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TAKEN FROM PAGE 525.

BY DR. McCANN:

since the next speaker's material covers areas - much of 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

his paper on the pulmonary function studies in men exposed for ten or more years to the inhalation of asbestos fibers.

BY DOCTOR GREGOIRE:

(Doctor Gregoire read a prepared paper which was to have been filed with the Saranac Laboratory. Transcript of his remarks is available in the event a formal paper was not filed).

BY DOCTOR McCANN:

There may be considerable discussion of these two papers, but I suggest that we take about a four or five minute recess for a stretch before we discuss them.

(Recess from 12:30 to 12:40 P. M.).

BY DOCTOR VORWALD:

May we all take our seats?

BY DOCTOR McCANN:

Will the meeting please come to order? Will you please come to order? Will all those who have not gotten their banquet tickets please do so before twelve o'clock, before twelve. The two papers which I have just heard by Doctor Wright and by Doctor Gregoire are now open for discussion.

BY DOCTOR HUGH-JONES:

I would like to make two comments really. The first is about Doctor Wright's paper with which I was extremely interested, and he put forward a suggested definition,

shall we say, of a way of measuring a man's capacity for overall work. There was one question I would like to ask him about that, and that is this, that many people, I think I'm right in saying, Taylor and Briggs originally did that which they called the crest load, the maximum work that people can do in a steady state. Other people have done the maximum ability to work as measured by the oxygen consumption which Doctor Wright has used.

Now, there is always one thing that worries me slightly about that, and that is this, that although you and I, for instance, might have very different powers to do our maximum, does that necessarily limit us at the ordinary work we're going to do in every day performance. In fact, the question is this, that does Doctor Wright have evidence to show that the performance at sub-maximal loads is necessarily worse in people who show a falling off of their maximum ability? It doesn't always seem to me to necessarily follow.

For example, I might have a reduced maximum ventilation or maximum ventilatory power of my lungs and, therefore, not be able to run, shall we say, a half a mile as fast as I could before. On the other hand, I might be able to walk at a slow rate for a long time perfectly well if my own thinking on that subject, and I would like his comments on that.

The other thing I want, and I hope people will excuse me because I'm not a statistician, I'm a male physiologist, and I have a certain amount of fears, and worries about statistics. I think you know about the same kind of known estimations that are given that if all the blood capillaries were put end to end, tnsy would stretch around the world. Somebody once said if all the statisticians were put end to end, that would be a good thing.

With those remarks, if I may make two technical criticisms on the statistics, and I hope you'll forgive me. The first is on the use of this correlation co-efficient. Doctor Wright was surprised at the extremely high co-efficient he got between the maximum breathing capacity combined with the ventilation equivalent for oxygen, and the maximum power to work. I believe that is an example of what is technically called a spurious correlation. He has got the same thing coming into the top and bottom of the fraction, namely, the ventilation in maximum breathing capacity in one case and in ventilation equivalent on the other, and I believe in his examples of comparing correlations, he should have been using partial correlations throughout, that if you are comparing the overall correlation, what you're observing is the amount one test relates to some other test, and the degree of that is a set thing if you're just comparing one set of tests. If you're comparing

another test to the first thing, in this case oxygen capacity for work, the reason why that correlates so highly may be due because it's partially correlated with your original test and I don't think you can put out or compare things on that basis unless you take a count of the partial correlations and particularly of the spurious correlations which may arise from fractions.

That is one technical point. There are two others. One is that it does seem to me that if people, and I would like to ask Doctor Gregoire this question, when he says that these tests are significantly different, what he precisely means. If he uses twice the standard error of the difference which I think he did, that assumes a normal distribution curve and in a lot of these things which he was comparing, he is using a fraction which I know and can demonstrate is not normally distributed.

I would like to ask him what he takes as a level of statistical significance when the thing is on askewed distribution, and then lastly, which I think is an important point, and I put it up in all humility because I'm not sure the real answer to it, and that is this, that is a great fashion in physiology to which many people have been addicted, and that is to express things in a percentage of the predicted normal.

Now, it does seem to me that what Doctor Wright

and Doctor Gregoire did in two of their slides was a much more valuable way of doing things, and that is they showed the regression line with these tests scattering about it, and I think instead of saying that somebody at that point is a hundred percent of a predicted normal, you should say he lies within plus or minus a certain scatter of what would be expected at that age. In fact, you should subtract the average fall with age and not express it as a percentage. To express it as a percentage assumes, for one thing, a linear regression. It assumes the thing goes about the mean which it doesn't in any case, and lastly, in the extremes, it is entirely incorrect and it's a thing in physiology, I think we ought to fight very seriously, that if we are going to use statistics, I think we ought to consult expert statisticians on those things, and I do make those comments in all humility because I do think a lot of the physiological conclusions can be erroneous.

I was extremely interested in Doctor Gregoire's conclusions, his last ones, about the differences between asbestosis and silicosis, and I have no doubt in my own mind that all he said was extremely correct statistically from that point of view, and I think it was a fascinating and a very valuable and able study though I would like to ask him whether he did take cognizance of the various other individual tests as far as their significance level was

concerned.

BY DOCTOR McCANN:

We're going to finish by your scheduled time, it will be necessary to limit this discussion and I'll ask Doctor Wright if he cares to answer Doctor Hugh-Jones.

BY DOCTOR WRIGHT:

Doctor Jones, I'm afraid you read more into my paper than I wanted to be in it. You have gone beyond now and are applying the peak oxygen uptake to a man's ability to shovel coal, and I have refrained from doing that deliberately, because this is what we measured, and that's all I want to talk about, what enters into a man's ability to perform every day his most complex;motivation alone, how many children he must feed at home is extremely important, why people become fatigued on their job is a most complex question. Why does the housewife who really, in many instances, has little physical labor to do, with our washing machines and so on, become dead tired at the end of the day? I wouldn't for a moment say, and I refrain deliberately from saying that peak oxygen uptake will tell you whether or not the man is able to carry out a full day's work.

I can show you, I'm sure you have many examples, of men that stay on the payroll. They break just as much tonnage underground as the next man who may have double his

peak oxygen uptake.

What I do believe the peak oxygen uptake gives you some information on is what his human engine is able to do in this precise piece of work.

Now, there are two extremes that this sort of falls in the middle of. There is the sudden burst of energy which a man may be called upon to do in running from a burning building, which a severe cardiac might be able to do. That's accomplished anaphobia. Then there is the other kind that you are referring to, the sub-maximal work that is carried out over a long period of time and that may not bear a relationship to the peak oxygen uptake.

As a matter of fact, it was the failure of its bearing relationship that led us to do this study originally, because we had observed just in a practical way, that men were - with a low maximum breathing capacity who had arterial saturation, who had a high residual of air, were nevertheless able to do a full day underground, doing a job that was certainly a sub-maximal job, so I agree with you fully. I'm glad you brought the point up that one can not transfer this sort of data in any exact manner to the question of whether or not an individual is able to do a day's work at sub-maximal labor.

I do believe, however, that it is a tool that lets the clinician find out how well he is able to estimate the

departure from normal.

Now, our statistical problem would take a considerable amount of time. I recognize the things you are talking about and would like to have more opportunity to converse with you in that regard. We were worried about whether or not we had the same background, two sides of the correlation, a thing that I believes was a serious criticism of Doctor Motley's data.

It's true that oxygen, oxygen uptake, is a factor that appears, and ventilation appears, but they are done under different circumstances and I do not believe they are the same.

It would be something like saying that a man who has one dollar is a millionaire because he possesses a dollar. Oxygen uptake, during work, when it's related to ventilation equivalent, is simply the amount of oxygen being used in relation to the amount of air being breathed at the time. It's totally different from maximum breathing capacity and it's totally different from peak oxygen uptake and I think we're on fairly safe grounds from that point of view.

You raise the question of askewed distribution. It's true that one of these correlations definitely is a curvo-linear distribution and that's the maximum breathing capacity against maximum oxygen uptake. The curve is in the

process of being fitted at the present time in an effort to see whether it would give us a better correlation than the formula we did use, which was a straight line formula.

I would like to say one thing that Doctor Gregoire perhaps won't be able to touch on, and that is when we say a thing is a certain percent of the predicted, we are taking into consideration the two standard deviations from normal. These are most of the time corrected curves for age or some other factor and the standard deviation of the normal predicted value has been calculated as, for example, with maximum breathing capacity in which we say there is such a figure as one hundred percent or a normal figure, the scatter around that regression line gives you a standard deviation if you wish to calculate it.

The scatter, for example, around the maximum breathing capacity, is such that ties the standard deviation of the predicted value requires you to consider all people over sixty-six percent as being within the normal range. Now, the matter of partial correlation is much too involved for us to discuss here. We can do that afterwards.

BY DOCTOR McCANN:

Do you wish to make further comment, Doctor Gregoire?

BY DOCTOR GREGOIRE:

I think he has covered it.

BY DOCTOR McCANN:

If not, I will proceed then to discuss the subject which was assigned to me, which concerned the cardio-circulatory aspects of Pneumoconiosis.

I might say at the outset in answer to a remark of Doctor Wright's, that I do not think the clinician should omit functional and physiological studies. The function of the clinician is to put the whole mess of things together. He's an integrator. He must take all aspects of the man concerned, into account, if it's going to make any sense.

(Doctor McCann's paper, from this point, was prepared, and a copy has been filed with the Saranac Laboratory.

BY DOCTOR McCANN:

In the printed record of these proceedings, I should like the names of Doctor Lovejoy, Hillfrank and others as co-authors of the paper which I have read. I'm afraid I haven't been too clear. I certainly have used up so much time, I'll certainly leave very little for discussion.

Doctor Waring will open the discussion.

BY DOCTOR WARING:

Doctor McCann and Members of the Symposium, Doctor McCann has, as always, presented factual matter as well as philosophical comments with such a happy facility that I envy him. I'm reminded of the story which I hope our British friends here will not find incorrect, about Sir Joseph

CURRENT RESEARCHES IN ANESTHESIA & ANALGESIA

Official Organ of the International Anesthesia Research Society

LAURETTE MCMECHAN, ASS'T. EDITOR, EXECUTIVE SECRETARY
318 HOTEL WESTLAKE, ROCKY RIVER, CLEVELAND 16, OHIO

February 3, 1953

Dr. James J. Waring
University of Colorado
Department of Medicine
4200 East 9th St.,
Denver 7, Colo.

Dear Dr. Waring:-

We are happy to give you permission to use the two illustrations from Drs. Whitehead and Draper's paper, namely numbers 1 and 4, with due acknowledgement to source of the original publication.

With kindest personal regards, I am,

Cordially and appreciatively yours,

Laurette McMechan

Assistant Secretary

TAKEN FROM PAGE 535.

BY DOCTOR WARING:

Doctor McCann and Members of the Symposium, Doctor McCann has, as always, presented factual matter as well as philosophical comments with such a happy facility that I envy him. I'm reminded of the story which I hope our British friends here will not find incorrect, about Sir Joseph

Lister, who was invited to attend a graduating exercise of one of the great universities in the British Mes, and he gave a magnificent address and at the end of his address, there was some demand from the audience that the resident professor of medicine should get up and make a few remarks. Being a modest gentleman, he was reluctant to do it, but the demand increased and finally he stood up and he said, "Ladies and gentlemen, when the English nightingale sings, all other birds should be still". Now when this Rochester nightingale,who is both physician and physiologist,sings, I think the Rocky Mountain magpie, perhaps, ought to shut up.

Now, he has emphasized many important things, and I can only touch on them in just a few moments. He indicts heavily emphysema and the physiological changes that accompany emphysema and I agree with all that. He sings in praise of carbon dioxide and I think very wisely, and also very cautiously so. He emphasizes that in past times, we have emphasized too much heart failure and too little lung failure, and one surely will have to agree with him on that.

Now, at the University of Colorado, we have had competent physiologists and bronchologists and since Doctor McCann was kind enough to send me a copy of his address to try and digest at the higher and more rarified altitude of the Rocky Mountain regions, this denser atmosphere within

and without, why I am grateful to him for letting me have that and I wanted to tell you perhaps something about the formal pharmical dynamics of carbondioxide as it has been studied by Doctor Whitehead and Doctor Draper, Doctor Goldenson and other men in the Departments of Physiology and Pharmacology at the University of Colorado School of Medicine.

So, may I have that first slide, please? Now, in 1908, Volhard talked about what he called 'oxygen pumpers' and the experiments which I will tell you about here will demonstrate something of this.

Now, if you will look at the slide, you will see that we have the ambient atmosphere outside; we have an airway depicted and we have the respiratory alveolae, and moving from left to right, we have the pulmonary circulation in the capillary bed.

Now, if, as was done by my colleagues, if an animal is first de-nitrogenated, that is if he is permitted to breathe one hundred percent oxygen for forty-five minutes until the nitrogen is pretty thoroughly washed out of his system, especially his repiratory airways and if then he is given pentothal of sodium intravenously until his respiration ceases entirely and if he is now continued in a one hundred percent atmosphere or as the circulation proceeds through his capillary bed, oxygen is picked up out

of the alveolar spaces and carried away and carbon dioxide comes into the alveolae. His respiration has ceased entirely under the influence of pentothal of sodium, but because the uptake of oxygen volume exceeds the indigenous CO_2 in the alveolar space, why a valent of pressure is created from the space to the alveolae and the oxygen which is alone in this animal's ambient atmostphere, the atmosphere then flows from his glottis down through his trachea and into his alveolae, is picked up and carried away, and the dog, without any artificial breathing whatsoever, and Doctor Whitehead calls this the fusion restoration rather than oxygen pumper as Vorhard described it, the animal will live without any form of artificial respiration just by virtue of this hemoglobin oxygen pump.

The oxygen is taken away with sufficient rapidity in the alveolae to set up a current, to set up a radium of pressure from the atmosphere down into the lungs, and the animal will continue to survive for forty-five minutes.

Now, he will die after that time if the experiment is continued for the reason that the carbon dioxide elimination gradually blankets the alveolar capillary membrane so that the oxygen is no longer able to move into the - into the arterial and capillary into the blood.

Now, the animal would die if he was immediately taken out from this and put in air, because then there would

be a great inflow of nitrogen and the nitrogen would serve in the same blanketing way and he would die very quickly.

Now, if, after say, say after twenty minutes the carbon dioxide has begun, has been steadily increasing, no longer is pentothal of sodium needed after twenty - between twenty and thirty minutes, because the carbon dioxide accumulation, as Doctor McCann referred to, is sufficient at this time and has an oxidizing influence upon respiration and for the last, say fifteen minutes or longer of the experiment, the animal is not breathing, but he does not require any longer pentothal of sodium to keep him in this state.

Next slide, please. Now, this slide shows you here up above the blood pressure and the picket fence here is the spirometer reading and the movements on the left here show the respirations up and down and then the pentothal sodium is given in sufficient quantity to stop his breathing entirely and that's where you see, over on the left, the point where the up and down respiratory movements quit.

Each one of the large moving down of the lines simply indicates the point at which the spirometer bell is filled again. The moving down simply means the point where the spirometer bell is filled in with oxygen;over here are the respiratory movements, and these figures here do not refer to minutes. These are the minutes down here, but

these refer to certain events in what's happening here.

Now, you can see, although respiration has quit here, oxygen is continued to be taken up by this oxygen hemoglobin from the bell. The bell is filled again, oxygen continues to be taken up, the bell is filled again, oxygen continues to be taken up, and so on.

At this point up in here, you will notice that he had a little fall in blood pressure and then a little rise and then here, this is a run of X-ray cystolic contractions which Doctor Whitehead showed very nicely with - were due not to fall in blood pressure and not to fall in carbon dioxide, but to too much pentothal, and then you notice that they disappear and the blood pressure falls slowly over here and after some sixty minutes over here, why with complete lack of circulation, there is complete stoppage of uptake of oxygen from the bell.

Next slide. Now, he showed very nicely in this slide here, time in minutes in here and oxygen saturation of the hemoglobin is here and here is the arterial saturation and the veinous saturation, the control period. This is during the period of abnema, of - during diffusion and this is after the period of abnema. You notice the period of arterial saturation maintains remarkably well for thirty minutes here as hypoxia develops. You notice the veinous saturation does the same thing and then very rapidly

at the termination of the experiment which is simply terminated by giving artificial respiration with oxygen.

Next slide. Now, this slide shows time in minutes down here, control period here, the abnea appeared here, the after abnea aperiod here, and the CO_2 in control percent here. You will notice that the arterial PH during the accumulation of carbon dioxide, and arterial PH falls, the veinous PH falls and the arterial and veinous CO_2 both rise quite remarkably. The PH falls down in the neighborhood, in the average around to 6.69.

The next slide, please. Now, here an interesting thing was done. This is similar to the other slide I showed you. There was a little rise in blood pressure here at the beginning of the experiment and a little fall. This is the respiratory movements here. This is where the abnea appear, or that period begins, but the oxygen uptake continues. The spirometer bell was filled again and the oxygen uptake gains again.

Now, at this point right here, the bell was held so that the bell could not fall and monometers were placed so as to record the negative pressure that would be created under these conditions, and you can see that this pressure fell quite remarkably here and amounted to about fourteen centimeters of water. In other words, the oxygen uptake by the alveolar capillary system, under these conditions,

and you can see that this pressure fell quite remarkably here and amounted to about fourteen centimeters of water. In other words, the oxygen uptake by the alveolar capillary system, under these conditions, was sufficient to create a negative pressure in the - or in the airway amounting to umpteen centimeters of water.

Next slide. Now, they subjected some animals to carbon dioxide inhalation, and Doctor McCann referred to this work of Doctor Stott, and there is one in our clinic out there, that work of Doctor Stott, and that was he emphasized the importance that should be attributed or the significance attributed to the fact that the emphysematous patient has a remarkable tolerance to CO_2. He lives in an atmosphere of low oxygen and a high atmosphere of CO_2.

Now, if you give this emphysematous patient carbon dioxide to breathe, he establishes it remarkably well until a point where he comes to a critical level. Perhaps Doctor Stott reported that when the CO_2 given to breathe was around about 9.28 percent, the emphysematous patient was remarkably comfortable, but when he was given carbon dioxide to breathe as high as 11.28 percent, he was very extremely uncomfortable.

Now, one other thing in relation to that, and that was this, both in these animals and in the human beings who were subjected to ventilation with high percentages of carbon

dioxide, Doctor Whitehead found that a small dose ofpentothal, while the CO_2 was being breathed at high concentration, could show amazingly the discomfort of this high CO_2 ventilation. A perfectly normal person breathes a high CO_2 concentration, why he becomes very quickly very uncomfortable and this discomfort is very easily controlled by the very small dose of pentothal sodium.

Doctor Whitehead found, in addition, that during the high concentration of CO_2, there was more barbiturate apparently taken up in the central nervous system than when there was low CO_2 and that suggests the clinical danger perhaps of a patient who has been given, for surgical purposes, a barbiturate and then that patient comes back to the ward and becomes anoxic because of an obstructed airway, and now, very quickly, he has a combination of high CO_2 and esthetic effect, and a high barbiturate can drive or can be driven into his central nervous system to add to his difficulties.

Now, one other thing in relation to this, and that is this, that when a patient breathes oxygen, a higher percentage of oxygen, I should have mentioned this earlier in one of the slides, when this patient breathes a high percentage of oxygen and he gets an obstruction of the airway, why there is no nitrogen, there is only a very small amount of CO_2 there early, and he can get very quickly a complete

collapsible lung or a collapse of a lobe or a segment of his lung, simply because the residual oxygen is only there and that is very quickly absorbed under these conditions.

Now, here you see the effect on a human being of breathing nearly ten percent CO_2, twenty percent, thirty and forty percent CO_2 and the remarkable effect on the PH breathing these different percentages of CO_2.

Next slide. Now, experimental slide of treating psychotic patients with CO_2 and with this type of experiment. In other words, it was thought that maybe that inhalation of higher CO_2 and the dropping down in PH might have an important influence upon the underlying abnormalities within the central nervous system that made a patient schizophrenic or at least so abnormal that he couldn't get along with the rest of us, and so they tried this on a number of patients and found that within a small number, that they were apparently helped by breating this high percentage of CO_2 with a change in their PH.

Now, they found also one other thing that was very interesting and that was that practically immediately the abnea ensues, the kidneys stop sereting urine and when the experiment was terminated and the respiration starts again, the kidneys immediately start secreting urine again, and they determined that this was a reflex by denervating one kidney

leaving the other kidney without any anesthetic around it, and they found there that the normal kidney not denervated by local anesthetic continued or stopped secreting immediately that the abnea was started. The other kidney that was denervated, why, continued to secrete urine, but at a lower rate than normal, and after the experiment was terminated, and a period of abnea was over here, why, the denervated kidney rapidly returned to a higher rate of secretion of urine and the one that was not denervated, why, resumed also its normal rate of secretion.

Now, I have reported this bedause I thought that these might have mono-dynamic influence or effects of carbon dioxide might bear an important relation to what Doctor McCann has been telling you.

(Applause).

BY DOCTOR VORWALD:

May I beg your patience just for a few moments. It is twelve o'clock and there is only one announcement, if you remember, the photograph which was taken yesterday. There will be a young lady in the foyer of the building for most of you who wish to have one. I am sure she will satisfy your needs, and so with that, let us be off to lunch.

(Session adjourned at 12:00 noon)

-oOo-