

1918

Francis W. Peabody, 1917

The Rockefeller University

Follow this and additional works at: <http://digitalcommons.rockefeller.edu/harvey-lectures>

Recommended Citation

The Rockefeller University, "Francis W. Peabody, 1917" (1918). *Harvey Society Lectures*. 14.
<http://digitalcommons.rockefeller.edu/harvey-lectures/14>

This Book is brought to you for free and open access by Digital Commons @ RU. It has been accepted for inclusion in Harvey Society Lectures by an authorized administrator of Digital Commons @ RU. For more information, please contact mcsweej@mail.rockefeller.edu.

CARDIAC DYSPNEA*

FRANCIS W. PEABODY, M.D.

Boston

EACH of the milestones reached in the continually advancing progress of clinical medicine corresponds closely to some forward step taken in what have come to be known as the "fundamental sciences." A new technical method or a new point of view which opens a fresh way of approach in anatomy, physiology, chemistry or biology is quickly seized upon by the physician in the hope that it may prove to be an addition to his armamentarium which will aid him to gain new knowledge of disease—its mechanism—its recognition—and its cure. The era inaugurated by Virchow gave to us as accurate a conception of the pathological morphology of the commoner diseases as the methods thus far developed would allow, and the last decade in clinical medicine has belonged essentially to biology and physiology. The study of dead form has largely given way to the study of living processes,—the growth of microorganisms and the abnormalities of function produced in cells and organs under various conditions of disease. The significant rôle played by physiology is manifest in many fields of clinical medicine, and the application of the methods and instruments of the physiological laboratory to the study of patients in the wards has broadened and in some instances revolutionized our conception of human pathology.

In scarcely any field has this affiliation between physiology and clinical medicine produced more interesting and stimulating results than in the study of the respiration. The application of modern methods permits the accurate determination of oxygen consumption, carbon dioxid production, the respiratory quotient, and heat production. With their aid we are rapidly gaining

* From the Medical Service of the Peter Bent Brigham Hospital, and the Department of Medicine, Harvard Medical School. Delivered March 17, 1917.

insight into the more fundamental changes of the intermediary metabolism which are met with in disease. The adaptation of recent physiological researches on the chemical control of the respiratory centre has led directly to the use of methods for determining the carbon dioxid content of the alveolar air in the study of disease. From this, and from analogous methods, we have learned much about those pathological conditions in which acidosis is a significant feature. Neither in the study of the gaseous exchange nor of the alveolar air, however, is the interest focused primarily on the respiration itself. Just as the urine is of value in the investigation of nitrogenous metabolism because of the end products which it contains, so the expired air and the alveolar air are chiefly of interest because they serve as indices of the intermediary metabolism. The respiration itself, the various forms which may occur in disease, the factors which may influence it and limit its efficiency,—these have occupied comparatively little attention. It is to some of these changes, and more especially to a consideration of the causes of the dyspnea which occurs in association with heart disease that the present paper is directed.

Before proceeding to a discussion of those factors which enter into the production of dyspnea, it will be well to state briefly the exact significance of the term itself. As ordinarily used the word is applied loosely to various abnormal types of respiration. Thus not infrequently rapid breathing or tachypnea is referred to as dyspnea, while even more often the increase of rate and depth of respiration which constitutes hyperpnea is characterized as dyspnea. Neither condition is, however, necessarily synonymous with dyspnea. Dyspnea, as the derivation of the word indicates, is a difficult or labored breathing, and there is implied in it an element of subjective discomfort. Hyperpnea on the other hand, merely signifies an increase above the normal value for the subject at rest in the volume of air breathed. Such an increase of the pulmonary ventilation, or as it is commonly called, of the minute-volume of air breathed may be due to a more rapid respiration or to a deepening of the respiration, but usually both factors take part in it. Whether or not in any

given instance the hyperpnea will amount to a true dyspnea depends on the degree to which the pulmonary ventilation is increased, and on the ability of the subject to raise his minute-volume to that degree easily. As will be seen, anything which prevents a person from increasing his pulmonary ventilation in a normal manner, will be an element in increasing his tendency to dyspnea.

It is extremely difficult to analyze with accuracy the fundamental cause of the subjective sensation which we know as dyspnea. How much is it due to fatigue of the muscles of respiration? How much is it due to a functional insufficiency of the respiration resulting in an inadequate oxygen supply to the tissues, and an incomplete removal of the waste products of metabolism? Without doubt both factors are involved and one is confronted by a vicious circle, in which waste products accumulated in the cells and blood augment the stimulus to the respiratory centre, and this in turn makes still greater demands on the already tired muscles of respiration.

In a general consideration of the respiration it is customary to subdivide the subject into two broad phases,—the external respiration, and the internal respiration. The former depends largely on the lungs, and the essential feature of it is that the pulmonary ventilation shall be such as to supply oxygen to the blood in the amounts required by the metabolism of the body, and to provide for the proper removal of the waste carbon dioxide. The internal respiration in which the circulation plays a prominent rôle, is concerned with the exchange of gases between the blood and the cells of the body. It is clear that if either the external or the internal respiration is inadequate to the task imposed upon it, dyspnea may result. Even when the external respiration produces a blood which is wholly normal as it leaves the lungs, there may be an improper gaseous exchange between the blood and the tissues owing to an imperfect internal respiration. Of the internal respiration, which is possibly the more fundamental phase of the respiration, physiologists and chemists know but little, and of its pathology clinicians know, if anything, somewhat less. The methods for studying even so gross a feature

as the rate of the blood flow are still imperfect, and chemical analyses are limited to blood from the peripheral vessels. The whole field of the internal respiration must, therefore, for the present, be left open, and we shall be restricted to a discussion of the conditions affecting the external pulmonary respiration.

One of the chief factors which have aroused interest in the study of the respiration in disease has been the recent advance made in our knowledge concerning the normal control and regulation of the respiration. The old discussion among physiologists as to the nature of the stimulus to the respiration was in a large degree settled by the classical paper of Haldane and Priestley¹ which showed that carbon dioxid is the essential stimulus, and indicated the extreme sensitiveness of the respiratory centre in that a rise of 0.2 per cent of the carbon dioxid content of the alveolar air caused the ventilation to be doubled. Subsequent investigations have tended to broaden this conception and to Winterstein² and Hasselbalch³ is due the chief credit of demonstrating that the respiratory centre responds not to carbon dioxid alone but to any increase of the acid radicles in the blood.

Since the presence of carbon dioxid and of other acids in the blood depends in general on the chemical processes in the body, it is evident that the basic factor in the regulation of the respiration is the metabolism. The respiratory centre controls the movements of the lungs and regulates them so that the pulmonary ventilation keeps pace with the metabolism. In a normal individual at rest, a minute-volume of approximately 5.0 liters of air suffices to remove the excess of carbon dioxid, and to supply sufficient oxygen for the needs of the body. If, however, the subject walks about the room his metabolism rises, more carbon dioxid is formed. the respiratory centre is more highly stimulated and the pulmonary ventilation is increased. The rise in metabolism associated with the walking may require an increase of the minute-volume of air breathed to three or four times its resting value in order that the needs of the tissues for a proper gaseous exchange may

¹ Haldane and Priestley: *Jour. of Physiol.*, 1905, xxxii, 225.

² Winterstein: *Arch. f. d. ges. Physiol.*, 1911, cxxxviii, 167.

³ Hasselbalch: *Biochem. Ztschr.*, 1913, xlii, 403.

be met. Such an increase in minute-volume is easily brought about by increasing the rate and depth of breathing and, indeed, a normal person is hardly conscious of any change in his respiration when he is breathing 15.0 liters a minute. With severe exercise the metabolism rises much higher, and in addition to the carbon dioxid formed, Ryffel⁴ has shown that lactic acid may be produced. Here, then, is an additional stimulus to the respiratory centre. In an attempt to determine how great a pulmonary ventilation normal persons were capable of, a series of observations have been made in association with Mr. F. C. Hall and Miss B. I. Barker. The experiments consisted in having young men,—doctors and medical students,—ride on a stationary bicycle until they were forced to stop on account of shortness of breath. Some of the subjects were athletes in excellent training while others were accustomed to a sedentary life. The subjects breathed through mouth-pieces, and valves were used to separate the inspired from the expired air. The expired air was passed through a Bohr air meter, and its volume measured for each half minute of the time during which the subject was riding. The rate of the respiration was counted from a continuous pneumographic record. The data obtained over each half minute consisted of the respiratory rate, the total volume of air breathed, and the average volume of each individual respiration. While there was a certain amount of variation among the different individuals in that some tended to greater increase of rate and others to greater increase of the depth of breathing, a number of interesting facts were elicited. Over the last minute and one-half of the ride, thus when dyspnea was most marked, and just before having to stop, the minute-volume of air breathed ranged from 47.6 to 80.0 liters. The larger minute-volumes were, of course, in general found in the larger individuals. Comparing these figures with the minute-volume at complete rest, it is found that these normal subjects could increase their pulmonary ventilation on an average of 10.7 times above the resting value. This gives a fairly accurate idea as to the great adaptability of the respiratory

⁴ Barcroft: *The Respiratory Function of the Blood*. Cambridge, 1914, p. 239.

mechanism to any demands that may be put on it, and one has a quantitative value for what we may call the "pulmonary reserve." Since the high minute-volume depends on an ability to increase the rate and especially the depth of respiration, it is not surprising to find a close relation between the highest minute-volume and the vital capacity, or the volume of air which can be expired after the greatest possible inspiration. There is also a relation between the volume of the individual respiration and the vital capacity, and it is rather striking that the deepest respirations while riding averaged only 33 per cent of the vital capacity. Curiously enough no definite differences were observed with regard to the respiratory mechanism between the trained and the untrained subjects. A point of considerable interest was the great difficulty experienced in making the subjects highly dyspneic, because they tended to stop riding on account of muscular fatigue rather than on account of shortness of breath. This was in part due to the fact that they were using muscles unaccustomed to heavy work, but it showed that in general the respiratory mechanism can normally adapt itself to any grade of metabolism that the body can produce.

Normally then, "the pulmonary reserve" is so great, and the minute-volume of air breathed can be so easily raised to many times the volume at rest, that dyspnea is only noticeable under conditions of rather severe exertion. What, however, are the factors which tend to decrease the "pulmonary reserve" or to make a person more readily subject to dyspnea? What must one consider as possible elements in the cause of any pathological dyspnea? Since the "pulmonary reserve" depends on the relation between the minute-volume of air breathed at rest and the highest minute-volume which the subject is capable of breathing, it will be greatest if the minute-volume at rest is low. Thus; first among the factors which may cause an abnormal tendency to dyspnea are those conditions which produce a high minute-volume at rest. Chief among these are an increase of metabolism and the presence of an acidosis. Secondly there are the factors which limit the ability of the subject to meet a demand for a higher pulmonary ventilation. Since an increase in minute-

volume depends on an increase of rate and depth of respiration it is evident that a high initial respiratory rate and more especially, anything which interferes with deep breathing will tend to reduce the pulmonary reserve. Finally it will be seen that still other conditions probably underlie the type of dyspnea which is associated with periodic breathing.

From this point of view, then, we may approach the question of heart disease in an attempt to determine whether or not these possible factors are present, and in how far they may be considered as elements in the production of dyspnea. It is important to appreciate that dyspnea is one of the commonest symptoms met with in patients suffering from cardiac disorders, and that it appears in a considerable variety of clinical conditions. We shall, therefore, expect to find that the causes of dyspnea are not necessarily the same in different cases, and that while the symptom has a comparatively simple basis in certain instances, in others it is complex and depends on a number of interacting factors. The dyspnea which is noticed on ascending stairs by a subject with a compensated valvular lesion is quite a different thing from the continuous dyspnea of the same person when in a state of acute decompensation, and this in turn may have different underlying elements from the dyspnea of the patient with cardio-renal disease, or the nocturnal attacks of paroxysmal dyspnea seen in an old man with chronic myocarditis.

Let us first consider the question of the metabolism in cardiac disease. The most satisfactory study of the basal metabolism in patients with heart disease was carried out at Bellevue Hospital, New York, in the calorimeter of the Russell Sage Institute of Pathology by DuBois and Meyer in an investigation in which it was my privilege to take part.⁵ Of fundamental importance was the demonstration by means of the close agreement between the methods of direct and indirect calorimetry, as well as by the finding of respiratory quotients which were within the normal limits, that the intermediary metabolism in heart disease follows a normal course. Sixteen patients were studied. The results showed that in compensated cardiac disease the metabolism is

⁵ Peabody, Meyer and DuBois: Arch. Int. Med., 1916, xvii, 980.

perfectly normal. Of twelve patients, on the other hand, who had some degree of dyspnea at the time they were studied, three showed a normal metabolism, and nine a metabolism that was distinctly above normal. In five of the latter the metabolism was increased from 25 to 50 per cent above the normal. The cause of the rise in metabolism is not evident. These, and other more recent observations from the same source⁶ indicate that it is not a necessary accompaniment of dyspnea, that it cannot be attributed to acidosis, and that it bears no definite relation to the level of the nitrogen in the blood. The subject has been further investigated in the Medical Laboratory of the Peter Bent Brigham Hospital⁷ in association with Dr. J. A. Wentworth and Miss B. I. Barker. The indirect method of calorimetry was used, the apparatus consisting essentially of a large Tissot spirometer for the collection of the expired air and the Haldane Portable Gas Analysis apparatus. By this method data are obtained regarding the minute-volume of air breathed which are lacking in the observations made with the large bed calorimeter. The results of the metabolism determinations in 24 instances agree essentially with those at the Sage Institute. They confirm the fact that in persons with mild grades of heart disease, in whom the lesion is comparatively well compensated, the metabolism is within normal limits, and they demonstrate again that in more severe cases, with or without dyspnea at the time of observation, the metabolism is variable, being frequently normal, but in some instances as much as 40 per cent above normal. In only two cases was the heat production more than 25 per cent above the normal however, and in general, the rise in basal metabolism is neither a constant, nor a particularly significant feature. Of more immediate interest in the study of dyspnea are the observations on the minute-volume of air breathed. These show that while patients with mild cardiac lesions, and only a slight tendency to dyspnea breathe a normal minute-volume of air, usually between 5.0 and 6.0 liters, the more severely affected patients who are either dyspneic while at rest, or who become so on very slight

⁶ Aub and DuBois: Arch. Int. Med., 1917, xix, 865.

⁷ Peabody, Wentworth and Barker: Arch. Int. Med., 1917, xx, 468.

exertion, tend to have a considerably higher minute-volume. In this group of subjects the minute-volume at rest ran as high as 11.6 liters while the average in 12 patients was 8.22 liters. There is, moreover, no definite relation between the minute volume and the metabolism, and a high minute-volume may be found in a subject whose basal metabolism is wholly normal. A similar increase in the minute-volume has been reported by Beddard and Pembrey^{*} and by other observers.

As to the cause of this increased minute-volume associated with a normal metabolism we have no absolute proof, but there is a very suggestive relationship between the raising of the minute-volume and the decrease of the vital capacity of the lungs. Practically all cardiac patients with a vital capacity of less than 60 per cent of the normal (see below) show a high minute-volume and a similar observation has been made in a case of pleural effusion. The decrease in the vital capacity of the lungs is probably associated with a lessening of the area of the respiratory surface, as for instance, by the production of atelectasis by collections of fluid in the pleural cavity. The dead space, consisting of the naso-pharynx, trachea, and bronchi, would not necessarily be affected and the resulting decrease in the respiratory surface, with a relative increase in the dead space would bring about a rise in the actual minute-volume of air breathed in order that the alveolar ventilation, which is after all the essential thing, should remain constant.

In patients with severe manifestations of cardiac disease, then, an increase of the minute-volume of air breathed while at rest is very commonly present, whether or not there is any associated rise in the basal metabolism. In such cases the high initial minute-volume will be a factor in the production of dyspnea in that it limits the "pulmonary reserve." By diminishing the difference between the volume of air breathed at rest, and the maximum volume the subject is capable of breathing, it makes him more readily susceptible to the production of dyspnea.

Let us turn to the consideration of a second condition which causes an increase in the pulmonary ventilation, and which may

* Beddard and Pembrey: *Brit. Med. Jour.*, 1908, ii, 580.

thus act as a factor in the production of dyspnea in much the same manner as an increased metabolism. This is acidosis. The respiratory centre is excessively sensitive to a shift in the reaction of the blood, and any considerable accumulation of acids in the blood stream causes a greater activity on the part of the lungs. Indeed the production of hyperpnea is perhaps the most characteristic effect of acidosis.

In the recent enthusiastic attention which clinicians have accorded to the subject of acidosis, the condition has been held responsible for a great variety of symptoms. It is not to be wondered at, then, that the relation of acidosis to dyspnea is a problem which has given rise to much conjecture and to a considerable amount of experimentation. Some observers, notably Lewis and his co-workers^{*} regard acidosis as one of the chief factors in the dyspnea seen in elderly persons with weak hearts and usually with kidney involvement,—essentially the cardio-renal group. It is important therefore to examine in some detail into the conditions associated with cardiac disease in which acidosis is present, and to consider in how far it may be regarded as responsible for the production of dyspnea.

As regards pure cardiac disease, one may state as the result of many observations on the carbon dioxid content of the blood and alveolar air, that there is no evidence indicating the presence of an acidosis in compensated cases. In patients with pure cardiac disease in a state of acute decompensation the question is less simple to answer. Not infrequently the alveolar air analyses show a low carbon dioxid tension, while the blood analyses show a normal or high tension. With the regaining of compensation and usually with the disappearance of continuous dyspnea, so that the patient is comfortable while at rest, the alveolar carbon dioxid rises quickly and the relation between the blood and the alveolar carbon dioxid becomes normal. How is this to be interpreted? It is possible that in these acutely sick persons the samples of alveolar air are not reliable, but this explanation is hardly satisfactory, and it is much more likely that the condition

^{*} Lewis, Ryffel, Wolf, Cotton and Barcroft: *Heart*, 1913, v, 45.

is a real one. Peters¹⁰ who has studied the question at the Presbyterian Hospital and who has found the carbon dioxid content of the blood considerably higher than that of the alveolar air, concludes, and most probably correctly, that there is an interference with the passage of carbon dioxid from the blood into the alveolar air. There is thus an accumulation of carbon dioxid in the blood, and an acidosis in which an excess of carbon dioxid is the essential feature. The possibility of the presence of other abnormal acids due to incomplete oxidation, a condition similar to the acidosis of asphyxia, cannot be definitely excluded, but at any rate, in the production of dyspnea in pure cardiac disease acidosis is a factor which only occurs in the most severely decompensated cases, and its influence in cases which recover is of short duration.

In cases of cardiac disease associated with renal insufficiency, on the other hand, the rôle played by acidosis is much more significant. Sellards¹¹ and Palmer and Henderson¹² showed the frequency with which acidosis occurs in chronic nephritis, and Straub and Schlayer¹³ described the low alveolar carbon dioxid tension in uræmia. Observations in our own laboratory have confirmed this work and helped to indicate the close relationship between acidosis and renal function.¹⁴ In general, cases of chronic nephritis with a normal phthalein output show no signs of acidosis; with the failure to excrete phthalein satisfactorily an acidosis develops which shows itself by an increase in the "alkali-tolerance test;" and when the phthalein output has fallen to zero, there is often a degree of acidosis sufficient to cause a fall in the carbon dioxid tension of the alveolar air. The recent work of Marriott and Howland¹⁵ shows that the acidosis is due to the inability of the kidney to excrete acid phosphate.

A study of numerous cases of renal and cardio-renal disease

¹⁰ Peters: *Am. Jour. Physiol.*, 1917, xliii, 113.

¹¹ Sellards: *Bull. Johns Hopkins Hosp.*, 1912, xxiii, 289; *ibid.* 1914, xxv, 141.

¹² Palmer: *Med. Communicat. Mass. Med. Soc.*, 1913, xxiv, 133.

¹³ Straub and Schlayer: *Munchen. med. Wehnschr.*, 1912, lix, 569.

¹⁴ Peabody: *Arch. Int. Med.*, 1915, xvi, 955.

¹⁵ Marriott and Howland: *Arch. Int. Med.*, 1916, xviii, 708.

shows that in the advanced stages, before and after the onset of uræmia, and even just before death, the alveolar carbon dioxid tension is usually not below 25 mm. This is in itself not a sufficient drop to cause a marked hyperpnea. Indeed in diabetes the increase in ventilation due to acidosis is not particularly noticeable until the carbon dioxid tension is approximately 15 mm. Considering, therefore, the comparatively mild grade of acidosis usually met with in chronic nephritis, one must hesitate to attribute to it too great a significance in the production of dyspnea. Occasional rare cases of nephritis present the clinical picture of coma and air hunger just before death, and simulate diabetic coma. In these the carbon dioxid tension is about 10 mm., and the air hunger may be relieved by alkali. Thus in a very small group of cases the acidosis may be the direct cause of a hyperpnea which is sufficient to produce dyspnea.

If, however, the acidosis which is commonly met with in chronic nephritis is not of itself intense enough to cause dyspnea, it is by no means true that it is a factor to be ignored. Its significance may be made clear by some experiments carried on at the Peter Bent Brigham Hospital¹⁶ which were devised as a means of studying the production of dyspnea in normal subjects and in persons with cardiac disease. In order to avoid the dangers and difficulties attendant on the production of dyspnea in persons with heart disease by exercise, and to allow of the investigation of comparatively sick patients in bed, the dyspnea was produced by a continually increasing percentage of carbon dioxid in the inspired air. The subjects breathed through valves separating the inspired from the expired air. The expired air passed through a plethysmograph which was calibrated so that its movements, recorded on the smoked drum of a kymograph, gave an accurate index of the volume of each respiration as well as of the rate of respiration. The total ventilation for each minute could thus be calculated. After leaving the plethysmograph the expired air was rebreathed by the subject. The carbon dioxid tension of the inspired air rose progressively during the experiment and its percentage was determined by the analysis of samples taken at

¹⁶ Peabody: Arch. Int. Med., 1915, xvi, 846.

frequent intervals. As the result of a series of observations it was found that in normal individuals a given percentage of carbon dioxid produced a fairly constant rise in the pulmonary ventilation. Thus when the inspired air contained from 4.2 to 5.4 per cent of carbon dioxid the minute-volume of air breathed was approximately twice what it was at the beginning of the experiment. Exactly the same relationship was observed in most patients with cardiac and renal disease. Their response to carbon dioxid fell into the normal limits. In a number of cases, however, in which the alveolar air showed evidence of an acidosis, abnormal findings were met with. Instead of the pulmonary ventilation being doubled by 4.2 to 5.4 per cent carbon dioxid it became doubled when only 2 to 3 per cent of carbon dioxid was breathed. In other words these patients were unusually sensitive to the stimulus of carbon dioxid, and it required much less than normal to cause a considerable increase of the pulmonary ventilation. That this effect was actually dependent on the acidosis was demonstrated by performing the experiment again after enough alkali had been given to overcome the acidosis and to bring the carbon dioxid tension of the alveolar air back to its normal value. Under these circumstances the patients reacted just like normal subjects. The explanation of these results is simple. With the development of the acidosis the so-called "buffer action" of the blood becomes diminished and the addition to it of small amounts of carbon dioxid which under normal circumstances would produce little change in reaction, causes enough shift in reaction to stimulate the respiratory centre. It seems fair to conclude from these experiments that while the degree of acidosis which is commonly met with in patients with cardio-renal disease is not sufficient to cause any decided increase in the pulmonary ventilation, nevertheless it may render the patients unusually susceptible to the production of dyspnea, and it is to be regarded as one factor in causing them to become short of breath on exertion. In severely decompensated cases, even the comparatively slight increase in the pulmonary ventilation while at rest may be sufficient to make the difference between comfort and discomfort in breathing. There is then a rational

basis for the administration of alkali to patients with acidosis, and in certain cases definite relief of symptoms may be observed.

Having discussed briefly the two chief conditions which cause an increase of the pulmonary ventilation let us now turn to the means by which the body responds to a demand for a higher minute-volume of respired air, and consider in what way these may be affected in heart disease. Such an increase in the minute-volume of air breathed is brought about by an increase of the rate or of the depth of breathing.

We may first give attention to the question of the depth of respiration and observe in how far a limitation in the capacity to breath deeply is to be regarded as a factor in the production of dyspnea in heart disease. In the experiments just described in which the subjects were made dyspneic by rebreathing air containing increasing amounts of carbon dioxid, one striking difference was noted between the normal subjects and the patients who had cardiac disease.¹⁷ While the former did not become extremely dyspneic until they were breathing from 60 to 80 liters of air per minute, the latter were forced to stop when they were breathing only 20 to 40 liters per minute. A study of the graphic records of the respiration during the experiments showed that this difference depended on the fact that the patients with cardiac disease were unable to increase the depth of their respiration as well as the normal subjects could. It is obvious that anything which prevents a person from breathing deeply is of profound importance as a factor in the production of dyspnea, for it immediately limits the extent to which the minute-volume can be raised, and this prevents him from meeting such increases of metabolism as he normally could. The inability to breathe deeply was found to correspond to a decrease in the vital capacity of the lungs.

It has long been known¹⁸ that the vital capacity of the lungs is often decreased in heart disease, but no particular attention has been paid to the fact. It seemed, however, that the condition merited systematic investigation, and in association with Dr. J. A. Wentworth a careful study of the subject has been

¹⁷ Peabody: Arch. Int. Med., 1917, xx, 433.

¹⁸ Arnold: *Über die Athmungsgrosse des Menschen*. Heidelberg, 1855.

made.¹⁹ The vital capacity of the lungs is the volume of air that can be expired after the deepest possible inspiration. In our experiments the observations were made by having the subject breathe in and out as deeply as possible through a rubber mouth-piece connected with a calibrated recording spirometer. The movements of the spirometer were recorded on the smoked drum of a kymograph, and the vital capacity was determined by measuring the length of the line which corresponded to the greatest expiration and inspiration. In order to decide whether the vital capacity of any given patient was normal or not, it was necessary to have standards for comparison, and since no wholly satisfactory data were at hand observations were made on a considerable group of healthy persons. Ninety-six normal men and forty-four normal women were studied. It was found that standards which were sufficiently accurate could be established if the results were classified according to sex and according to height. Various other factors which influence the vital capacity of the lungs could be fairly neglected as they were not particularly significant in the group of cases which we have studied. Thus old age causes a decrease in the vital capacity, but the majority of our patients were at a time of life when this did not play an important part. Athletic training increases the vital capacity but this rarely affected our results, for in pathological cases it is the decrease that is significant. When placed in their appropriate groups according to sex and height it was found that 134 of the 140 normal subjects had a vital capacity of 90 per cent or more of the normal figure.

Having thus established normal standards of the vital capacity of the lungs for men and women of different heights, it was possible to compare with them the results obtained in patients with heart disease. One hundred and twenty-four cases have been studied and about 224 records have been made. It is convenient to classify these patients according to the vital capacity into four groups each of which presents rather definite clinical characteristics, and it will be seen that there is a very close relationship between the decrease in vital capacity and the tendency to dyspnea. Briefly summarized the results obtained are somewhat as follows:

¹⁹ Peabody and Wentworth: *Arch. Int. Med.*, 1917, xx, 443.

TABLE I.

Group	Vital Capacity, per cent.	Number of cases.	Mortality, per cent.	Symptoms of decompensa- tion, per cent.	Working, per cent.
I	90+	25	0	0	92
II	70-90	41	5	27	54
III	40-70	67	17	39	7
IV	under 40	23	61	100	0

Certain cases were tested several times and, owing to changes in the vital capacity they appear in more than one group. In the "Mortality" column they are included only in the lowest group into which they fell. "Symptoms of decompensation" indicates dyspnea while at rest in bed or on very slight exertion. Under "Working" are included only those actually at work, and able to continue. Many other patients in Group II were able to work, but they are not included as they were still in the hospital.

Group I consists of 25 cardiac patients in whom the vital capacity was 90 per cent or more of the normal standard. Thus in these cases the vital capacity does not fall below the limits found in healthy persons. All of them had well compensated hearts, and dyspnea was scarcely a more prominent symptom in their histories than it would be found to be in a similar group of normal individuals. About 90 per cent of them were working, and the others were limited in their activities by cardiac pain or palpitation rather than by dyspnea. They were thus nearly all in extremely good general condition, and in many the cardiac lesion was merely an incidental finding. Group II consisted of 41 cases whose vital capacity was between 70 and 90 per cent of the normal. These patients differed from those of the group with a higher vital capacity in that practically all gave a definite history of dyspnea on any unusual exertion. The majority, however, were able to work, and the rest, with two possible exceptions, could lead a satisfactory, though somewhat restricted life. Several of them had passed through periods of more or less severe cardiac decompensation, and they are to be regarded as borderline cases whose activities must be somewhat limited, but who, under favorable circumstances, show little evidence of cardiac insufficiency. Group III consists of 67 patients in whom the vital capacity was between 40 and 70 per cent of the normal.

These cases are much more severely handicapped than are the members of Group II and practically all suffer from dyspnea on moderate exertion. Those with a vital capacity only slightly above 40 per cent are confined to bed or can do little more than get about the house, while those with a vital capacity approaching the upper limits can walk fairly easily, but they usually avoid the stairs or hills. Only 7 per cent of this group were still at work. Attacks of severe cardiac decompensation occur with considerable frequency among those patients, and 17 per cent of the number have died. Group IV consists of 23 cases with a vital capacity of 40 per cent or less. All of them were severely decompensated and the majority were confined to bed. Dyspnea is either constantly present or it is produced by the slightest exertion. The prognosis for patients who fall into this group is bad. A few patients whose vital capacity has fallen as low as this during their first attack of decompensation have subsequently recovered so that they could lead a fairly active life, but most of them made comparatively little clinical improvement and 61 per cent have died.

These observations demonstrate the important rôle played by decrease of the vital capacity in the production of dyspnea in heart disease. In a surprisingly accurate manner the degree to which the vital capacity is decreased corresponds to the tendency to dyspnea. Patients who have no unusual tendency to become short of breath almost invariably have a normal vital capacity, and those who become dyspneic readily have a vital capacity which is depressed in accordance with the severity of the symptom.

But what, it may be asked, is the cause of the decrease of vital capacity in heart disease? The answer to this question is that there are many causes, some of which are obvious and easy to appreciate, while others still remain obscure. Anything which interferes with the free movements of the lungs, or the entrance of air into them, will decrease the vital capacity. Thus pleural effusions, fluid in the peritoneal cavity, emphysema and pulmonary oedema may be reckoned among the more gross conditions affecting it. These and other similar factors seem to explain

the more severely decompensated cases, but there is a large group of patients with slight symptoms in whom the physical examination gives no clew to the reason for a decreased vital capacity. Further investigation into the cause of the decreased vital capacity in these subjects is clearly indicated, and the work of Siebeck²⁰ points to a promising line of approach. His comprehensive study of lung volumes in heart disease suggests that the low vital capacity depends on a change in the elasticity of the lungs which results from an engorgement of the pulmonary vessels due to back pressure from the left side of the heart. If this conception is correct then the vital capacity of the lungs is an index of the state of the pulmonary circulation, and as such is of considerable clinical significance. It is probable that in many cases the earliest evidence of cardiac insufficiency occurs in the pulmonary circuit but the usual methods of examination afford no means of detecting it. One clinical fact which is quite in accord with the theory that decrease in vital capacity with its attendant dyspnea is associated with a disturbance of circulation through the lungs is the common observation that dyspnea is an earlier symptom in disease of the mitral valves than it is in disease of the aortic valves.

If this relation between the vital capacity and the tendency to dyspnea is generally true when one compares a large series of cases with somewhat arbitrarily chosen normal standards it becomes more so when one follows the individual patient and watches the changes in the vital capacity which are coincident with changes in the clinical condition. As long as the clinical picture remains constant the vital capacity is found to be the same, but when cardiac insufficiency becomes more marked, and dyspnea more noticeable, the vital capacity falls. Similarly, an improvement in the general condition and a lessening of the dyspnea is associated with a rise in the vital capacity. This parallelism is, indeed, so definite that the determination of the vital capacity seems to assume a practical significance. Dyspnea is, of course, only one symptom of heart disease but it is a very common symptom, and it is an important one because the degree of dyspnea

²⁰ Siebeck: *Deut. Arch. f. klin. Med.*, 1910, c, 204.

or of the tendency to dyspnea is a valuable index of the state of cardiac efficiency. The clinical records of cardiac patients abound with statements about dyspnea but these are always of limited worth for they are based on either the history as given by the patient or on the gross examination of the physician. Dyspnea is, moreover, such a difficult condition to analyze or to describe, that any objective method which allows one to obtain accurate quantitative information regarding it will serve a useful purpose. Such information the determination of the vital capacity appears to furnish even if only in a somewhat rough way. In many instances the observations have proved to give a more reliable conception of the clinical condition of the patient than has been obtained from either the history or the physical examination. This of course is true only in cases in which dyspnea is the presenting symptom, and does not hold for the group of patients whose cardiac lesion manifests itself by other symptoms such as pain or palpitation. However the latter includes only a relatively small number of cardiac cases, and in a surprisingly large proportion of cases records of the vital capacity give important and helpful data as to the present status and the prognosis. They are often of much greater significance than are records of the pulse rate or blood pressure, and they seem to be a useful, although indirect index of the cardiac reserve.

But, as we have already seen, the increase of the minute-volume of air breathed which accompanies a rise in metabolism is brought about not only by a greater depth of respiration but also by a higher rate of respiration. What, then, is the relation of rate of respiration to the problem of dyspnea in heart disease? The facts are simple and well known by all, so that the subject may be briefly dismissed. With the exception of the extremely mild cases of cardiac disease, which are in a good state of compensation, most instances have a respiration rate which is somewhat above normal, and the more severely affected the case the more rapid the respiration. Now there is, roughly speaking, a maximum rate to which the respiration can rise without losing much of its efficiency. The extraordinarily rapid breathing seen in some hysterical patients, is of course economically wasteful.

The maximum efficient respiratory rate will vary considerably in different individuals and under different circumstances, but it is interesting for purposes of comparison to note that the average highest rate of our normal bicycle riders was 34 per minute. Assuming some such figure as this for the high limit of efficient respiratory rate, it is obvious that the individual with a low initial rate while at rest has a marked advantage. The greater the difference between the rate of respiration at rest and the maximum rate of efficient respiration, the greater is the reserve. With an initial rate of ten the respiration rate can be raised more than three times before the maximum of efficiency is reached, but with an initial rate of seventeen it can only be doubled. Thus the high rate of respiration which is found in severely affected cardiac patients is a significant factor in decreasing their reserve and increasing their tendency to dyspnea.

Having considered some of the general conditions which bear on the problem of dyspnea in heart disease we may now turn to a special type of respiration which deserves mention both because it is common in clinical practice and because its mechanism involves other considerations than those which have been as yet discussed. This is the periodic type of breathing, which reaches its highest expression in the classical Cheyne-Stokes respiration. Careful observation, and more particularly the studying of records made with the pneumograph impress one with the fact that the association of periodic breathing with heart disease is much more frequent than is generally recognized. It appears in cardiorenal cases, in aortic disease, and in advanced myocarditis, and it is most often characteristically seen in patients who suffer from attacks of nocturnal dyspnea. A history of the onset of dyspnea in the evening is often given by patients with myocardial weakness, and if they are watched it will usually be found that periods of dyspnea alternate with periods of apnea. During the apnea the patient dozes off and goes to sleep. With the beginning of respiration he rouses a little, and at the height of dyspnea he wakes up to find himself intensely uncomfortable and often gasping for breath. His discomfort disappears with the cessation of dyspnea, and during the period of apnea he falls

asleep again. Such attacks are sometimes referred to as "cardiac asthma," but the name is singularly ill-chosen for one of the most characteristic features of the true asthmatic attack is that the breathing is continuously rapid and labored. The volume of air expired has been measured in a few cases of mild periodic dyspnea and the total minute-volume has not been found to be remarkably high. The chief difficulty, and the reason for the discomfort appears to be that the patient is breathing only part of the time. The periods of apnea may last for half a minute, so that the patient is virtually breathing his minute-volume in the remaining thirty seconds. If he were to breathe the same minute volume of air regularly, over the whole minute, much less discomfort would be experienced. The volume of the individual respirations rises to much above the normal, and since the vital capacity is usually decreased, the deepest respirations may approach the maximum of which the patient is capable.

What can one say as to the fundamental cause of this type of dyspnea? The question is unfortunately one which remains incompletely answered, but some facts have been gathered which throw light on it. The suggestion has been made that the attacks are associated with an acidosis. As opposed to this it is difficult to conceive of an acidosis of such sudden onset, and moreover the typical feature of the respiration in acidosis, such as that seen in advanced diabetes, is hyperpnea with deep regular breathing. The clinical picture is quite different from that of periodic breathing. However, to settle the problem more definitely Dr. F. T. H'Doubler has studied the carbon dioxid content of the blood in a number of cases during the attack of dyspnea and either before or after it. Some of the patients who had advanced cardio-renal disease showed a slight decrease in the carbon dioxid tension, but this was rarely below 25 mm. and not sufficient to account for the dyspnea. Moreover there was no significant fall in the carbon dioxid tension during the attack of dyspnea as would be expected if the attack were dependent on a further increase in acidosis.

Douglas and Haldane²¹ consider that the essential cause of Cheyne-Stokes respiration is oxygen lack, and they state that

²¹ Douglas and Haldane: Jour. Physiol., 1909, xxxviii, 401.

"the periodic breathing is produced by periodic occurrence and disappearance of the (indirect) excitatory effects of want of oxygen" which "may be due to abnormal deficiency in the alveolar oxygen pressure" or "to effects on the circulation of changes in the breathing or to both causes combined." This explanation accounted satisfactorily for the periodic breathing observed by them on the expedition to Pike's Peak.²²

The frequency with which the attacks come on at night is a feature of interest. Periodic breathing is a normal phenomenon which occurs in many healthy persons during sleep, and in hibernating animals. Straub²³ has shown that during sleep the alveolar carbon dioxid tension rises, and he attributes this to a decrease in the excitability of the respiratory center. Morphine, which depresses the respiratory centre, often produces periodic breathing. May it not be that the periodic breathing in heart disease is associated with a change in the excitability of the centre? In favor of this suggestion is its nocturnal occurrence, and the fact that in mild cases it often ceases if the patient is roused or in any way excited. To test the question further, some observations have been made with Mr. F. C. Hall on the effect of caffeine, a respiratory stimulant, on Cheyne-Stokes respiration. The number of cases as yet examined is comparatively small but in nearly all a definite, though very transient cessation of the periodicity of the breathing, often associated with subjective improvement, resulted from the administration of considerable doses of caffeine. Several other drugs produced no noticeable effect. Morphine, in the few instances studied, caused no change or increased the periodicity, but its administration was therapeutically beneficial, for it depressed the central nervous system so that the patients did not rouse during the periods of dyspnea.

Whether Cheyne-Stokes respiration and periodic dyspnea in heart disease are due to oxygen lack in the sense of Douglas and Haldane or to a depression of the excitability of the respiratory

²² Douglas, Haldane, Henderson and Schneider: *Trans. Royal Soc. London*, 1912, cciii, Series B, 185.

²³ Straub: *Deut. Arch. f. klin. Med.*, 1915, cxvii, 397.

centre, or possibly to a combination of the two, is a problem which still awaits solution.

Such then, are at least some of the factors which contribute to the cause of that common but singularly complex symptom of heart disease—dyspnea. In its final analysis the problem resolves itself into the question of what we have called the “pulmonary reserve.” The degree to which any individual manifests a tendency to dyspnea depends on the relation between the volume of air which he breathes while at rest and the maximum volume which he is capable of breathing. The ability to meet adequately the needs of an increased metabolism such as occurs with muscular exercise, depends on the “pulmonary reserve.” In normal persons, as has been seen, the “pulmonary reserve” is great, and healthy young men can increase their pulmonary ventilation to approximately ten times the volume required by their resting metabolism. But in patients with heart disease the circumstances are much less favorable, and various conditions arise which cut down the “pulmonary reserve” and make them more readily subject to dyspnea. An increase of metabolism, or the development of an acidosis may raise the volume of air breathed while at rest, while an increased respiratory rate or a decrease of the vital capacity of the lungs will make the maximum ventilation of which they are capable much lower than the normal. A decrease of the “pulmonary reserve” results, and even moderate exertion causes a rise of metabolism and a pulmonary ventilation which produces the subjective sensation of dyspnea. The degree to which these different factors are present in any given case is extremely variable. The earliest and most constant feature in the production of dyspnea is apparently a fall in the vital capacity and it is often met with quite unaccompanied by any of the other factors which we have considered. In advanced cases of cardiac disease the situation becomes much more complicated. The vital capacity drops still lower, the rate of respiration rises, the metabolism increases, and an acidosis may appear. Finally the picture is still further confused by the onset of periodic respiration, and it becomes, indeed,

quite impossible to determine which element is most responsible for the patient's unhappy state.

Our conception of the etiology of dyspnea in heart disease is still vague and incomplete. Some little insight we have obtained, but further knowledge must come from the careful investigation of the individual case, the discovery of other factors in the cause of dyspnea, and the systematic grouping of the separate types of dyspnea. Only by such studies can we hope to reach our ultimate aim—the proper treatment and the relief of dyspnea in heart disease.