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ON

THE CAUSE AND SIGNIFICANCE OF DYSPNOEA
IN PULMONARY DISEASE.*

BY

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THE occurrence of respiratory distress is one of the most common and important symptoms in diseases of the lungs. This symptom may be described by the patient in many ways. Indeed it may vary from an urgent complaint without any conspicuous or even obvious change of rate to a very pronounced objective disturbance with or without the patient indicating any inconvenience. It may usually be stated that "dyspnoea" is the conscious desire for increased pulmonary ventilation. But this is not absolutely correct, as there are certain pathological conditions in which increased pulmonary ventilation occurs without conscious distress on the part of the patient. Nevertheless, in cases which exhibit such an increased respiratory function its significance is none the less important. In fact its diagnostic and prognostic import is frequently in inverse ratio to the distress or discomfort it gives the subject. Therefore the disturbances of function and structure which give rise to respiratory abnormality in pulmonary diseases should be clearly understood.

THE POWER OF ADAPTATION.

The underlying causes of dyspnoea are numerous and frequently are to be found in structures far removed from the lungs. Consequently those causes which result from pulmonary diseases may be looked upon as local, in spite of the fact that their effects may influence many other remote and important functions. But being localized there is a definite and concrete opportunity for their investigation and interpretation. In order that this may be accomplished, certain biological phenomena must first be considered. These are concerned mainly with the power of adaptation which the animal body seems inherently to possess. It is a well known fact that an organism if suddenly plunged into a radically new environment will rapidly succumb. If, however, the change of environment be brought about slowly it will gradually acquire in the same or succeeding generations an unexpected tolerance or even a relish for an ordinarily impossible situation. Adaptation occurring in one generation is amply illustrated by the acquired capacity of aviators and mountaineers to attain altitudes and even accomplish severe physical exertion in such a rarefied atmosphere as some authorities had predicted was theoretically impossible without certain artificial aids. These predictions must surely have been made without knowledge of the powers of adaptation of the animal organism. Examples might be cited of an almost similar power of adaptation of unicellular organisms to gross changes in their environment. Dallinger¹ showed how successive generations of flagellates gradually accommodated themselves to changes in the temperature of their environment. This was increased from 60° to 158° F. by slow graduations over a period of seven years. In view of these facts due allowance must be made for the different responses, both local and general, which may result from disturbances of respiration in pulmonary diseases. It would obviously be illogical to compare the effects of interference with respiratory function in bronchopneumonia and emphysema or those resulting from laryngeal obstruction due to diphtheria and tracheal obstruction due to a slowly growing mediastinal tumour.

RESPIRATORY FUNCTION AND THE CONSEQUENCES OF ITS
DISTURBANCE.

Respiration primarily is necessary for the acquisition of oxygen and elimination of carbon dioxide by the organism. Oxygen is absolutely necessary for all forms of function.

Further, although so essential there are no known reserves, which is contrary to the case of many other almost equally important supplies. In regard to the elimination of carbon dioxide the reserve powers for dealing with its retention are much more adequate provided a simultaneous and acute deprivation of oxygen does not occur. Want of oxygen makes the respiratory centre and probably all the other tissues more sensitive to their normal hydrogen-ion concentration, which is influenced by that of the arterial blood. If the circulation rate through the tissues remains normal or is increased a lowering of the carbon dioxide content of the arterial blood will lower its hydrogen-ion concentration and consequently will effect the reaction of the tissues. Thus the effect of acute oxygen want is to produce a moderate degree of dyspnoea which is not so much due to the lack of oxygen as to the fact that the organism has not sufficient time to lower the hydrogen-ion concentration of the blood by removing carbon dioxide. Hence the pulmonary ventilation is increased in order that this may be accomplished. If a more insidious oxygen want should occur there will be a slight increase of pulmonary ventilation, which lowers the carbon dioxide pressure of the alveolar air and thus of the arterial blood, and so the tissues gradually reduce their carbon dioxide pressure and thus their hydrogen-ion concentration. Therefore there is no demand for violent pulmonary ventilation. The respirations, however, will gradually become shallower and shallower and to some extent faster, but at no time giving distress, until eventually inspiration and expiration are so diminished that the respiratory movement practically ceases. This may be called the anoxaemic type of respiratory failure so characteristic of uncomplicated oxygen want which occurs in mines with increasing "black damp." It is also tragically revealed by Tissandier in his diary of the famous balloon ascent of the "Zenith" in 1875.

There are practically no pulmonary lesions which solely produce a retention of carbon dioxide. This is accounted for by the fact that carbon dioxide is twenty times more soluble than oxygen, and also on account of the peculiar character of the former's dissociation curve, which allows it to be removed from the blood entering the lungs at an almost constant rate in proportion to the degree of pulmonary ventilation. If, however, there be acute oxygen want and carbon dioxide retention a most violent form of dyspnoea is produced. Most characteristic examples of this condition are to be found in acute laryngeal obstruction due to diphtheria and in certain cases of spasmodic asthma. Furthermore, such a condition can be experimentally produced and studied in man by introducing a resistance to inspiration and expiration.² If the resistance be comparatively moderate it will only produce a slowing and slight augmentation of the respirations. If, however, it be increased further, or if exertion be undertaken with moderate resistance, the respiratory effort will become more violent until a sudden climax will be reached, when it will suddenly become excessively rapid and shallower until it ceases altogether. This may be termed the asphyxial type of respiratory failure.

Before leaving the discussion of the causes of dyspnoea in pulmonary diseases it remains to account for another type of respiratory disturbance. Respiration, besides being controlled by the relative proportions of oxygen and carbon dioxide (as a regulator of the hydrogen-ion concentration) in the tissues, is also influenced in a very profound degree by a nervous reflex. The chemical conditions may be said to determine the total pulmonary ventilation, but to some extent the Hering-Breuer reflex may be considered to have a leading role in arranging how this shall be accomplished. Under relatively normal conditions if there be a demand for increased pulmonary ventilation this is accomplished by increasing the depth of respiration rather than by increasing the rate. In other words, the points at which inspiration ceases and expiration begins are moved farther and farther apart until a maximum is reached. On further demand being made, the rate begins to increase conspicuously. If these demands be sufficiently severe it will be soon impossible to increase the rate except at the expense of the depth. At this point the high tide of respiratory efficiency is reached. A continuance of the demand leads to a decrease of the

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supply proportionate to the increase of rate and decrease of the depth, so in the end the rate reaches a relative infinity and the depth zero, and respiration ceases.

THE DYSPNOEA OF VARIOUS PULMONARY DISEASES.

1. Laryngeal and Tracheal Obstruction.

Lesions producing obstruction in the larynx or trachea lead to symptoms very similar to those which are found in experiments with artificial resistance. Particularly is this the case if the obstruction be acute, as in laryngeal diphtheria. In such circumstances there is no time for accommodation. The breathing at first is, if anything, slowed, with increased depth and obvious difficulty. After a short time, or if the obstruction becomes more complete, deep blue cyanosis develops, the respirations become more and more rapid, shallower, and eventually asphyxial respiratory failure occurs. It has been shown by Schafer⁷ that an almost similar condition occurs in double vagotomy, the animals dying within twenty-four hours of asphyxia. During this period the breathing is slowed, which has led to the conclusion that this is a direct result of section of both vagi. It is probably due to the laryngeal obstruction resulting from the paralysis of the vocal cords. If the animal survives the first twenty-four hours, accommodation seems to occur and recovery may eventually take place.

Respiratory failure in such cases is undoubtedly due to the fatigue of the respiratory centre, brought about by a combined oxygen want and carbon dioxide retention. If the obstruction be more insidious in its course a considerable degree of accommodation of the tissues may take place and very pronounced stenosis may occur without signs of respiratory failure, even although anoxaemia and carbon dioxide retention occur, as demonstrated by direct examination of the arterial blood and also by the deep blue type of cyanosis.

Complete collapse of one lung may lead to no respiratory symptoms at rest, except for the first few minutes. The reason for this is that although the lung be collapsed and non-functioning, so also is the circulation through these tissues. Therefore comparatively little non-aerated blood returns to pollute the general circulation. If, however, a partial stenosis of one bronchus occurs which leads to deficient aeration of the alveoli supplied by this bronchus, the circulation through this region will continue almost as freely as previously, and the blood, being partly aerated, will return to pollute the general circulation.

2. Bronchial Obstruction.

It is seldom that acute bronchitis leads to any interference with respiratory function provided that the inflammation does not descend to the small ramifications of the bronchial tree. In spasmodic asthma, on the other hand, a very good example is found of diffuse bronchial obstruction. As the attacks come on suddenly, and may be of different degrees of severity, it offers a very good opportunity for the study of acute dyspnoea due to pulmonary lesions. It may be stated that in practically all cases of spasmodic asthma there occurs a more or less pronounced arterial anoxaemia. This results from interference with the proper ventilation of some of the alveoli. A variable number of these, depending upon the severity of the attack, are probably almost completely cut off from adequate ventilation. Dyspnoea and hyperpnoea result from the acute oxygen want, which is accentuated by either relative or absolute retention of carbon dioxide. If the lesion is not of a very diffuse character, leaving many areas of alveoli undisturbed, the dyspnoea soon brings about a sufficient elimination of carbon dioxide to more or less relieve the symptoms. This elimination is accomplished on account of the greater solubility of carbon dioxide as compared with oxygen, but of more importance is the character of the two dissociation curves. The blood passing through a normally functioning alveolus can only become 99 per cent. saturated with oxygen. This is usually not sufficient to make up for the desaturation which occurs in other alveoli which are not properly functioning. The carbon dioxide, however, may be removed in such an increased amount from normally functioning alveoli as to completely, if not more than completely, compensate for the retention occurring in the pathological areas. In this way

carbon dioxide may be eliminated with such rapidity as to produce a relative apnoea through its excessive reduction in the arterial blood and tissues. This apnoea may last for a few minutes, and then hyperpnoea may ensue as the carbon dioxide reaccumulates. In this way successive paroxysms of asthma may appear to occur, with some minutes' intervals between each. This, however, is not a true remission and exacerbation of the asthma, but is due to an excessive degree of periodic breathing. In such cases the urine is usually faintly alkaline. On the other hand, the distribution of the asthmatic obstruction may be very diffuse, leading to a partial lack of ventilation of a great number of the alveoli. The increased ventilation which results is not sufficient to decrease the carbon dioxide in the general alveolar air, and therefore in the mixed arterial blood, and persistent symptoms of acute asphyxia result. In such instances the urine is strongly acid. Thus we see that there may be in asthma both an anoxaemic and asphyxial type of dyspnoea.

TABLE I.—Gases in the Arterial Blood of Cases of Lobar Pneumonia.

No.	Day of Disease.	CO ₂ c.cm. vol. per cent. in 100 c.cm. of Arterial Blood.	Oxygen per cent. Saturation of 100 c.cm. of Arterial Blood.	Remarks.
1	5th	—	83.00	Some delirium.
	8th	—	82.00	Delirious.
	8th	—	91.00	On oxygen.
	9th	—	91.00	On oxygen.
	10th	—	84.00	Semi-delirious; off oxygen.
	11th	—	95.00	Crisis.
	15th	—	95.50	Convalescent.
2	6th	—	88.80	
3	5th	—	92.00	
4	5th	—	87.90	
5	6th	—	87.87	
6	9th	42	86.58	Slightly delirious.
7	8th	—	89.66	
8	8th	42	82.13	Delirious; pH 7.48.
9	7th	41	80.06	Semi-comatose.
10	6th	44	91.56	
11	4th	48	93.00	pH 7.41.
	5th	44	92.00	pH 7.48.
	6th	46	91.00	pH 7.44.
	7th	46	91.00	
	10th	46	90.00	pH 7.42.
12	—	52	95.00	Before pneumonia.
	2nd	67	89.00	
	6th	45	84.00	Delirious.
	7th	47	93.00	On oxygen.
13	7th	42	93.00	pH 7.54.
14	6th	39	80.00	pH 7.45.
	8th	45	92.00	On oxygen; pH 7.46.
	10th	43	92.00	On oxygen; pH 7.42.
	24th	54	95.00	Convalescent; pH 7.34.
15	9th	48	63.00	Moribund; pH 7.33.

3. Lesions of the Alveoli.

It is a frequent observation in cases of acute bronchitis that when the lesion extends to the alveoli, giving rise to a bronchiolitis or bronchopneumonia, the character of the breathing immediately changes. I have already mentioned how rare it is to have respiratory distress when the inflammatory lesion is confined to the larger bronchi. But, as soon as alveolar inflammation or irritation occurs, the rate of the respirations increases and synchronously the depth

becomes much less. This is probably one of the most important causes of tachypnoea. It is frequently observed in lobar pneumonia, bronchopneumonia, infarct and oedema of the lung, and its detailed consideration will be taken up later.

In acute lobar pneumonia the respiratory distress as subjectively experienced by the patient is most acute during the first few days. This is during the period of early consolidation, when the exudate is forming in the alveoli, but yet the pulmonary circulation is still more or less active. During this period there may be a considerable reduction of the oxygen saturation of the arterial blood and an increased carbon dioxide content. This is undoubtedly due to the pollution of the general circulation by non-aerated blood coming from the consolidating lung. As the circulation becomes more and more cut off this condition rapidly changes. While there may still be arterial anoxaemia, the carbon dioxide content of the arterial blood becomes progressively less. When the consolidation has become complete and the circulation through this area has been almost completely cut off, it will be found that the carbon dioxide content has reached an abnormally low level (Table I). There has been considerable discussion as to the cause of the continued increase of the respiratory rate at this stage of lobar pneumonia. By many it has been considered to be due to a specific influence of the pneumococcus toxin on the respiratory centre. If this were the case, however, one would expect it to occur in pneumococcal infections which do not affect the lung.

The dyspnoea in bronchopneumonia as well as the cyanosis is usually of a much different type. The patient frequently complains of very urgent desire for increased pulmonary ventilation, in distinction frequently to the cases of lobar pneumonia in whom the hyperpnoea is not of an urgent character (except probably in the first thirty-six hours), although it may be complicated by the occurrence of pain. The type of cyanosis frequently gives us a clue as to the reason for the urgency of the dyspnoea. It is usual in bronchopneumonia for the patient to exhibit a full purplish colour, in distinction to lobar pneumonia, where the skin is either of a good pink colour or assumes a pale grey hue. This latter type of cyanosis, which is a very serious omen, may occur in the terminal stages of both diseases.

The reason for the urgent dyspnoea and purplish cyanosis in bronchopneumonia is to be found in the fact that there is usually besides an oxygen want also a relative or an absolute carbon dioxide retention (Table II). This has

TABLE II.—*Gases in the Arterial Blood of Cases of Bronchopneumonia.*

No.	Day of Disease.	Oxygen per cent. Saturation of 100 c.cm. of Arterial Blood.	CO ₂ c.cm. vol. per cent. in 100 c.cm. of Arterial Blood.	pH.	Remarks.
1	6th	75.0	70.0		
	6th	98.0	72.0	7.5	On oxygen.
2	6th	85.0	54.0	7.33	
3		79.0	85.5	7.27	On oxygen.
		18.0	85.3		Not on oxygen.
4	9th	93.5	51.0	7.47	
5		97.0	—		
6	10th	90.0	—		
	13th	86.0	53.0		
7	10th	89.0	—		

been amply demonstrated, as will be seen from Table II, and is probably brought about through the following conditions. In bronchopneumonia the inflammatory lesion begins in the smaller bronchioles and extends into the alveoli in an irregular manner. Complete consolidation does not occur in all the inflamed areas. As a consequence a certain amount of circulation persists through damaged alveoli in which the alveolar air is not being properly aerated. This may be due either to a stenosis of the bronchioles, a

swelling of the alveolar epithelium, or an actual exudate into the alveolar spaces. If the first two conditions are the most important an increase of the partial pressure of oxygen in the inspired air may overcome this obstruction to oxygen diffusion by increasing its inward diffusion pressure, and more or less complete oxygenation of the pulmonary blood may result. If, however, the oxygen saturation of the arterial blood is not increased by administration of oxygen it is probable that circulation persists in inflamed areas to which the oxygen cannot penetrate, and venous blood returns to the left side of the heart to pollute the general arterial blood. The same reason which prevents the inward diffusion of oxygen interferes with the outward diffusion of carbon dioxide. Thus there is an absolute retention of carbon dioxide in spite of the increased pulmonary ventilation.

In oedema of the lungs a similar state of affairs occurs. If the oedema be uniformly distributed the epithelium of the alveoli in the greater part of the lungs becomes swollen. There is a serous exudate into the alveolar spaces and a free diffusion of the blood gases is interfered with. Many of these cases exhibit the violent dyspnoea associated with an asphyxial form of respiratory distress and also the deep blue cyanosis which usually accompanies it. Such cases obtain considerable relief by inhaling air sufficiently enriched with oxygen. In some cases the lesion is so serious as to require the oxygen in the inspired air to be increased to 80-90 per cent. It is very gratifying in cases of mitral stenosis in which this pulmonary complication develops to observe the relief and rapid improvement which occurs on the proper administration of oxygen.

DYSPNOEA IN CHRONIC ALVEOLAR LESIONS.

In chronic diseases where damage to the alveoli is the outstanding lesion dyspnoea of a less urgent type is met with. This is particularly so in emphysema. Here the lung through a number of years has gradually lost its elasticity through destruction of the alveolar walls and fibrosis of the interstitial tissue. The total volume of the lungs is greater, but the alveolar surface, therefore the functioning surface of the lung, is decreased. Further, through the lack of elasticity, the normal churning movement which respiration imparts to the air in the lungs is diminished and thus the free diffusion of gases is impaired. The patients suffering from emphysema usually develop a pronounced degree of cyanosis, with comparatively little dyspnoea when at rest. The cyanosis is of a deep purplish colour and is accentuated by the polycythaemia which so frequently occurs in cases of chronic oxygen want. There is also found to be a pronounced change in the alveolar air in these cases. The partial pressure of oxygen is greatly below normal, sometimes diminishing to between 70-80 mm. partial pressure, while that of the carbon dioxide may conspicuously increase.

The chronicity and insidious development of this lesion produces a very good example of adaptation. As the lesion slowly develops carbon dioxide retention and anoxaemia occur. The carbon dioxide retention is compensated for by an increase in the "alkali reserve," so that the blood has a greater capacity for combining with carbon dioxide and at the same time maintaining the normal hydrogen-ion concentration. This condition is probably also reflected in the tissues. In order to compensate for the diminished partial pressure of oxygen in the alveolar air, and also diminished saturation of the arterial blood, polycythaemia occurs, thus increasing the oxygen capacity of the blood. There is at the same time a moderate change in the oxy-haemoglobin dissociation curve, indicating that the blood can take up more oxygen at a diminished partial pressure than normally. This brings about a greater oxygen saturation of the arterial blood than normal at the same partial pressure of oxygen in the alveolar air.

There is also found in cases of emphysema an increased capacity for breathing air enriched with carbon dioxide.² This is shown in experiments where the emphysematous person breathes without discomfort a concentration of carbon dioxide which would produce in a normal individual a pronounced degree of dyspnoea. In the former there is very little increase in rate or depth of respiration until a concentration of 6 to 7 per cent. carbon dioxide is being

inhaled. When, however, symptoms begin to appear the maximal intolerance is rapidly reached. This is probably to be explained by the fact that as soon as any increase in pulmonary ventilation is demanded the lungs are physically incapable of responding, and therefore an acute crisis in the respiratory effort occurs. This probably explains in great part why individuals suffering from emphysema may tolerate changes in their blood gases which a normal person would find the greatest difficulty of enduring, but if a very moderate increase of pulmonary ventilation be demanded it leads to an acute onset of symptoms.

In fibroid phthisis the occurrence of dyspnoea and other respiratory symptoms in a great part depends upon the condition of the lungs at the moment. If there be complete fibrosis of a part with obliteration of the circulation and no surrounding inflammatory area then there may be comparatively few signs of respiratory embarrassment. The condition is very analogous to a complete unilateral pneumothorax. In such cases the lung is completely collapsed, the local circulation through the pulmonary artery has practically ceased, and the healthy lung is sufficient to supply all the needs of the moment. In large areas of fibrosis or partial atelectasis the circulation may continue to some extent. This blood will not be properly aerated, and on joining the general arterial blood it will reduce the oxygen saturation and increase the carbon dioxide content of the latter. The severity of the dyspnoea and other symptoms which result will depend upon the proportion in which the aerated blood be diluted with non-aerated blood. Similar conditions occur in extensive pulmonary tuberculosis.

DYSPNOEA DUE TO NERVOUS LESIONS.

Reference has already been made to the character of dyspnoea which appears to result from a disturbance of the normal respiratory reflex. In normal respiration the inspiration and expiration are initiated at certain intervals, thus producing normal depth of respiration, which is increased if there be a demand for increased ventilation. If the respiratory reflex be upset the inspiration and expiration become abnormally short, and on increased demand either remain so restricted or become more so. Therefore increased ventilation is accomplished by an increase of rate rather than of depth. This condition can be simulated in animals by the production of minute pulmonary emboli, by damage to the alveoli by irritant gases, etc. In man pulmonary infarcts, which in themselves are not large enough to produce any interference with respiration, may produce this peculiar disturbance of the respiratory rhythm. It is also significant that it is practically always associated with lesions occurring in the capillaries or the alveoli. It would appear that the pulmonary reflex becomes intolerant of more than a very restricted pulmonary expansion. The result is that in spite of increased total ventilation of the lungs, signs develop which are indicative of deficient respiratory function.⁴ This has been explained on the hypothesis that the ventilation is not uniform, many alveoli being poorly ventilated while others may be excessively so. The excessive ventilation of certain alveoli allows for an abnormal removal of carbon dioxide. This excessive removal compensates for the diminished removal of this substance in the poorly ventilated alveoli. The small increase in the oxygen saturation is insufficient to compensate for the desaturated blood coming from the poorly ventilated area. As a consequence a certain degree of arterial anoxaemia may result. It is probable that this type of respiration plays a very important role in the disturbed respiratory function of lobar pneumonia and other pulmonary lesions.

On the other hand, there is evidence that this type of breathing may be the result of either psychological or central causes. It is the typical dyspnoea which occurs in cases of neurasthenia and in convalescence from disease. In these conditions the normal reflexes are preternaturally hypersensitive and in a very irritable condition. As the nervous equilibrium becomes established this dyspnoea disappears and the individual may return to normal condition. If, however, there be anything which perpetuates the neurasthenic state this type of breathing remains. In hysteria cases of very abnormally rapid respiration sometimes occur—in fact, it is within most people's experience to see cases of

hysteria with a respiratory rate of 100 or more. In some of the more aggravated of these, pronounced cyanosis appears and collapse may result. In these cases the respiratory rate as a rule returns to normal during sleep, or hypnosis, and very probably is not present when the individual considers himself alone. The exact mechanism of the disturbance of such reflexes is not at present satisfactorily explained.

In cases of encephalitis lethargica pronounced disturbances of respiration occur. These are quite independent of any local pulmonary lesion as far as can be determined. In a case of encephalitis lethargica reported by Harrop⁵ the respiratory rate ranged between 40 and 50 a minute, the arterial oxygen saturation was 80 per cent., but contained only 25 per cent. by volume of carbon dioxide, and there was a pronounced increase in the arterial pH, it being 7.59. As Harrop states, it is evident that the condition was one of uncompensated carbon dioxide deficit, due to the rapid shallow breathing which had produced an abnormally great pulmonary carbon dioxide excretion, with an increase in the ratio $\text{BHCO}_3 : \text{H}_2\text{CO}_3$, and therefore in the pH. This explanation seems quite logical, and the excessive removal of carbon dioxide as compared with the absorption of oxygen is to be explained by the greater diffusion constant of carbon dioxide as compared with oxygen. At post-mortem examination it was found that there was an extensive pulmonary lesion which in some respects resembled the lesion of early influenzal pneumonia. We have found in these cases that instead of an excessive carbon dioxide elimination there is generally a carbon dioxide retention. The only exceptions are those cases where the extent of the pulmonary lesion is insignificant as compared with the healthy portion from which a large quantity of carbon dioxide may be removed by means of the excessive ventilation.

Contrary to the case recorded by Harrop, Barach and Woodwell⁶ have reported two cases of encephalitis lethargica in whom the respirations were between 40 and 50 a minute and of pronouncedly shallow character. The patients breathed in a jerky manner and there was evidence which suggests a paralysis of the respiratory muscles. In both these cases there was extreme cyanosis, the arterial blood was 61 to 65 per cent. saturated with oxygen, and in one case contained 62 volumes per cent. of carbon dioxide and in the other 51 volumes per cent. On the administration of oxygen the oxygen saturation of the arterial blood increased in the first case to 85 per cent. and in the second case to 82 per cent., while the carbon dioxide content increased to 88 per cent. and 62 per cent. In both of these cases there was, in addition to very pronounced arterial anoxaemia, a carbon dioxide retention. The administration of oxygen to some extent relieved the anoxaemia but also brought about an increase of the carbon dioxide content. In the second case, from the carbon dioxide dissociation curve it was demonstrated that there was an uncompensated carbon dioxide acidosis, pH 7.22.

It is obvious that the case reported by Harrop and those reported by Barach and Woodwell, although similar in certain characteristics are quite dissimilar in others. In the cases of Barach and Woodwell the carbon dioxide retention may be explained on the grounds that there was probably a paralysis of the respiratory muscles. If this were the case their results would be quite intelligible, in that very inadequate pulmonary ventilation was taking place in spite of the increased respiration rate. As a consequence the air in the greater part of the lungs was remaining in a stagnant condition. The administration of oxygen would increase the partial pressure of this gas into the alveoli and thus to some extent relieve the arterial anoxaemia, but would have no effect on the carbon dioxide retention. In the first case reported by Barach and Woodwell the respirations slowed from 45 to 34 during oxygen administration, and it was in this case that the greatest increase of carbon dioxide retention occurred. This could be explained by an absolute decrease in the demand for pulmonary ventilation due to the partial removal of the anoxaemia. In the second instance it is not easy to explain the carbon dioxide increase in the same manner, as the respiratory rate remained comparatively constant.

This now brings us to consider the respiratory function when there is a paralysis of the respiratory muscles due to a

spinal lesion. The conditions which ensue are very analogous to those which occur with increased respiratory resistance. There is an inability of the respiratory muscles to ventilate the alveoli adequately, and thus a pronounced degree of arterial anoxaemia and carbon dioxide retention occurs. The oxygen want can be to some extent overcome by the inhalation of oxygen, but the increased elimination of carbon dioxide cannot be accomplished. If relief of the spinal lesion can be expected within a reasonable time, properly controlled methods of artificial respiration may be instituted in order to reduce the uncompensated carbon dioxide acidosis which is apt to occur. This may be helped in some degree by the administration of alkalis in large quantities.

TREATMENT OF DYSPNOEA.

The treatment of dyspnoea in pulmonary diseases is very unsatisfactory unless the cause can be removed. In cases of respiratory obstruction, laryngeal diphtheria, or asthma, the first object to be attained is removal of the obstruction. If this be accomplished the relief is extremely prompt, as when the bronchial spasm is relieved in asthma by the administration of adrenaline.

We have at present few drugs which we know from actual observation relieve the dyspnoea which occurs in many pulmonary lesions. The evidence upon which respiratory stimulants are given is at present very scanty, and there is comparatively little proof to indicate that they are at all efficacious. On the other hand, the proper use of oxygen and carbon dioxide is of the greatest importance. In all acute cases which show any degree of cyanosis oxygen should be administered promptly and in sufficient quantity. This can only be done if proper methods are employed. The use of the so-called funnel method is to be condemned, as the quantity of oxygen allowed to pass through the funnel is usually ludicrously inadequate, and there is evidence to prove that it does not enrich the inspired air. On the other hand, the use of properly fitting masks and the regulation of the amount of oxygen given, or the use of a nasal catheter with a similar control, gives very good results (Table III).

TABLE III.—Showing the Effect of Oxygen Administration on the Cerebral Symptoms in Cases of Lobar Pneumonia with Lowered Oxygen Saturation of the Arterial Blood.

No.	Inspiring Air enriched with Oxygen.	Oxygen per cent. Saturation of 100 c.cm. of Arterial Blood.	Cerebral Symptoms.	No.	Inspiring Air enriched with Oxygen.	Oxygen per cent. Saturation of 100 c.cm. of Arterial Blood.	Cerebral Symptoms.
1	—	83	Slight delirium.	3	—	80	Semi-comatose.
	—	82	Delirious.		+	94	Quite rational.
	+	91	No delirium.	4	—	84	Delirious.
	+	92	No delirium.		+	90	Slight delirium.
	—	84	Very restless.	5	—	81	Semi-delirious.
	+	97	No delirium.		+	93	No delirium.
2	—	89	Restless.	6	—	79	Delirious.
	+	98	Very comfortable.		+	98	No delirium.

The ideal, of course, would be to place the patient in an atmosphere rich in oxygen without the disturbance and discomfort of the mechanical appliances already mentioned.

Up to the present sufficient attention has not been given to the therapeutic use of carbon dioxide. In many cases it might be expected that a pronounced decrease in the carbon dioxide content of the arterial blood and of the tissues occurs, as in the case reported by Harrop. In such instances the administration of carbon dioxide after a proper manner would most probably have very beneficial results. The work of Yandell Henderson and Haggart on the acapnoea which they have shown follows upon operative and other procedures needs thorough clinical investigation.

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³ Scott: *Arch. Int. Med.*, 1920, xxvi, 544. ⁴ Haldane, Meakins, and Priestley: *Journ. of Physiol.*, 1919, lii, 420. ⁵ Harrop: *Journ. Amer. Med. Assoc.*, 1923, lxxxi, 452. ⁶ Barach and Woodwell: *Arch. Int. Med.*, 1921, xxviii, 421. ⁷ Sharpey Schafer: *Quart. Journ. Exper. Physiol.*, 1919, xiii, 251.

A COMPARISON OF THE KAHN AND WASSERMANN TESTS ON 500 SERUMS.

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THE Wassermann test for syphilis is so complicated that it can only be carried out by a highly trained and skilled pathologist working in a well fitted laboratory. Many workers have attempted, with varying success, to produce a simpler test which should be more delicate and reliable, and Kahn, in America, evolved a "precipito-agglutination" test¹ which, in its recent modification,² seems to combine simplicity, brevity, and delicacy. Antigen and serum are mixed in varying given proportions and shaken, and the reading made; after a short period of incubation it is shaken again and a final reading taken.

It was considered that it would be of interest to compare this test with the Wassermann test in a series of serums from cases of treated and untreated syphilis and non-syphilitic cases. Accordingly 500 serums were taken at random from the Venereal Diseases Clinic at St. Thomas's Hospital; in no instance was a patient seen by the authors, and no analysis of results was attempted until the series was complete.

The Wassermann test performed was No. 1 method Medical Research Council (Report Series No. 14), the routine test in this laboratory. The Kahn test was modified slightly from that described,² and the technique was as follows:

1. *Preparation of the Antigen.*³—"Fresh beef heart is freed from fat, fibre, and blood vessels, and passed several times through a meat chopper. It is then spread in a thin layer on a porcelain platter and dried by means of a revolving fan. The dried material is broken into small particles and passed three times through a coffee grinder. Fifty grams of the dried heart muscle is then placed in a 500 c.cm. Erlenmeyer flask; sufficient ether is added to cover the dried material with an inch of fluid and it is placed in the ice-box. After twenty-four hours' extraction the supernatant ether is yellowish; it is then poured off and replaced with fresh ether. This is repeated daily for three days. On the fourth day the supernatant ether is water-clear. The ether is then filtered off and the ground muscle spread on paper and dried at room temperature until no odour of ether is detectable. This requires several hours' drying. To 20 grams of this material 100 c.cm. of absolute alcohol is added and the whole extracted for nine days in the ice-box and a day at room temperature. After this period the alcoholic extract is filtered off. A total of 70 c.cm. of alcoholic antigen is usually thus obtained." Four milligrams of cholesterin are added to each cubic centimetre of alcoholic antigen.

2. *Titration of the Antigen.*—This was carried out as described by Kahn, though the reading did not appear so simple as suggested. It seemed, however, to be satisfactory to use equal parts of antigen and saline with each of the two antigens employed.

3. *The Test Proper.*—Tubes and racks, as for the Wassermann test, were employed. Pipettes were made by drawing out glass tubing and calibrating with mercury, marks being made with grease pencil to indicate volumes of 0.15, 0.05, 0.025, and 0.0125 c.cm. No doubt these could be obtained from an instrument maker, but they can easily be made by any pathologist. The same pipette is used throughout any given batch of tests. Three rows of tubes are set up, three tubes for each test. Into each tube of the first row is introduced 0.05 c.cm. of diluted antigen (obtained by pouring an equal quantity of 0.85 per cent. NaCl solution on to the neat antigen and inverting the tube several times), the point of the pipette being placed on the bottom of the tube. Similarly each tube of the second row receives 0.025 c.cm. of antigen, and of the third row 0.0125 c.cm. The three tubes for each test then receive 0.15 c.cm. of the patient's serum previously heated to 56° C. for half an hour. Controls are set up with antigen and saline instead of serum. The racks containing the tubes are then shaken vigorously for three minutes (either by hand or by fixing the rack to a vaccine shaker) and a preliminary reading is then taken. This is carried out with the aid of an X6 hand lens and a reading apparatus, as described by Dreyer and Ward for the Sigma test.⁴ (An ordinary electric light with a black shade answers the purpose quite well.) The tube to be examined is held nearly horizontally in front of the black background, behind which is the light, and examined with the lens, the tube being moved slightly to set up a movement in any granules which may be present. After this preliminary reading all racks are placed in a water-bath at 37° C. for one hour, again shaken for one minute, and then read a second time.