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We will proceed to the first paper on the program by Doctor Leonard Bristol, on the incidence of clinically manifest diffuse obstructive emphysema. Doctor Bristol.

BY DOCTOR BRISTOL:

Doctor McCann, Ladies and Gentlemen of the Symposium: I should like to state at the outset that this is a preliminary report. It is a combined study of the Departments of Physiology, the Radiology of the Trudeau Foundation and the physiological data in this paper has been compiled by Doctor George Wright and his staff. I should like to have it clearly understood that my part in this work was that of a radiologist.

The word emphysema is derived from the Greek and literally means a blowing. Strictly speaking, it is defined as a swelling produced by gas or air diffused in a cellular tissue. It is a term of broad general meaning and, therefore, when it is employed for descriptive purposes, one must define clearly what is meant by its uses.

The clinical diagnosis of chronic pulmonary emphysema is not simple to make. No physician should have difficulty in establishing a diagnosis of far advanced emphysema, but it requires the most keen clinical insight to diagnose correctly a mild to moderate emphysema. A large proportion of moderate emphysemas are overlooked while many cases so diagnoses are not confirmed by pathologic study.

In a recent publication, Fernon states: There is no consistent relationship between the clinical severity diffused by lateral pulmonary emphysema and the extent of the process seen in necropsy. This, in general, has been our experience. Histologically, pulmonary emphysema is a condition in which the alveolae are distended, distorted and interrupted. Continued air sacs within a lobule may coalesce and adjacent lobules may fuse to form large air spaces. As a result of this, the total respiratory surface is reduced and the pulmonary capillary bed is diminished. The pulmonary elastic tissue is frightened and appears to be reduced in amount. It is surprising that one of the chief clinical and physiological features, namely, air with an obstruction, has not, with the exception of a recent paper by Spain and Amberson, been described by histologists.

The term emphysema as used in medicine is very ambiguous and as - is far too often employed in a very loose manner. Therefore, it is imperative that we think clearly as to what is meant when we use it. Several varieties of this condition are recognized. A simple but satisfactory classification has been devised by Rubin -- may I have the first slide, please -- as follows:

Obstructive emphysema caused by mechanical interference with respirators. The subdivisions be neath that, as you can see it, are chronic hypertrophic bulbous forms,

two, common obstructive emphysema caused by obstruction, in the thoracic change. The lungs expand to fill a barrel shaped chest, referred to as senile or postule emphysema. Interstitial emphysema condition characterized by tissue trauma of the lungs; for compensatory emphysema, a state of physical enlargement of the alveolae to meet anatomic readjustment and increased functional demands resulting from loss of tissue and, five, combined forms of emphysema, one component usually being predominant.

At this time, emphysema may develop suddenly or slowly and is usually bi-lateral and generalized. This condition may occur independently of any pulmonary disease, as a complication of long standing bronchial disease or may be associated with other diseases or malformations of the lungs or chest.

For purposes of discussion in this paper, we shall limit our consideration to diffuse obstructive emphysema for the chonric hypertrophic form, The salient clinical feature of which is airway obstruction. Whatever the obstructive agent, the mechanics of this condition are such that air entering the lung during inspiration is exeplled with difficulty during expiration, the difficulty in turn leads to a reduced maximal breathing capacity, a high residual air and in its advanced stages, to a retention of carbon dioxide in the lungs and hypoxia.

These physiological data can be recorded accurately in relation to an individual's total respiratory capacity. I should like to present a case of classic diffuse structural emphysema. This slide represents a film in full inspiration and full expiration, the production on your left being the inspiration microgram and the one on your right in full expiration.

I should like to direct your attention to the lack of rise of the diaphragms in the expiratory film and the failure of this patient to empty his lungs on expiration. The information to be gathered from this slide is that the patient has a low maximum breathing capacity and a higher residual air. We have predicted maximal breathing capacity of twenty-two liters per minute at determined thirty-one; residual air, predicted 1.36 and determined was 1.54.

The data on this slide shows that the patient has an elevated carbon dioxide content, an abnormally low hemoglobin saturation with .02. There is an elevated PCO_2 and a low PO_2. These are evidences of markedly impaired ventilation of the blood.

Diffuse obstructive emphysema is known to be one of the complications of silicosis. Simple discreet nodular silicosis is seldom associated with clinically manifest diffuse obstructive emphysema. On the other hand, conglomerate silicosis is almost always complicated by some degree of

diffuse obstructive emphysema. We do not mean to imply that chronic pulmonary emphysema is never detected in an individual who has discreet nodular silicosis, but raise a question as to its underlying cause when the two are associated.

Is it directly related to the pulmonary deposition of quartz or is it entirely an independent process? Emphysema has been alleged to be a complication of asbestosis. This problem will be discussed by Doctor Gregoire. Emphysema is also alleged to be caused by the inhalation of coal dust. Emphysema has been observed in granular beryllium workers, but is by no means always present. Emphysema is also observed in persons exposed to all manner of inert dust and some go so far as to associate these inert dusts in a causal relationship.

Now, to establish a causal relationship between emphysema and the inhalation of any foreign material, requires the demonstration of a high presence of emphysema in those so exposed as in a similar group not so exposed.

We propose to explore the question of whether or not there is a higher incidence of emphysema in those exposed to the inhalation of inert dust than in those not so exposed, in an attempt to prove or disprove a causal relationship between such inert dust and the development of diffuse obstructive emphysema.

The first step in such a study is to discover the

relative incidence of emphysema in a dusty and non-dusty trade. As mentioned before, diffuse obstructive emphysema is difficult to diagnose by means of history or physical examination, except in advances cases. Hence, it is imperative that we look for more refined methods.

In recent years, clinical physiologists have devised accurate techniques in the study of the normal and abnormal functions of the lungs. These various lung function studies offer a method of appraising pulmonary disabilities objectively. If we again refer back to our original case which, as you will recall, was that of a patient with diffuse obstructive emphysema, it will be seen that there was the presence of a low maximum breathing capacity. This test measures the maximum volume of air that can be breathed in a unit of time. The patient also had a high residual of air. This represents the amount of air remaining in the lungs following a maximal respiratory effort.

Also, there was a retention of carbon dioxide and hypoxia. Obviously, it is impractical to employ these methods in undertaking a study of a large series of individuals. Therefore, wehave attempted to find a more practical procedure. The maximum breathing capacity is known to correlate highly with the volume of air that can be expelled in a unit time.

Gensler has shown that the maximum breathing

capacity correlates highly with the volume of air expired in one sector. In a similar study carried out in our physiology laboratory, Wright and his co-workers found that the volume of air expelled in eight tenths second following the beginning of the most rapid expiration possible, correlated with the maximum breathing capacity of .758 with a standard error of .750. It will appear from these studies that the air expelled in eight seconds during such a maneuver and hereafter referred to as E2, is to a limited extent a substitute for the maximum breathing capacity test in mass surveys.

May I have the next slide, please? It would appear logical that the enclosed area within the silhouette of the thoracic cage at full inspiration would bear a relationship to the total volume of air within the lung, that the silhouette of the thoracic cage at full expiration would bear a relationship to residual air. The possibility of using the ratio between these two areas is a substitute for the actual residual air total volume ratio, has occurred to several investigators.

On this slide, a-3 refers to the area at full expiration and A-1 to the area of full inspiration.

In 1933, Gertado and his co-workers showed that there was a significant correlation between residual air and total volume ratio and the area enclosed within the

thoracic porages on a film taken at full expiration, provided that - in a similar area on full inspiration. Five years later, in another communication, he stated that contrary to previous results, the correlation between the ratio, area at maximum expiration divided by area at maximum inspiration and the maximum residual air divided by total capacity, was low and insignificant, but no explanation of this statement was ever made.

May I have the next slide, please? Recently, George Wright has studied two hundred and thirty-four cases and showed a good correlation of the residual air total volume ratio with the area of radiological inspiration, area of radiologic inspiration, the co-efficient being .772 and with a standard error or .02, and the remainder of this paper, this radiologic ratio will be referred to as A-e, A-1.

This is the regression formula showing that high correlation of stock that Wright obtained in this study. You will notice in the right-hand corner is marked 134 cases but since this lamp slide was made, he has studied a hundred more, making a total of 234 cases. From this regression formula, we can see that there is a high correlation between the area expiration and area of inspiration, with the percentage of residual air.

Now, this lantern slide represents a full

expiration of a normal healthy male. The area of the film, the area of the film on your right is referred to as A-3 and the area of full inspiration on your left represents A-1. These measurements are determined by a clinimeter and you can see the tracings which have been made especially on the expiration film, to determine from these traces.

The work we wish to report on this morning represents a study of 713 men in the General Electric plant in Schenectady, by means of inspiration and expiration films and measurement of maximum expiratory velocity. The men studied made up three distinct groups, one, all but two of those currently employed in the iron and steel foundry, or 237 persons; all but eight of those currently employed in the porcelain division or 193 persons; workers from the tool and dye and punch press divisions, 229 persons; these last were chosen by random sampling, but were allowed to refuse if they did not want to participate in the study. Fifty more men from salary personnel were also studied.

Most of these have been employed more or less sporadically than the laboring group of the divisions mentioned. The non-dusted group, at the same age distribution as did the dusted groups. Each man had the following study: Roentgenograms were made on a four by five flat film, the films taken as follows: One, full inspiration, two, four tenths of a second after beginning of the most rapid

expiration possible; three, eight tenths of a second after the beginning of the most rapid expiration possible, and four, in full expiration.

We are not reporting on the four tenths or eight tenths seconds films at this time. All exposures were set at one tenth of a second, The kilowatts and high amperes being slightly over exposed for the film in that period.

The expired air was caught in a spirometer with two indicators, one of which was stopped at either four tenths or eight tenths second after expiration was begun. The other registered the full vital capacity. The volume of air blown into the spirometer during the four tenths or eight tenths second period is considered to be representative of maximum expiration velocity. The maximum breathing capacity was measured in 233 of the 713 men.

The following data have been calculated regarding the maximum expiratory capacity. The first three lines are representative of - define our symbols. E-1 equals the volume of air expired in four tenths of a second at the fastest expiration possible. E-2 represents the volume of air expired eight tenths of a second at the fastest expiration possible and E-3 equals the vital capacity at fastest expiration possible. RE equals the co-efficient oc correlation.

Now, I'd like to draw your attention to this line

here, apparently E-2 correlates highly and best with the actual maximum breathing capacity. This is all the more significant when one realizes that we were studying a group of individuals who are almost normal from the standpoint of their maximum breathing capacity. As indicated by the fact that their mean maximum breathing capacity was 135 liters per minute and the median 140 liters per minute. If we had had a larger proportion of persons with a pathologically low maximum breathing capacity, we probably would have had an even higher correlation co-efficient.

If one would accept the contention that the E-2 is a fairly representative measure of the maximum breathing capacity especially for group studies, one can derive further information from the study. One hundred and six men had a maximum breathing capacity that fell within one standard deviation of their predicted normal figure, and a hundred and sixty fell within two standard deviations. The mean E-2 for the hundred and six men was 2.934 liters, and for the hundred and sixty men, it was 2.836 liters.

One may, thus, take the figure of 2.836 liters as the mean E-2 for a group of men who have normal maximum breathing capacity.

Of the entire group whose maximum breathing capacity was measured, 32 have values outside the range of normal, that is beyond two standard deviations on th low

side. The mean maximum breathingcapacity of this low group was eighty-eight liters per minute and their mean E-2 is 2.198 liters, in contrast to the normal group. It is apparent that the E-2 will disclose the presence of a low maximum breathing capacity.

If one starts with the premise that those mean with a normal breathing - maximum breathing capacity, that is within two standard deviations of their predicted, comprise a group which is, as a whole, free of emphysema, then their mean E-2 plus two standard deviations and their mean A-3:A-1 ratio plus two standard deviations can serve as a control for comparison with other groups.

The mean maximum breathing capacity of 160 men, within two standard deviations of predicted, covering ninety-five percent of their group, is 139.97 liters, and is 97.17 percent of predicted values. The E-2 of this group is 2.836 with the standard deviation of .551.

Next slide, please. From this data, is it - itis seen that the mean E-2 of these 713 men compares well with the mean E-2 of the 160 men whose mean maximum breathing capacity was 97.17 percent of predicted values. The only exception was in the iron foundry group and this difference was only slight, the difference being .164 which is slightly more than twice the standard error of the difference.

So, therefore, there is just as many pathological

E-2's in all groups, and insofar as E-2 correlates highly with maximum breathing capacity, we can state that there are just as many people with low maximum breathing capacity in the non-dusty trades as there are in the dusty trades.

The next question we must ask ourselves is what is the percentage of men within the various groups who fell below two standard deviations of the mean E-2 of 2.836. Next slide, please. From this chart, we can see that there was one out of fifty-six in the steel foundry or 1.8 percent, five percent in the iron foundry, 31 percent in the porcelain division, 5.8 in tool and dye, 8.3 in punch press and 9.3 in salaried personnel. There were as many men in the non-dusty trades who fell below two standard deviations as there were in the dusty trades.

This demonstrates quite conclusively for the group studied, this, that there were as many men, if not more, in the non-dusted group who have a below normal E-2 as there are in the dusty occupations.

Next slide, please. The mean A-3:A-1, that is area of expiration over area of inspiration, from the radiological films, from the films of those men having a normal maximum breathing capacity, is .615 with a standard deviation of .05$. Now, it is reasonable to assume from this information, that there is some increase in residual air in the foundry and porcelain workers, but not enough to cause

a reduction in the E-2, and by inference, the maximum breathing capacity. The number of men in this group who have a pathological A-3, A-1 ratio, in other words, more than two standard deviations from the men of normal mean, is demonstrated on the next slide.

The steel foundry, 7.9 percent; iron foundry, 5.8 percent; porcelain division, 5.9 percent; tool and dye, 1.8 percent, punch press, 5 percent; salaried personnel, 2 percent. Now, from this we can readily see that the number of men who have an increased residual air is slightly higher in the dusted versus the non-dusted groups.

Now, in conclusion, I should like to say that this has been an exploratory study made in an effort to obtain information as to the degree of emphysema present in certain occupations. The E-2 of all groups was approximately the same, and the A-3:A-1 ratio in the foundry and porcelain divisions departed only slightly from that in the group of men employed in the non-dusty trades. Because E-2 has a high correlation with maximum breathing capacity and the A-3: A:1 ratio correlates highly with residual air, it is easy to assume that these studies in mass survey will render reliable information as to the quantity of emphysema present in any particular group.

These methods failed to reveal any presence of significant change among the various groups studied. If

the pulmonary deposition of dust is the cause of an increase in the incidence of emphysema, then one would expect, from this investigation, to find it clearly demonstrable, the difference between the two groups studied, such a difference was not apparent.

In closing, I should like to reiterate that this is a preliminary report and that the information to date suggests that there is just as much emphysema in the non-dustry trades as in the dusty trades. Thank you.

(Applause).

BY DOCTOR McCANN:

Doctor Bristol's paper is open for discussion.

BY DOCTOR BENNETT:

Doctor Bennett, New York State Workmen's Compensation Board. I believe the paper and the presentation of its biostatistical data should have had the age groups referred to, because this may well be the universal statistical computation, namely the study of emphysema in various trades. However, the age group is an important thing.

BY DOCTOR McCANN:

Are there any other comments? Doctor Hugh-Jones?

BY DOCTOR HUGH-JONES:

Mr. Chairman, I would like to congratulate Doctor Wright and Doctor Bristol on this - on their work. One of the very difficult things, indeed, is to find practicable

tests which one can use in the field, and they're tackling something which is exceedingly difficult to do, and that is to find a suitable combination of things to define physiological values. They have set about doing something which other people have similarly tried to do, and one of the difficulties has been always in relating a group of tests to define a particular syndrome, if we like, in this case emphysema.

Now, one of the difficulties is that although you may get a high correlation of any one test, unfortunately, the error of prediction is very great. Could I make my point clear with the blackboard? If you have a relationship which they demonstrated, between one function such as, shall we say, a maximum voluntary ventilation and the time of the vital capacitor, then you will find a certain static about the regression line.

Unfortunately, if the correlation is low or even as high as .7, when you predict one from the other, you get a high scatter about this line, and one suggestion that we have tried to work out in overcoming this difficulty, is to use what is, statistically, a discriminate function and that is to combine a series of tests to maximize a difficulty or a difference.

I don't know whether I can make my point clear, but if you will accept for a moment that the clinician can

define gross emphysema as compared with the normal, and Doctor Bristol adequately desdribed that as a possibility, then you can take the different tests, for example, they give maximum ventilation, residual capacity, Co_2, or the tests predicted from them, and find what combinationit might be, three times the predicted M. B. C., plus four times the predicted residual capacity from error of the films, and get a statistical function which maximizes the change from normal to abnormal.

When that is done, you enormously improve the difficulties of any one test being significant, and I would suggest that as a method in using these predicted tests. You can get a discriminate function which gives the maximum difference in accepted normal and extreme emphysema, and then apply that in the field to these other things, using the simple predicted tests. Thank you.

BY DOCTOR McCANN:

Are there any other comments? Doctor Fletcher?

BY DOCTOR FLETCHER:

I just want to ask two simple questions. I was also interested in the age standardization, which, of course, perhapsis not vital, but you did tell us that some men were allowed to stand down from being tested, but you didn't tell us the percentage of the total population that took advantage of that privilege.

The other small point I would just like to correct is your statement that as far as coal miners are concerned, that fibrosis is always associated with emphysema, which is quite a common association, but not always.

BY DOCTOR HUEPER:

What was the labor turn-over in the various groups you tested? I think in dusty occupations, you should usually have your higher turn-over and, therefore, shorter exposure time. If you can manage statistics that way very beautifully.

BY DOCTOR HERMAN:

The general statement was made about dusty occupations. Nothing was said about the degree of dustiness, extreme dustiness, any comments to be made on that?

BY DOCTOR McCANN:

Any other comments? Doctor Bristol, would you like to answer these questions?

BY DOCTOR BRISTOL:

I should like to have Doctor Wright answer these questions, as he is in a better position to do so than I am. Doctor Wright.

BY DOCTOR WRIGHT:

That's all right. The questions have all been, of course, very pertinent. Doctor Bristol took some pains to say this is a preliminary report and when the final

report is made, most of these questions will be answered, in particular the ones about the dust exposure and the labor turn-over.

Neither of those have been the subject of scrutiny as yet. Data is available and is in the process of being looked at. I can say that the - there were a large number of men, I attempted to say the vast majority in the dusty trades, that had been in employment twenty, twenty-five, thirty years. I'm sure that Doctor Vosburgh, who is in the audience, can give you a little more information on that, if anyone wants to ask him personally. That will be in the final report.

The age distribution, I can tell you roughly about. It ran from approximately twenty-five to seventy and we took pains in choosing our control group, to have the same age distribution.

Now, the matter of obtaining volunteers in the tool and dye and punch press, in the dusted trades, we obtained all of the people except two in the foundry, and eight in the porcelain. Those were people who were away on holidays and we couldn't get them. There were no refusals, and I don't think that our relation was seriously impaired by the lack of those ten individuals. There were relatively few individuals who refused when requested, in the tool and dye and punch press. That was a random sample and then the

people picked were asked if they would volunteer. There were some refusals; I can't tell you precisely how many.

I'm afraid that maybe we won't be able to tell you that at all, because I'm not sure that records were kept as to how many refused, but I will look into that. It's a good question and, for the sake of completeness, we should have it.

Doctor Hugh-Jones' suggestion is a good one. You will see in the next paper that we attempted to get at that to some extent by full time correlation procedure. I'm not certain that that's the same thing he's talking about. I believe that his procedure is a little bit different and it is one that I'm not familiar with. I certainly will get together with you afterwards and see if we can't improve our data.

Did I leave anybody out?

BY DOCTOR BRISTOL:

The complication of conglomerate.

BY DOCTOR WRIGHT:

Oh, yes, perhaps Doctor Bristol didn't make it clear enough. I think he did say, commonly or almost always, in regard to emphysema being a complication of conglomerate disease. We certainly have had the experience in the vast majority of conglomerate silicotics, of demonstrable evidences of emphysema. We have one, I published a

very striking case of no emphysema.

BY DOCTOR FRIEDMAN:

Doctor Wright, in the dusty trade groups that you analyzed, what percentage of significant pulmonary dust disease did you find in the dusty groups?

BY DOCTOR WRIGHT:

You mean how many have radiological evidences of silicosis?

BY DOCTOR FRIEDMAN:

How many have radiologic evidences and how many were disabled by our other standards of function studies?

BY DOCTOR WRIGHT:

Well, insofar as the number who had radiologic evidences, there were some. That will be in the final report. Doctor Bristol is just getting ready now to review on large film all of these cases. There were some, perhaps Doctor Vosburgh could give us a rough estimate. Other methods of study were not carried out in these individuals. I wish that such an opportunity were made available to us.

BY DOCTOR FRIEDMAN:

Now, in the dusty trades, you analyzed then, there isn't necessarily a very great hazard that could have been corrected previously with proper hygienic industrial methods. You may have entered into places where improvement had already taken place.

BY DOCTOR WRIGHT:

On all of these people, I think the employment records will show they have been there twenty, twenty-five years.

BY DOCTOR FRIEDMAN:

And you know how many years they worked in hazard- our concentration and how many years not?

BY DOCTOR WRIGHT:

Yes, we have a letter - we have all that information on cards, and it is being gone over now. That will be in the final report.

BY DOCTOR McCANN:

If there is no further discussion, we will proceed to the next paper, and we're going to change the order of the program so that Doctor Wright's paper will precede that of Doctor Gregoire. Doctor Wright.

BY DOCTOR WRIGHT:

Mr. Chairman, Ladies and Gentlemen: Before presenting the material in my paper, I would like to make one comment to amplify, to some extent, one of the things that I think was rather important that was brought out by our Chairman, and that is the importance of the clinician in these various studies, and the position that gadgeteering and attempts to measure with some precision has in such studies as we are making.

TAKEN FROM PAGE 505.

BY DOCTOR WRIGHT:

Mr. Chairman, Ladies and Gentlemen: Before presenting the material in my paper, I would like to make one comment to amplify, to some extent, one of the things that I think was rather important that was brought out by our Chairman, and that is the importance of the clinician in these various studies, and the position that gadgeteering and attempts to measure with some precision has in such studies as we are making.

I find myself in full agreement with him on the question of the importance of the clinician and the tendency to rely on laboratory procedures. This reliance, in clinical medicine, is a manifestation partly of the tremendous burden that is put on a physician. I think it's also, to some extent, a false reliance in that we can see figures and understand figures more easily than we can the things that go into forming an opinion.

I do believe, however, that Doctor McCann would be the first to say that we need these gadgets and these methods of measurement if for no other reasson than to apply some sort of a test to our clinical accounts, our clinical abilities.

The clinician has been going on for years expressing opinions, and lacking all - most always wanting to know, but lacking more precise methods of confirming his opinion, and I would think that perhaps one of the greatest functions - more precise measurement - is that of applying some sort of tests to clinical abilities, and it is somewhat in that vein that our work has been carried out and the study that I am to report this morning was done.

May I have the first slide? Because this is a mixed audience, I am going to take just a few moments to prepare some background for the comments that I am going to make, and I have hopes that my medical colleagues will forgive

me for this crude diagram which, to my mind, portrays in an easily understood manner, the vital functions of respiration.

The respiratory apparatus is in essence, a bellows, an air pump through which blood circulates for the purpose of being ventilated. Air enters into a bellows and the action of that bellows is all important. The air is then distributed through the bellows and being constantly replaced, maintains its way, with a higher pressure of oxygen and a lower pressure of carbon dioxide than existed in the blood that flows through it.

The veinous blood returns to the lung from the periphery, carrying a high load of carbon dioxide and being low in oxygen. As the blood circulates through the bellows, gas passes across a very thick membrane which separates the blood phase from the gas phase of the lung, oxygen going into the blood and carbon dioxide coming out. The blood then returns to the left side of the heart and is pumped out through the tissues.

You have, in essence here, a pump and a diffusion service. That is the lung proper, and then we have, of course, a system that is intimately involved, it simply can not be separated from the lung, namely, the circulatory system, a pumping system which pumps the blood into the lung, accepts blood back from the lung and then pumps it out to the tissues.

Now, the vulnerable points of such an apparatus are, of course, immediately apparent. The apparatus is vulnerable from the point of view of air flow into and out of the lung, namely, from the pipes. Any airway obstruction will, very obviously, interfere with the capacity of this apparatus to behave as an air pump.

Improper distribution of gas in this bellows will lead to regional poor ventilation and possibly even -- actually it does occur -- areas of lung that are not ventilated at all. If these areas are still circulated, the veinous blood that flows through such areas does so to no purpose whatsoever. The bellows itself is vulnerable. It is a pump in the same sense that any other mechanical pump operates. Loss of power or loss of deformability or ease of being changed in volume, will obviously impair its activity as a pump. The system is very vulnerable at that thin membrane which separates the blood from the gas phase. If it becomes thickened or otherwise changed, you can readily understand that gasses may have trouble in getting across this barrier and then, of course, the circulatory system itself is vulnerable, the total area which can receive blood or the cross-sectional area of the vasuular bed may be diminished, so the blood is pumped through with difficulty. Blood may dam back in the lung, because of failure of the pumpon the left side to move the blood along as it leaves

the lung. The circulatory aspect is going to be covered by Doctor McCann.

I don't, however, in our presentation, want you to lose sight of the fact that a lung is not just an air pump; it's intimately associated with the circulation.

Now, for a good many years, the - these intimate and distinct functions of respiration were not amenable to very precise study, but during the past twenty years, methods have been developed which will permit a fairly precise measurement of the activities of the respiratory apparatus especially the study of the vulnerable points that I have just mentioned.

I would like to say, at this point, that Doctor McCann and his group, Doctor Kotler, who is in the audience were and continued to be pioneers in this study. Areally tremendous amount of the work that we are talking about today stems from it, their own laboratory, and I just think this is a rather appropriate time to recognize their role in studies of respiration in this country and abroad.

Now, some thirteen years ago, Doctor Gardner became interested in the functional aspects of the effects that the inhalation of dust might have on lung and circulation and it was because of this interest that I came here. I might say also that it gives me some pleasure to say that it was through Doctor McCann's efforts that this was made

possible. I doubt if many of you know that the initial building of the laboratory came about as a result of contributions for a number of years from the Department of Medicine, not only of money, but of time and helpful instruction. We began our studies in the only way that we knew how at the time, namely, to study the individual actions of the respiratory apparatus. These procedures are those that you have been told about here by others that have talked on the subject of pulmonary function.

We measured the size of the bellows, the so-called pulmonary volume; we measured the stroke volume of this air pump, then the vital capacity. We measured the power that this pump has to deliver air per minute, namely, the maximum breathing capacity. We have attempted, with relatively little success, to measure the distribution and mixing of gasses in the lung. With some greater success, we have been able to measure the impairment, if any, for the passage of gasses from the gas phase to the blood phase, and this is done in two ways, by studying the blood gasses of the blood after it has emerged from the lung, namely the degree to which the hemoglobin is saturated with oxygen and the degree to which carbon dioxide has been removed from the blood, and in a little more precise way, we have measured the pressure head that exists between the oxygen and carbon dioxide in the gas phase and the oxygen and carbon dioxide in the blood

phase.

One of the great shortcomings, and I think it is still a shortcoming, although a lot of work is being done on it, is that we have not been able to measure with nearly the same degree of accuracy, the role of the circulatory apparatus. I await with great eagerness the day when maximum cardiac outputs can be measured, and when the pressure relationships about which Doctor McCann will tell you, that govern the flow of blood through the lung, can be measured under conditions of stress.

After about four years of work, measuring these various things, these individual functions of the lung, we came to the realization that we were not really doing what we had set out to do. It is through, we could recognize, failure of the blood to be properly ventilated. We could recognize impairment of the pumping action of the lung or the respiratory apparatus. We could recognize poor distribution of gasses, and I have been guilty, as have others, of calling these disabilities, and thereby, we have confused some of our legal friends, because we have failed to be precise, and say these were disabilities for certain things.

A low maximum breathing capacity is a disability for breathing power. A poor arterial saturation is a disability for blood gas transfer and that is all that the disability is. That's all we have measured, and we and

others have sometimes not been careful to say whether or not this disability to breathing power is a disability in terms of a man's ability to work.

After, as I say, about four years of effort along these lines, we were repeatedly struck with the fact that certain men were remaining on the job doing a full day's work who had considerable impairment of breathing power, who had some degree of arterial unsaturation, who had abnormalities of the pulmonary volumena, and thick-headed as we were, took a long time to realize that we should be much more careful in the use of that word disability, and should define it precisely every time that it is used.

The word itself means exactly what it says, loss of an ability, and we should be careful to say what ability. Because of this discrepancy, we, as have many others before us, cast about for some way of trying to relate these specific disabilities to the general ability of a person to perform as a physical engineer - engine.

Now, you may use various procedures in this regard. The earning power of a man is the - to some extent, a measure of his ability to perform as a physical engine, but it is not a very precise one, and many factors are involved in that, perhaps I'll have occasion to say more about that this afternoon.

As doctors, we were, of course, interested in the

human body, and therefore, it is or would be nice if we could find some way of measuring the integrated man, what he can do in the way of physical performance. Some work has been done along these lines, measuring peak abilities to - for physical output, for example, the wonderful records that have been set in distance running and in other forms of physical feats, is, in a sense, a measure of an ability.

There is a more precise way of getting at it. The human engine is a great deal like an ordinary internal combustion engine. Fuel is burned, oxygen is required in that burning, and carbon dioxide is the result of that burning, and just as you might rate the power output of any engine in terms of its oxygen consumption, the human body can be studied in essentially the same way.

The next slide, please. One can study maximum performance abilities by having the individual walk on a treadmill rather than run on a circular one-mile track, and tremendous amounts of excellent work has been done in the Peck Laboratory at Harvard, studying fine athletes and some of that data I will show you in just a moment.

We have studied men from the point of view of their greatest ability to put out physical energy, by having them walk on a treadmill. We chose that rather than the bicycle because in this country, our people are not accustomed

to riding a bicycle. In addition, the exercise involved is not as free as it is in walking.

This is simply a picture of a man walking on a treadmill while various measurements are being made. Next slide. Studying the individual in this way, at increasing intensities of physical exertion, certain measurements can be made, as represented in this slide. This is of a person who has been walking or who has been walked at a constant speed, as you see, in the forward right-hand column, three and a half miles an hour, but increasing the level on which he walked until finally a level is reached which is the utmost that he can accomplish; in other words, a higher level, the walk is terminated at an earlier period than we have or had chosen.

These walks were all of six minutes duration and, by increasing the grade on which the man walks, we finally get to a point where the man can not walk for the full six minutes; he must get off and normal individuals, because of some severe leg weakness and some degree of breathlessness.

Now, it's apparent that the human engine is quite similar to the internal combustion engine. The oxygen uptake, as you would well expect, shown in the far left column, increases and gets up to a peak oxygen uptake of 2,950 [illegible] centimeters of oxygen. Now, that, then,

is the greatest ability that this individual had for oxygen uptake. If you would plot that out, you would see that as the last two exercises were carried out and a plateau was reached, there is very little increment in those last two exercises, and we have some data to show as in others, that a plateau is reached in oxygen uptake at a time when the minimum ventilation or breathing facility of the lungs can still be augmented and this has led along with other evidence, to the conclusion that in the normal man, the circulation is the governing factor for peak physical output of moderate duration. We're not talking now about short bursts of energy output.

I believe that I won't need to labor the point any further, but can simply say that it is generally accepted that the - one of the measures and perhaps one of the best at present available, of a man's ability to perform, as an integrated being, is the height to which he can increase or raise his oxygen uptake. This is certainly a function not only of respiration but of circulation, and I believe is primarily a function of circulation or chiefly so.

The other tables that I will show you, will indicate, as Doctor Motley stated, that we have enormous respiratory reserves, far greater than we do circulatory.

Now, we have chosen as our measure of the ability of this human engine to perform, this peak oxygen uptake,

and each man studied in the data that I will show you was carried in a series of walks of this sort to the peak oxygen uptake. The first two or three exercises can be done in one day. Subsequent ones, especially those requiring, when you get near the top, you can't do more than two in one day, because it's very strenuous work. It's very time-consuming, as you can see, so that what will be referred to as maximum oxygen uptake, is this bottom figure on the left-hand side, your left-hand side, and expressed in square meters of surface area, liters per minute, and what we have attempted to do or what we have accomplished in our study over the last ten years, is to run various tests of specific respiratory function in conjunction with this measurement of peak oxygen uptake.

Next slide. Now, here are forty-one normal men carried to the peak oxygen uptake on the treadmill. On the, on the left you see plotted on the oribt, the oxygen uptake in liters per square meter of body surface, and here the age in years. There is a loss of ability, as the man becomes older, which is only common sense, that fits in with what you all know.

The degree of spread is interesting in that I did anticipate there would be a greater variation. It is a good sized variation, standard deviation is approximately thirteen percent of the mean and that means that an individual

might -- well, I'll say more about that this afternoon -- really with normal mean bearing.

The next slide shows some abnormal individuals in respect to peak oxygen uptake. I might also say that the resting oxygen uptake is indicated, the amount of oxygen intake for a level walk is also indicated showing what reserves we possess. These are abnormal individuals and, to confirm the notion that peak oxygen uptake is a pretty good measure of a man's ability to perform, I have plotted data taken from a paper that appeared in Science, by Robinson Dill, and their co-workers, on peak power of physical performance of some of our fine athletes.

The very top figure is the data from Don Lasch, whom many of you will remember was our very fine two-mile runner, and very fine cross-country runner. The three that are plotted below him are Glen - Gene Benske, Glen Cunningham and Archie San Romani, who were also very fine distance runners. They have a perfectly phenomenal ability for oxygen uptake. Lasch could sustain that level not for five or six minutes but for twenty minutes.

Now, this is an ability that is far beyond anything that is possessed by the rest of us mere mortals. The average normal individual, as indicated by the very heavy line. These are some pathological subjects. The squares, filled in squares, are emphysemas. There is one

pneumonectomy over here, who still possesses a quite good ability. Some of the silicosis and asbestosis cases are scattered around.

Next slide. Now, I would like to show you a series of correlation c o-efficients in which we attempted to disclose or find out which of these specific measurements seem to parallel a man's greatest ability for oxygen uptake and, by inference, his ability to perform as a physical engine. The vital capacity correlated in a rather surprisingly good fashion. I have been one who, in the last ten years, has belabored the position of the vital capacity measurement. I'm not retracting all that I said about it, but I must say that this gave me some reason for surprise and I think Doctor Hugh-Jones, in his paper the other day, also said that they were somewhat surprised to find a way in which vital capacity correlated with ability of a man to perform.

This data, I must say, that I've got, is obtained on 180 individuals, and embraces all manner of pulmonary disease. There are sarcoid, there are pulmonary glanulomas, emphysema, bronchiectases, non-specific pneumoconiosis that we were able to diagnose, silicosis, asbestosis, exposure to dust, men with linear exposure and so on, a conglomerate group and ranges all the way from people who can just barely walk on the level at one and a half miles an hour for

five minutes, to men who had astounding abilities to perform, and it is, I believe, going to be possible with further working of our data to find out that there are specific diseases in which the vital capacity does give the erroneous information, and others in which the information is more reliable.

As you run down, you can see that there is very little improvement in the correlation when the vital capacity is expressed as a percent of the predicted, in other words, where you attempt to correct for age and surface area. Now, the residual capacity, or the residual air also correlates with a quite high correlation, as you would well expect, and as those have shown in the normal individuals, the correlation is very poor; in order to disclose the correlation, one must add in other people, namely, those who have had some impairment of their residual capacity.

It's rather interesting to show what Doctor Gregoire will later show, that in asbestosis, there is no correlation whatsoever.

Maximum breathing capacity correlatex somewhat better than does the vital capacity.

The next slide. Splitting up the maximum breathing capacity, you see that in normal individuals, the correlation drops considerably, and I think this is further evidence that we possess far greater reserves for breathing

power than we do for circulation. If the maximum breathing capacity in normal men was a strong determinant of ability to perform, the correlation should be higher and I'm sure that when we are able to measure cardiac output during peak exercise, we will find a very high correlation. However, when you have impairment of the breathing pump as occurs in asbestosis and silicosis, the correlation is somewhat improved, especially in silicosis.

Next slide. The ability of the lung to remove carbon dioxide from the blood is, I think, one of the very important ones, and we were curious as to how that might correlate, and there is a correlation, but it is of a rather low order. Very poor correlation, as you see, between aerterial hemoglobin saturation during exercise - these were blood samples removed while the man was walking on the mill - very low correlation between any of the gas exchange measurements and peak ability to work.

I rather wish that Doctor Motley were here because he could correct me if I'm wrong in my impression that he left, that perhaps I'm wrong in this, because as I understand what he said, his belief is that the single best indication of whether a man is normal or not fram a respira - tory point of view, is whether his blood gasses are normal, and I think you see here a fairly convincing demonstration that a man's ability to work depends relatively little on

his arterial saturation.

This is not difficult to understand if one will recall the great civilizations have been built at altitudes where every one was unsaturated, and today some of our productive mines operate with some physical energy expended on the part of the men, at altitudes where everyone is to some extent, unsaturated. To be sure, compensations on the part of the body do occur, but the same thing is true in the diseased man, as Doctor McCann will undoubtedly describe to you, so that arterial blood gasses were surprisingly poorly correlated.

Now, the O2V, that is a term that I must define for you, and could apply on one of the previous slides. It is what we refer to as the ventilation equivalent. It is obtained by dividing the minimum ventilation by oxygen uptake, and expressed, it's simply an expression of the breathing load, it's the amount of air that a man must breathe for a certain amount of energy expended, and it is surprisingly constant in normal people, has a very narrow range of variation.

Now, you see here a fairly high correlation, herein higher than we had anticipated, .60, and I shall jump now, just to the very last one, in which we had a multiple correlation. Incidentally, we had multiple correlations with most of these, and I'm only showing this one,

because it is the highest that we obtained. If one combines maximum breathing capacity and ventilation equivalent as a single factor, and I will show you some scattergraphs in a moment on that to point that out, then the correlation equivalent is a surprisingly high one, .904. This came as somewhat of a surprise to me. I still have difficulty in believing that it means what it seems to suggest, namely, that there is this very high dependence on M.B.C. and O2V when one wishes to study peak abilities to perform.

On the other hand, it is somewhat common sense, isn't it, because maximum breathing capacity is, in essence, breathing power. Ventilation equivalent is, in essence, breathing load and the ability of an ordinary engine to perform is certainly directly related to the power of the engine and to the load that one puts on it.

Next slide. Now, we were interested in whether or not this correlation would hold up, of M. B. C. and O2V versus oxygen uptake when one divided the data by diseases, and you will see that the correlation did hold up. Again, for normal individuals, the correlation is nowhere near that which we found in diseased individuals. This was another evidence that breathing reserves are much greater than circulatory reserves.

Next slide. Now, it's always well to look at scattergraphs, because as Doctor Hugh-Jones pointed out,

the correlation co-efficients usually look much better than do the scattergraphs, and the scatter will show you at once the wide variation which can also, of course, be expressed by the standard deviation which I will show you. This is vital capacity versus maximum oxygen uptake and there is, of course, this general slant, which is defined by the correlation co-efficient.

The standard deviation is large, as is shown by this wide scatter, making it, of course, very difficult to use the vital capacity as a good measurement in an individual, but for class studies or group studies, it is a better tool.

Next slide. This shows a maximum breathing capacity against peak oxygen uptake, and you will see at once that there is a - somewhat less scattered effect, still over large, and there are some exceptions that are always more interesting. Here, we find three individuals way down here all alone. These three persons were cases of pulmonary granuloma in beryllium workers, who possessed a normal maximum breathing capacity, but whose ability to exercise was very limited because of the very high ventilation equivalent, and when you correct the ventilation equivalent, they fall back into the body of the chart, as you will see in the next slide. Leave this one on just a moment.

You see, if you take above the average peak oxygen

uptake above 1.3, the scatter is tremendous, much more so than is true in the lower percentages here, indicating that respiratory reserves are far greater than circulatory or at least in relation to work. This shows you the M. B. C. and 02V combined as a factor, and here you have a scatter that is certainly far less, again more scattered in the range of normal, because the M. B. C. has undue weight at this or in this portion of the distribution of our data. But here we have a quite nice distribution.

The next slide. As I say, it's one that surprised me. I throw this on primarily so that you can see the coefficient of variation which defines mathematically the degree of scatter around the regression line. Vital capacity twenty-one, 1,984 maximum breathing dapacity and very great - very gratifyingly, much smaller for the combination of M. B. C. and 02V.

The next slide brings you back again to the same distribution of M. B. C. over 02V using, coming down now to zero instead of standing at three, with a drawing of a grid which combines the regression line and the standard deviation on the two sides.

The next slide -- or, that's all, I think. I want to summarize this rather long period of work by saying that as one would almost have anticipated, and I presume if I had gone to an engineer and said, "Now, look, we would

like to know what determines peak oxygen uptake", he would say, "Well, what's the load and what's the power", and we could have avoided all this work, because it's just a common sense correlation. I believe that the correlation is a rather surprising one. I can certainly say it's a surprising one to me. I don't understand why it's so high. I would think that circulation should have entered into this more than it did. We had no one in the series who had been in or was in congested failure. I'm sure we had some early cor pulmonales in the group. Undoubtedly, we have had some cardiac patients in this series, severe cardiacs, we would have found a little different result.

I believe that this type of study applied to the cardiac group would be very rewarding. In closing, I would like to say that this study is the end result of the labors of a large number of persons. I simply have the pleasure of presenting it to you. It's been carried on over the past ten years and the men who have worked in the laboratory have all taken a part in it. Thank you.

(Applause).

BY DOCTOR McCANN:

since the next speaker's material covers areas - much the same area, I think it would be better to defer the discussion on the two papers until we can have the two papers together, so I'll now ask Doctor Gregoire to present