor Mider read a prepared paper, which is on file with the Saranac Laboratory).

BY DOCTOR RHOADS:

Certainly a very comprehensive dissertation on this subject. It's most unfortunate to suspend these experiments at this stage of medical science. I am most interested to hear advocated the correlation of clinical observation and epidemiological studies. May I ask you the reference to the serial work, which is new to me, I think others might be interested in that since it hasn't appeared yet.

BY DOCTOR MIDER:

It has appeared in Lithgow & Finkel, Observations

on Lung Pathology Following the Inhalation of Radioactive
^{Cesium}
Serials, Abstract of Federation Proceedings, Page 360, 1949.

BY DOCTOR RHOADS:

Thank you very much indeed. I know many would be interested in this reference. I might also point out again in defense of the tobacco studies, that there has been some increase in cancer among women. Furthermore, much of the known cancer of women, may be adino-carcinoma, compared to carcinogenic.

Now, you're used to the term alleged increase, in man as not seriously meant. Do we not agree that the increase is real?

BY DOCTOR MIDER:

I think you and I can, Doctor Rhoads; I think Doctor Levin will join us, but there are still some die-hards who will not.

BY DOCTOR RHOADS:

This very interesting paper is open for discussion now.

BY DOCTOR FREDERMAN:

I would like to ask Doctor Mider a question. You referred to the effect of coal dust on the incidence of cancer and you made the statement, I believe, that you did not think it had any effect, particular effect, upon the incidence of cancer. Now, we have seen -- or something to

that effect. Will you re-state - will you re-state your remark on that, Doctor Mider?

BY DOCTOR MIDER:

I don't know if I can; all I said was that the mere - or what I meant to say was that the mere presence of large quantities of coal dust in the lungs of miners over the years has apparently not been associated with any considerable frequency of pulmonary cancer.

BY DOCTOR FRIEDMAN:

That's the point. Well, now, I wanted to ask you a question. Do you know whether or not it actually has established the inhibition or has prevented the incidence of cancer in these individuals, because in our own group, we have been impressed with the fact that we have seen very few cases of pulmonary carcinoma in coal miners, and with respect to the incidence of the disease in the rest of our hospital population.

BY DOCTOR MIDER:

Well, come to think of it, I think Doctor Pinkes's experiments will bear out that contention, though I have no opinion on it myself.

BY DOCTOR REARDS:

Can you give us your figures on that?

BY DOCTOR FRIEDMAN:

Out of three thousand cases, we have only had five

cases of carcinoma and I just sent one case to Doctor Vorwald that we're not even sure is carcinoma.

BY DOCTOR VORWALD:

And I'm sorry to say Doctor Vorwald hasn't examined the sections yet so I can't comment.

BY DOCTOR FRIEDMAN:

It's not likely that we're missing it, because we do extensive diagnostic studies and, in view of your comment, I thought perhaps you might have some other information on the studies.

BY DOCTOR RHOADS:

I think some of this might be clarified further; three thousand cases of what?

BY DOCTOR FRIEDMAN:

Three thousand cases of coal miners pneumoconiosis.

BY DOCTOR RHOADS:

In Wales?

BY DOCTOR FRIEDMAN:

No, in Alabama; I thought you said Mayo Clinic, in Mayo, and we only have either four or five cases.

BY DOCTOR LYNCH:

That's clinically, Doctor?

BY DOCTOR FRIEDMAN:

Pathological diagnosis, and a fifth case is in debate; we're not sure it's a carcinoma or not, because

Doctor Vorwald is one of those to express an opinion.

BY DOCTOR RHOADS:

Then if I may summarize, in three thousand autopsied individuals ...

BY DOCTOR FRIEDMAN:

No, three thousand clinical cases, those in which we have been able to establish a definite diagnosis of carcinoma of the lung, we have only been able to prove it in surgery, and the autopsy table in four or five cases.

UNIDENTIFIED SPEAKER:

Do most of your miners chew or smoke?

BY DOCTOR FRIEDMAN:

They do everything. Well, they smoke an awful lot when they come off the job; they chew; they smoke; they drink, they eat all sorts of food.

UNIDENTIFIED SPEAKER:

Do they smoke as much?

BY DOCTOR FRIEDMAN:

Well, we ask in our social history, we ask the amount of cigarette smoking they do or cigar smoking or tobacco, whatever type of tobacco they use, and I believe it would be safe to say that the average coal miner would smoke between three quarters and one and a quarter packs of cigarettes a day.

BY DOCTOR RHOADS:

Doctor Mider has a comment on these interesting remarks.

BY DOCTOR MIDER:

In what age group did these three thousand individuals fall, did you say?

BY DOCTOR FRIEDMAN:

You're asking me a lot of questions and I haven't prepared statistics on it, but they run - the oldest coal miner whom I took care of, I think, is eighty-six years of age and the youngest one whom I've taken care of as a coal miner is around twenty-four or twenty-five, so you see I have not - I have not taken the statistical analysis, but that's roughly the spread.

BY DOCTOR MIDER:

This brings up the subject that has been brought up before today and that is an adequate frame of reference for judging the incidence of cancer in a population, whether it is excessive, lower than normal or higher than normal. Certainly, we have not had adequate standards of reference in the past. Can you bear me back there?

We have not had adequate standards of reference in the past. In the United States at least, autopsy statistics cover a relatively small proportion of decedents. The use of mortality statistics imply that cancer is not curable. Well, that may be debatable. Cancer now is

reportable by law or by regulation in twenty-eight of these United States and the district of Columbia, and Alaska.

BY DOCTOR RHOADS:

After death?

BY DOCTOR MIDER:

No, cancer. It would seem practical then to derive tables of incidences of anatomical types of malignant neoplasms in relation to both age and sex for the principal types we're interested in and from these calculate the expected occurrence of cancer of these various types in sizeable populations in which we are interested.

Now, the method for that was devised by Gurtis and, to the best of my knowledge, it was first published of all places in the American Journal of Obstetrics and Gynecology, in 1946. The New York State Department of Health, through its Bureau of Cancer Control, I think largely due to the efforts of Doctor Levin, has made such tables for the year 1945 to the year 1947. I wonder if he would like to comment on this type of standard of reference which might improve our criteria for saying that this occupational or this environmental group has or has not an increased incidence in cancer.

BY DOCTOR RHOADS:

Doctor Levin, you already showed one such reference in your slide this morning.

BY DOCTOR LEVIN:

Yes, I was going to ask Doctor Friedman if he would mind telling us how long he had been practicing medicine?

BY DOCTOR FRIEDMAN:

I have been practicing medicine since 1941.

BY DOCTOR LEVIN:

That's a period of observation of ten years?

BY DOCTOR FRIEDMAN:

Less than that, because I haven't practiced to make a living since 1945 or '46.

BY DOCTOR LEVIN:

I don't think that's particularly pertinent. In a period of ten years, you wouldn't have observed your three thousand cases for more than a fraction of their life span. Now, if you observed three thousand males, according to the tables Doctor Hider was talking about, according to our data that come from all the hospitals, laboratories and physicians practicing medicine in New York State throughout their life span, in our three thousand cases, if they had neither more nor less lung cancer than were expected, there should be thirty cases.

Now, if you also watched them for ten years, it's quite possible that you observed just a lot of the normal incidence of lung cancer in three thousand men. Of course, if we knew what the age of these people were when you first

saw them, and of course, what the ages were when you last saw them, we could use the tables that Doctor Mider was referring to and give you something a little bit more refined. I think it's a kind of observation that you can not bank on as far as it goes, is worth following up more precisely and may actually lead to something that is a more precise type of data, you can't tell. The tables are available if anyone would like them; you can have them.

BY DOCTOR FLETCHER:

Let me comment once more on this terribly dangerous habit of trying to form statistics on hospital population, and I really do feel - I reproved Doctor Friedman for it yesterday, but he apparently is quite unrepentant.

Doctor Cochrane, - I did describe to you a survey that Doctor Cochrane has done in the Rhondda Valley in South Wales where he has X-rayed a complete mining community. Now, it was very interesting in the course of that X-ray survey where he X-rayed over nine thousand miners and ex-miners, I'm sorry I haven't got the detailed figures here, but they'll be available for the record - he didn't actually pick up on the X-ray a single case of pulmonary neoplasm among that whole population, although he did pick up two intrathoracic - what you - what do you call them, you know, pains?

BY DOCTOR RHODES:

Mediastinal pains?

BY DOCTOR FLETCHER:

Two terms, you know, it's astonishing. You pick it up, but not a single neoplasm, but within a year of the survey, there had been again -- I'm quoting from memory -- there had been four deaths from that neoplasm in that group. Now, we shall have actual figures for the actual mortality from neoplasm on this actual group of miners extending over the years, with accurate age distribution, and I think we should be able to give a fair answer to the effect of coal dust on the incidence of neoplasm in that group.

In the meanwhile, I think that Professor Gough's experience, with an enormous experience of post mortem work in coal miners in South Wales, he thinks that there is no influence at all of coal dust on neoplasms. He sees just as many neoplasms in miners as in non-miners. But I don't pay any greater respect to that by the evidence from the post mortem department than I do to Doctor Friedman.

BY DOCTOR RHODES:

Doctor Friedman?

BY DOCTOR FRIEDMAN:

I want Doctor Fletcher to know I did learn yesterday, and that today I didn't make any definite conclusion. I was merely asking a question. I don't think you should have reproved me again today.

BY DOCTOR VOIGT:

During very recent months, years really, I have become increasingly distressed by efforts of some who incriminate a dust which has been inhaled into the lung, deposited in all areas of the lung, which might be seen as present in an area of malignancy as the causation for that malignancy. I refer specifically to the asbestos body which occurs in tumors developing in the lung, and I should like to have someone comment upon the validity of that sort of reference or not. Doctor Mider may like to comment.

BY DOCTOR RECHARDS:

Doctor Mider?

BY DOCTOR MIDER:

Doctor Mider doesn't like to comment on that, but it seems to me that it's your possible hope, probably your hope, that sort of argument, and not susceptible to scientific proof or reputation; it's a state of mind, is it not?

BY DOCTOR RECHARDS:

Doctor Levin?

BY DOCTOR LEVIN:

Coming back to Doctor Mider's very interesting paper, I wonder if you would mind commenting on this question which may be un-ir. In view of the facts regarding experimental pulmonary neoplasms in animals such as the mouse, what justification could you educe for drawing any

conclusions whatsoever regarding the effect, pro or con, of various agents in the mouse, in what way would that have any bearing on the neoplasms in the man, in view of the marked differences that you have?

BY DOCTOR REOARD:

There is a question for you.

BY DOCTOR MIDER:

It seems to me about the only information that we can obtain from the mouse and man, in relation to man, is that information which has afforded us basic factors of information in carcinogenesis and is duplicated in some measure by what little we know about carcinogenesis in the human species and in other species.

In general, with some very definite exceptions, comparable approaches in man and in the mouse have led to comparable results. We must remember that the experimental cancer approach came out of the clinic and that, as far as we know today, there seem to be only five unadulterated substances which are capable of causing cancer in man that we know of, X-rays, ultra-violet rays, trivinyl arsenic, benznaphthalene and more recently, benzedrene.

Each of these agents is alleged - and I think with adequate evidence - to produce one or more types of neoplasms in experimental animals. Though one can not differentiate from one species to another directly without some

evidence that this is one, I do think that the study of pulmonary tumors in the mouse and of other tumors in other species have contributed to our basic faculty - our basic factual information as to what to expect in searching for human carcinomas.

I wish Doctor Smith would interject some remarks here. He knows a great deal more about this situation than do I.

BY DOCTOR SMITH:

I think the difference is that I don't know anything about it. I'd like to say that the reference Doctor Rhoads asked for and very properly called to your attention, that is the abstract by Lithgow and Finkel, describing tumors in the lungs of animals that have been allowed to inhale radioactive serum, is an abstract that I have - that I read carefully and couldn't understand. I believe if you look it up, you may encounter the same difficulty, so I wrote to Doctor Lithgow and he replied that - I asked Doctor Lithgow if he meant that he had, in fact, gotten tumors and if so, what sort of tumors he got. He replied that he did mean that he had gotten tumors and that they were epidermoid carcinomas.

Now, since he was talking about a matter of pathology and not a statistical question, I was inclined to accept what he said as fact, and I think it stands as an

evidence that this is one, I do think that the study of pulmonary tumors in the mouse and of other tumors in other species have contributed to our basic faculty - our basic factual information as to what to expect in searching for human carcinomas.

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BY DOCTOR SMITH:

cf p 80-81
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Now, sir, ~~he was talking about a matter of pathology and not a set of logical questions, I was inclined to accept what he said as fact, and I think it also is as an~~

extraordinarily important advance, because it represents, inasfar as I know, the first experimental success in producing in animals the type of carcinoma that forms a really major segment of the lung cancer problem in man, and as far as commenting on that general problem goes, I think that we are right there faced with a very important comment on it, in that here we are talking about an experiment which is so recent that it is in literature only in abstract form and yet the statisticians tell us and the clinicians have long known that lung cancer has become perhaps the outstanding clinical problem in males. We are faced with a real and a serious situation, and as far as our ability to study that situation experimentally goes, we have very little experience to guide us and that we urgently need more studies of suspected carcinogens by isolation techniques.

BY DOCTOR RHOADS:

Well, that's an arbitrary statement, Doctor. I would like to, with all deference to Doctor Mider, you referred to the five carcinogens which have included man, all having shown activity in the experimental animals. Did you yourself not question the animal experiments with arsenic?

BY DOCTOR MIDER:

Oh, excuse me, that's right.

BY DOCTOR RHOADS:

Are there other comments? (No response). If not,

then we will proceed with the next paper. Doctor Anna Baetjer, Pulmonary Cancer in Experimental Exposures to Chromium.

BY DOCTOR BAETJER:

Oh, don't you want to give them a little rest first? After all, they don't all have rubber rings like I do.

BY DOCTOR RHOADS:

She says they don't all have rubber rings like she does, so don't you want to give them the rest period. We'll will take a short recess then.

(Recess from 4:20 to 4:25 P. M.).

BY DOCTOR RHOADS:

Will you take your seats, please, so we can go on with the program. Will you please be seated; will you please be seated so that Doctor Baetjer can be heard? Gentlemen, will you please be seated? Our next speaker would like to be heard and we'd like to hear her.

Will the meeting please come to order. The next paper is by Doctor Anna Baetjer, Associate Professor, Environmental Medicine, Johns-Hopkins School. She will discuss pulmonary cancer in relation to exposure to chromate. Doctor Baetjer.

BY DOCTOR BAETJER:

Doctor Rhoads, Ladies and Gentlemen: First of all, I'm going to have to justify why I should stoop to do