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*J Clin Invest.* 1932;11(6):1321-1341. <https://doi.org/10.1172/JCI100480>.

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## STUDIES ON CHEYNE-STOKES RESPIRATION

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(Received for publication June 6, 1932)

### PART I

#### CHANGES IN CONCENTRATION OF GASES IN THE BLOOD

Cheyne-Stokes respiration is characterized by rhythmic changes in breathing in which periods of respiratory pause alternate with periods of slowly increasing and decreasing respiratory activity. It may be accompanied by phasic variations in the functions of the heart, nervous system and other organs, and has more recently been found to be associated with periodic variation in the concentration of the gases in the blood. It occurs as a symptom in diseases of the heart and kidneys especially, in meningitis and in encephalitis, and in certain intoxications such as morphine poisoning and oxygen lack. The development of this type of breathing has been ascribed to many causes—disturbances in the gaseous exchange in the lungs, of the circulation, of the activity of the respiratory and vasomotor centers and to so-called sub-cortical influences. Objections to all these hypotheses have been entered with the result that no satisfactory understanding of the subject has been attained. It is of value, therefore, to record further observations of Cheyne-Stokes respiration and its attendant or resultant phenomena.

The phenomenon concerning which it seems now important to accumulate more experience, is the behavior of the gases, carbon dioxide and oxygen, in the blood under the circumstances which attend this type of respiration. For this purpose, samples of arterial blood taken from patients exhibiting this abnormality were studied. A few analyses of arterial blood have already been reported by Gollwitzer-Meier (1), Uhlenbruck (2), and Resnik and Lathrop (3). Their studies show that variations in the concentration of the gases in the blood do occur during different phases of respiration<sup>1</sup> and that at some point during the respiratory cycle, oxygen saturation of the blood usually reaches normal limits. The average carbon dioxide content in the blood is reported in some cases to be increased, in others decreased, and in others normal. In former studies only one or two samples of blood were, however, taken; but in order to ascertain the extent of the variation in the concentration of the gases in the blood during a cycle of Cheyne-Stokes respiration it is

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<sup>1</sup> In this paper the Cheyne-Stokes *cycle* is described as divisible into a respiratory *phase* and an apneic *phase*.

necessary to collect from a continuous flow of arterial blood, separate, immediately successive samples as rapidly as possible. For this purpose a needle of the type usually used in puncturing arteries was connected with a nine-way stopcock.<sup>2</sup> With its aid, samples could be rapidly obtained. A somewhat similar method has recently been published by Klein (4). The blood was collected under liquid paraffin; the oxygen and carbon dioxide content were estimated by the method described by Van Slyke and Neill (5), and the hydrogen ion concentration according to that of Hastings and Sendroy (6).

Two patients were selected for study in whom Cheyne-Stokes respiration was observed in the hospital over a period of several months, and who, because of decreased mental activity, were not disturbed by the procedure of arterial puncture. A long period of observation was regarded as important in order to be certain of the continuous presence of this type of breathing. As is well known, there are cases in which Cheyne-Stokes breathing occurs in a transient manner, as for example in cases of heart failure and morphine poisoning or in normal individuals during a sojourn in rarefied air. Since the transient type may be distinct from the continuous, it is unknown at present whether the results of the observations now reported are applicable to cases of Cheyne-Stokes respiration in general.

*Case I.* The first patient, S. H., male, aged 52, Hospital number 7599, was admitted to the hospital on December 5, 1930. The diagnosis was hypertension and cardiac insufficiency. After a long period, during which he was kept under the influence of digitalis and was obliged to rest in bed, he gradually improved. For about three months before discharge the periods of Cheyne-Stokes respiration had been constantly present; but for the last three weeks, after considerable betterment, they had become intermittent. He then left this hospital.

In the only study made of this patient four samples of blood were taken, the oxygen contents of which varied between 15.1 and 18.5 volumes per cent (79.9 and 98.2 per cent of saturation), while those of the carbon dioxide varied between 42.2 and 50.1 volumes per cent. The number of samples was too small and the time during which they were taken was, in the case of each sample, too long to construct a curve, but the results are shown schematically in Figure 1. They give only an approxi-

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<sup>2</sup> This stopcock was made of glass and first used in January 1931. Blood entered through an opening in the bottom of the center plug emerging on the side. Eight perforations through the jacket in a circle at the level of the opening in the center plug lead by rubber connections to openings into the lower ends of the glass sample tubes. The sample tubes are held by a stout rubber band against the outer surface of the jacket. The whole apparatus is then filled with paraffin oil. By revolving the jacket with the sample tubes fixed to it, the tubes can be successively and rapidly connected to the arterial needle or cannula.

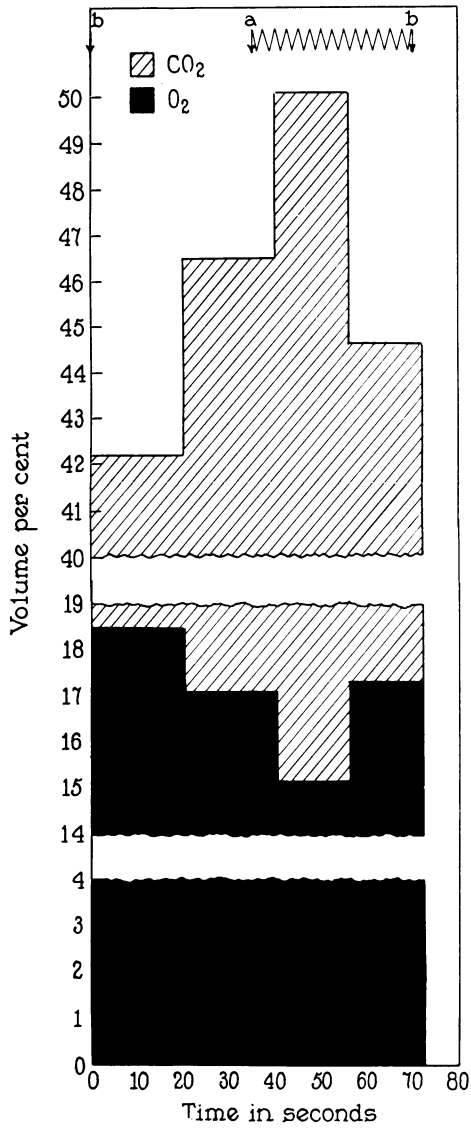


FIG. 1. CHART OF THE VARIATIONS IN CONCENTRATION OF OXYGEN AND CARBON DIOXIDE IN BLOOD OBTAINED FROM THE RADIAL ARTERY DURING A CYCLE OF CHEYNE-STOKES RESPIRATION (CASE I).

Arrows "a" mark the onset of dyspnea, arrows "b" the onset of apnea.

mate account of what the course of events must have been. The true maxima and minima were undoubtedly greater than the levels actually obtained in the samples, but whatever their magnitude they were probably attained within the period of time during which the samples characterized by the extreme values were collected. The greatest oxygen concentration was found to occur during the first half of apnea. It decreased during the second half of apnea and the first part of the respiratory phase, wherein it reached its minimum and began to increase again. The maximum was reached as before at the beginning of apnea. The concentration of carbon dioxide varied in an inverse direction. The mean concentrations of both gases occurred at about the beginning of the respiratory phase and either mean concentrations or values between this level and the maximal oxygen and minimal carbon dioxide concentrations occurred at the end of the respiratory phase.

*Case II.* In the second patient, S. G., male, aged 56, Hospital number 7745, admitted April 24, 1931, there had developed first right, then left hemiplegia several years before admission. Pareses of all the extremities, and aphasia still persisted. Arterial hypertension was present, but there were no signs of cardiac insufficiency. In the first study (Figure 2) four samples of blood during a single cycle were secured, and one sample during the whole of the next succeeding one. By superimposing the results obtained during the first cycle upon those of the second, it becomes obvious that the longer the time consumed in collecting a single sample, the greater the deviation of the values found from what must have been the actual or extreme values. The oxygen content varied only between 16.1 and 16.9 volumes per cent (89.1 and 93.0 per cent of saturation) and the carbon dioxide between 40.8 and 45.6 volumes per cent. That in this instance the range of variation in the concentration of the gases in the blood was so much less than in Case I may have been due to the fact that the phases of apnea and dyspnea were shorter. The oxygen minimum lay, however, at the same point as in Case I, but the maximum was found to fall, not in the first part of the apneic phase but during the last few respirations. Respiration therefore stopped when maximal oxygen and minimal carbon dioxide concentrations were reached, while it began when they attained mean values. The oxygen content, furthermore, decreased more slowly than it increased. The hydrogen ion concentration of the blood varied with the changes in concentration of the gases, reaching the peak of acidity (pH 7.40) at the time of the carbon dioxide maximum, and decreasing to pH 7.44 at that of the carbon dioxide minimum.

In the second study of this patient (Figure 3), eight samples of blood were taken during two cycles of Cheyne-Stokes breathing. The oxygen content varied between 16.6 and 18.2 volumes per cent (83.7 per cent and 98.7 per cent of saturation), the carbon dioxide between 40.5 and

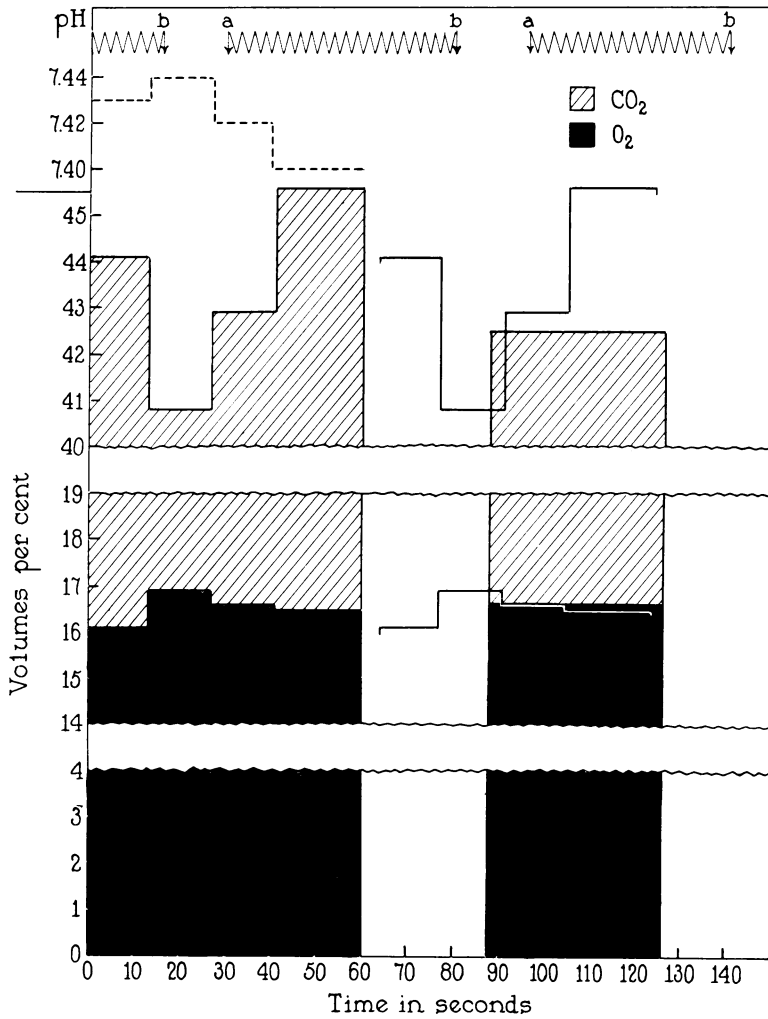


FIG. 2. CHART OF THE VARIATIONS IN CONCENTRATION OF OXYGEN AND CARBON DIOXIDE IN BLOOD OBTAINED FROM THE RADIAL ARTERY DURING A CYCLE OF CHEYNE-STOKES RESPIRATION (CASE II).

A fifth sample of long duration obtained during the next succeeding cycle illustrates the "leveling" effect. The solid line represents the changes in gases of the blood found during the first cycle reproduced in chronological relation to the second cycle. The broken line traces the change in hydrogen ion concentration.

45.4 volumes per cent. That these changes were greater than those obtained on the previous occasion may have been due to the greater length of the Cheyne-Stokes cycles, or to the shorter time during which each sample was collected. The time at which carbon dioxide was at its maximum and oxygen at its minimum bore the same relation to the

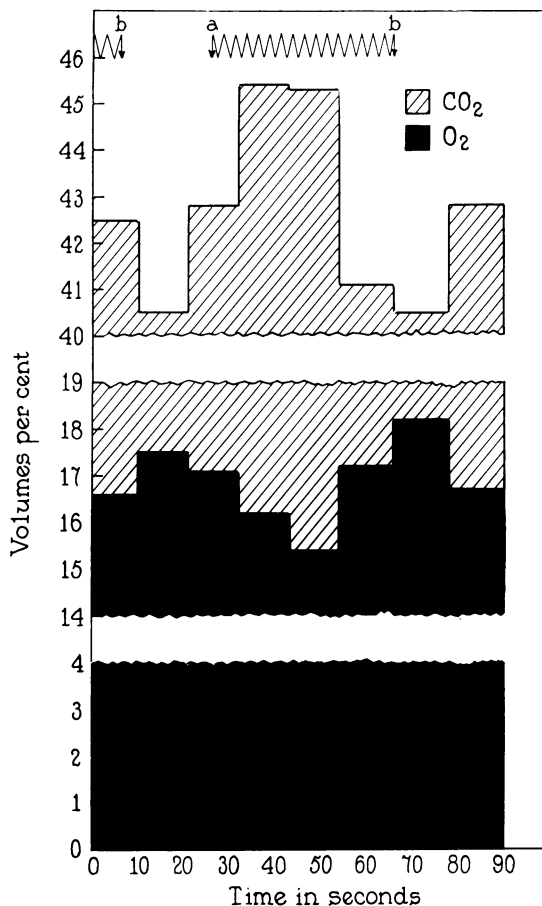


FIG. 3. CHART OF THE VARIATION OF THE GASES IN BLOOD OBTAINED IN A LATER STUDY ON THE PATIENT SHOWN IN FIGURE 2.

respiratory cycle as in the previous observation in this patient. The oxygen maximum lay in the first part of apnea. Concentrations of both gases were approximately near the mid-level when the respiratory phase began. In this study too, oxygen concentration decreased and carbon dioxide concentration increased more slowly than these increased and decreased respectively.

## DISCUSSION

In these observations the minimal concentration of oxygen in blood taken from the radial artery occurs constantly during the respiratory phase of the Cheyne-Stokes cycle, and the maximum at the end of this phase, or at the beginning of apnea. The maximal and minimal concentrations of the carbon dioxide occur at the time of the minimal and maximal concentrations respectively of oxygen. Similar results have been reported by Klein (4).

In order to set forth accurately the relations in time between the Cheyne-Stokes cycle and the concentration of gases in the blood leaving the lungs, one must recall the fact that any given concentration at this site precedes its arrival at the radial artery by the time of transmission, which being but two or three seconds, changes the relations only by insignificant amounts. By referring to Figure 3, it becomes apparent that the first few small respirations have little effect on the gases of the blood. The peak of saturation with oxygen is attained, moreover, just before or immediately upon the end of respiration, and indicates that the last few respirations also are quite ineffective.

Because of the different conditions attending the exchange of oxygen and of carbon dioxide between blood and lungs, the changes in their concentrations, though always opposite in direction, are not always inversely proportional. Aside from this relation, the amount of each gas present influences, as is well known, the concentration of the other. The question arises, therefore, how far the concentrations of gases in the blood are determined by variations in alveolar tension, and how far by the varying concentrations of the gases present in the blood itself. This problem has its importance, but the facts which are known are insufficient to analyze the processes which are involved.

The concentration of hydrogen ions in the blood shows changes consistent with the variations found in that of carbon dioxide. These variations are, however, relatively speaking small, due to the presence of the usual buffers of the blood. Since it is known that hemoglobin takes up one half molecule of carbon dioxide for each molecule of oxygen lost, without change in hydrogen ion concentration, the actual range of variation is still smaller than might be expected because decrease in oxygen takes place simultaneously with increase in carbon dioxide.

If changes in concentration of gases or of hydrogen ions in the blood control phases in the Cheyne-Stokes cycle, the levels of their various concentrations at the beginning of the respiratory phase take on new significance because it is at this point that, considered collectively as a stimulus, they may be assumed to have reached the threshold value of the respiratory center. Should this suggestion concerning the chain of events be correct, it would afford in man an opportunity to ascertain the threshold value of the respiratory center. The importance of know-



ing this value lies in the fact that it indicates a definite stage of irritability, readily discerned by a change from inactivity to activity in the organs controlled by the center. If the composition of the blood which is taken from the radial artery is identical with that which arrives at a corresponding time at the respiratory center (due regard being paid, of course, to differences in distance and in the nature of the arterial channels), the threshold of irritability of the respiratory center to carbon dioxide and oxygen lies at about the mean concentration of these gases in the blood, and also at the mean value of the hydrogen ion concentration, between pH 7.40 and 7.44. The last respiration may be a sign, furthermore, that the stimulus derived from the concentration of the gases in the blood has fallen below the threshold value. The impression has been gained in the course of these observations that the threshold changes; that it is lower when the intensity of the stimulus derived from the blood is decreasing than when it is increasing. The problem of the function of the respiratory center with regard to stimuli of increasing and decreasing strength has been so little studied that for the moment further discussion seems unprofitable.

From studies of the analyses of the gases in the blood alone, an explanation of the mechanism of Cheyne-Stokes respiration is not to be expected. For this reason objections may be raised to the conclusions of Klein. His observations and the results he obtained from them are, however, in close accord with those now described. By locating, in the phases of the Cheyne-Stokes cycle the instants of maximal and minimal saturation of oxygen in blood taken from the radial artery, he demonstrated that the oxygen saturation was lowest at about the height of dyspnea and greatest at the beginning of apnea. He then showed, by means of injections of Congo-red into an arm vein that, in patients with Cheyne-Stokes breathing, 18 to 22 seconds passed before the dye appeared in the radial artery, while in normal individuals only 8 to 12 seconds were required. From the increased time of flow he calculated the time at which the blood in the lungs would be most and when least saturated with oxygen. Maximal saturation (in the lungs) occurred at or just before the height of the respiratory phase, but breathing continued until blood saturated with oxygen arrived at the respiratory center. Respiration then stopped. The response of the respiratory center delayed by the slow rate of circulation shown by the experiments with the dye with respect to conditions at the site of ventilation (the lungs) he terms "Nachhinken." After complete saturation of the blood in the respiratory phase, over-ventilation, he believes, occurs with loss of carbon dioxide. Apnea then follows. If the time required for blood to flow from lungs to center is so important a factor as believed by Klein in maintaining periodicity of respiration, changes in the rate of flow should alter the length of the respiratory cycles. But this relation does not exist. If it

did, the breathing of normal persons should be periodic in character, the cycles, of course, being shorter since the time required for their blood to reach the respiratory center is but half that found by Klein in Cheyne-Stokes respiration. There are, besides, cases in which the time of flow is prolonged without bringing on Cheyne-Stokes respiration. If a decreased rate of flow were, moreover, responsible for cyclic breathing, the method by which the cycles should disappear is by becoming shorter and shorter. This, however, is not the case in our studies. When increased concentrations of carbon dioxide were administered during Cheyne-Stokes respiration, the cycles remained of about the same length and their disappearance was occasioned by gradual decrease in the intensity of the mid-point of the respiratory phase and by the gradual encroachment of this phase upon the phase of apnea. When, on the other hand, oxygen was administered, the cycles attained twice the usual duration. There is no evidence at hand, however, to show that the circulation time is prolonged by oxygen. Uhlenbruck also speaks of "Nachhinken" of the respiratory center as a result of local difficulties in circulation or in the diffusion of gases.

If, instead of assuming that the time of arrival of blood at the respiratory center and at the radial artery are simultaneous, various intervals of time are assumed and the resulting relations between the beginning of respiration and the concentrations of gases in the blood at the respiratory center are examined, it becomes possible to distinguish on a curve representing changing values of the stimulus of the blood, which portion is capable of arousing the respiratory center. In these observations at the beginning of the respiratory phase the blood in the radial artery was found to have a composition represented on this curve by "a" (Figure 4). Should blood leaving the lungs at the same time, and having the same composition, not arrive at the respiratory center until, for example, about 15 seconds later, it would have the same composition as that obtained from the radial artery 15 seconds before the respiratory phase began, that is to say, one similar to "b"; or, should the difference in time be greater, a composition similar to "c" or "d." But these assumptions are all physiologically improbable since blood of low carbon dioxide concentration, having weak stimulating value, would then be associated with respiratory activity, while that of much greater concentration of carbon dioxide, with apnea. On this calculation the arrival of blood of identical composition at the radial artery and at the respiratory center cannot differ by more than 10 or 15 seconds.

Should blood from the capillaries of the lungs take, for example, about 15 seconds to reach the radial artery, it would have at the beginning of respiration the same composition as that obtained from the radial artery 15 seconds after respiration began, that is to say a composition similar to "b'" (Figure 4). But this relation is likewise physiologically

improbable because the blood in the lungs would then exhibit the effects of ventilation (decrease in content of carbon dioxide) before respiration began. Such a situation is illustrated in Figure 4 where "b'" would necessarily represent the blood in the lungs at the beginning of the respiratory phase if it took as long as 15 seconds to reach the radial artery. The interval of time cannot be greater than this in our observations. From the location of these limits it becomes apparent that the values actually found to be associated with the onset of the respiratory phase lie in the mid-zone of the portion of the curve which is capable of arousing the respiratory center.

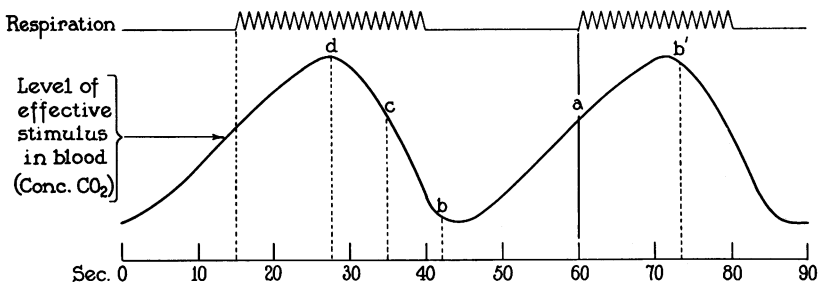


FIG. 4. SCHEMATIC REPRESENTATION OF VARIOUS RELATIONS OF THE LEVEL OF STIMULUS IN THE BLOOD (CONCENTRATION OF CARBON DIOXIDE), TO THE PHASES OF THE CHEYNE-STOKES CYCLE.

The time relations as drawn are based on the composition of blood obtained from the radial artery. Imagine the respiratory curve shifted to the right so that the beginning of the respiratory phase falls at  $b'$ , 13 seconds after  $a$  instead of at  $a$ , in order to obtain the relation between blood in the capillaries of the lungs to the phases of respiration if the time of blood flow from lungs to radial artery were as great as 13 seconds: or to the left to  $b$ ,  $c$  or  $d$ , in order to obtain the relation between blood in the respiratory center and the phases of respiration if blood took 18, 25 or 32 seconds longer to reach the medulla than the radial artery.

#### SUMMARY

By collecting a series of samples in immediate succession and during the briefest periods consistent with securing amounts sufficient for analysis from the continuous stream of blood flowing from the radial artery, it has been possible to analyze the influence of Cheyne-Stokes breathing on the concentration of the gases in the blood.

In the blood drawn from the radial artery, maximal oxygen and minimal carbon dioxide concentrations occur during the end of the dyspneic or first part of the apneic phase. The minimal oxygen and maximal carbon dioxide concentrations occur during the earlier part of the respiratory phase. At the beginning of active respiration, the gas concentrations lie at about a mean value.

## PART II

## OBSERVATIONS ON THE EFFECT OF INHALING OXYGEN AND CARBON DIOXIDE

Oxygen lack of the respiratory center is often regarded as the cause of Cheyne-Stokes breathing. This condition is ascribed in some cases to a lack of oxygenation of the blood in the lungs, in others to anoxemia produced by undue slowing of the general or local circulation, and in still others to difficulty in the passage of blood in the respiratory center. Opinions such as these are based on observations of Cheyne-Stokes breathing in normal persons at great elevations above sea level, on Cheyne-Stokes respiration brought about by the inhalation of gas mixtures low in oxygen and on clinical investigations of persons exhibiting the Cheyne-Stokes syndrome. The theory is supported, furthermore, by reports of improvement in condition following the administration of oxygen. Several authors (7, 8) have described cases in which Cheyne-Stokes respiration was brought to an end and regular breathing reestablished by the inhalation of oxygen as well as by the inhalation of carbon dioxide. Recently, Uhlenbruck (2) reported that the result with oxygen was transient, regular breathing occurring during the first few moments of administration only. Because the theory of oxygen lack is important both in attempting to analyze the nature, and in the therapy of Cheyne-Stokes respiration, its effect on the form of Cheyne-Stokes breathing was studied in detail.

The administration of oxygen was effected in some instances by inhaling from a mask connected through a rubber bag with an oxygen tank, in others, by enclosing the patient in an oxygen tent. The most satisfactory method was to place the patient in an oxygen chamber. We place special emphasis on the long duration of observation which the last mentioned method permits. Observations made when a mask is used are unsatisfactory because of increase in the dead space and the consequent possibility of rebreathing carbon dioxide, and also because of the danger of leak about the mask. Another objection results because patients sometimes change the type of breathing when a mask is applied to the face. Records of respiration were made by a Marey tambour connected by tubing with two rubber bags held in place against the chest by a canvas belt. The transmission was by air. The lever of the tambour wrote in ink on glazed paper moved by a revolving drum. The tracings were used only in calculating time relations; for volumetric measurements they were useless. To secure volume curves a Roth-Benedict spirometer and mask were used. The objections to this method are the same as those mentioned above. A more serious objection, due to progressive decrease in oxygen content of the gas in the spirometer, was overcome by increasing the total volume of the apparatus to about 20 liters. This large capacity was obtained by joining several large glass

bottles in series in the respiratory circuit. Oxygen variations under these conditions were less than 3 per cent.

Before the administration of oxygen, records were made of the patients in room air over a period of several hours. In some patients Cheyne-Stokes breathing persisted continuously during this period; in others, it alternated with periods of regular respiration. Transitions between the two were frequently observed in passing between the waking and the sleeping state (Figures 5*a* and *b*). In studying the effect of inhalation

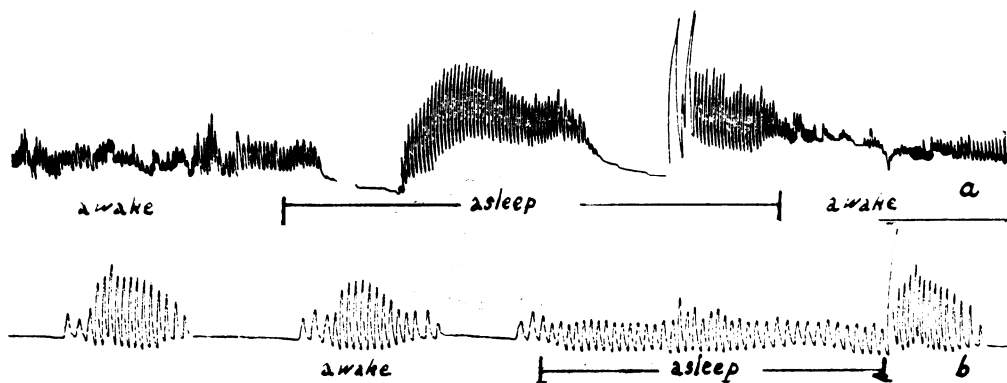


FIG. 5. KYMOGRAPHIC TRACINGS OF TRANSITION TO (a) CHEYNE-STOKES RESPIRATION ON FALLING ASLEEP AND (b) IN ANOTHER INDIVIDUAL TO CONTINUOUS BREATHING ON FALLING ASLEEP.

In this figure as well as in Figures 6, 7, 8, 9 and 12 the tracings have been reduced to four-fifths of their original size.

of oxygen only patients who were subject to continuous Cheyne-Stokes breathing were observed, except one in whom this type of breathing was present constantly while he was awake.

Carbon dioxide was first administered to some patients in order to secure curves to be used in comparison with those obtained when oxygen was used. Inhalation of 5 per cent carbon dioxide by mask stopped the occurrence of apneic phases after two minutes; only the frequency of respiration then showed periodic variations. As soon as carbon dioxide was withdrawn, Cheyne-Stokes respiration recurred. No after effects suggesting exhaustion of the respiratory center appeared. In an experiment of long duration, carbon dioxide was administered in a gas-tight chamber in which the gas could be slowly increased and accurately analyzed, and in which the oxygen content was maintained practically constant. By this means the details of the onset of continuous breathing were recorded. A period of control is illustrated in Figure 6*a*. When the carbon dioxide content reached one per cent, the respiratory phases began to increase in duration (Figure 6*b*) while the apneic phases became

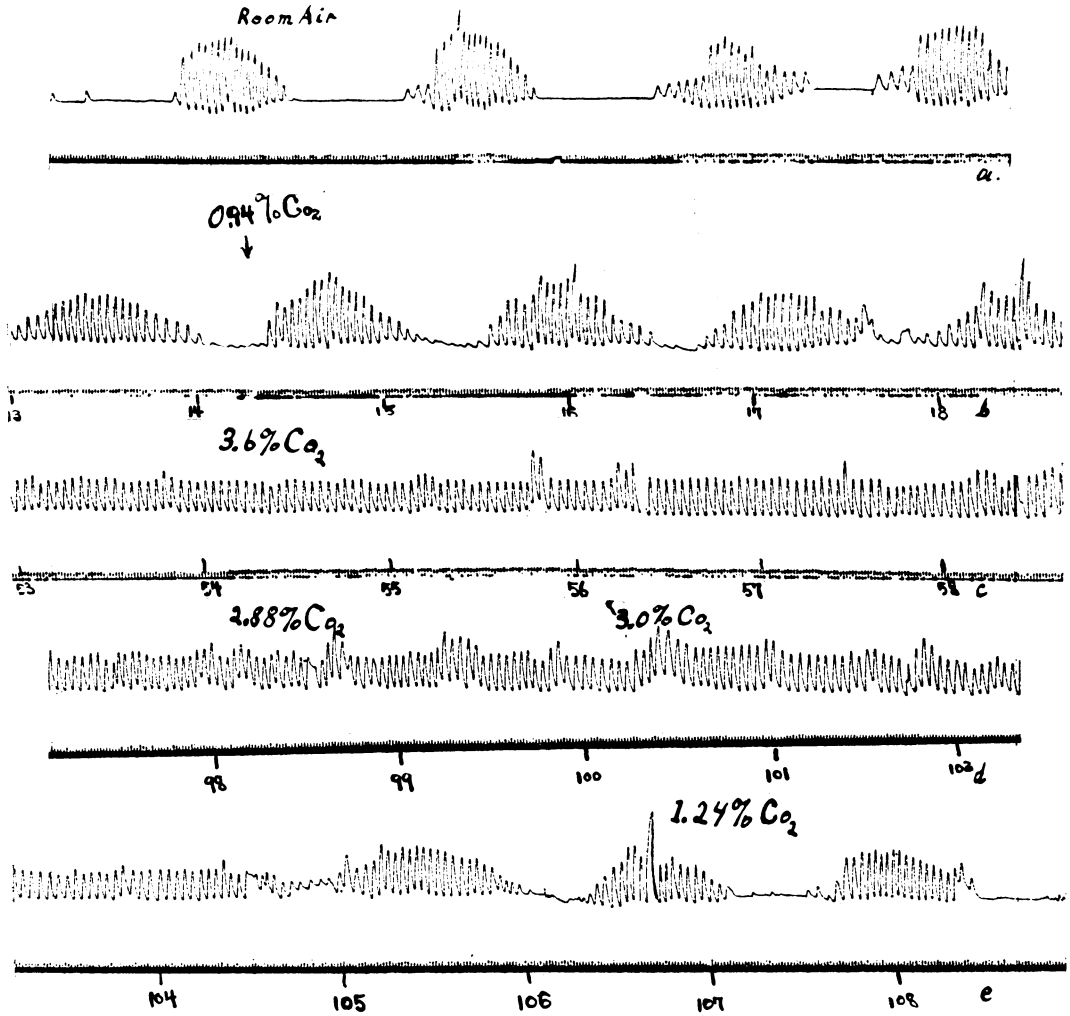


FIG. 6. TRACINGS OF CHANGES IN FORM OF RESPIRATION SHOWING THE GRADUAL DEVELOPMENT OF CONTINUOUS BREATHING DURING THE INHALATION OF INCREASED AMOUNTS OF CARBON DIOXIDE.

Note the gradual encroachment of the dyspneic upon the apneic phase in *b* causing a disappearance of the latter without change in the duration of the whole cycle.

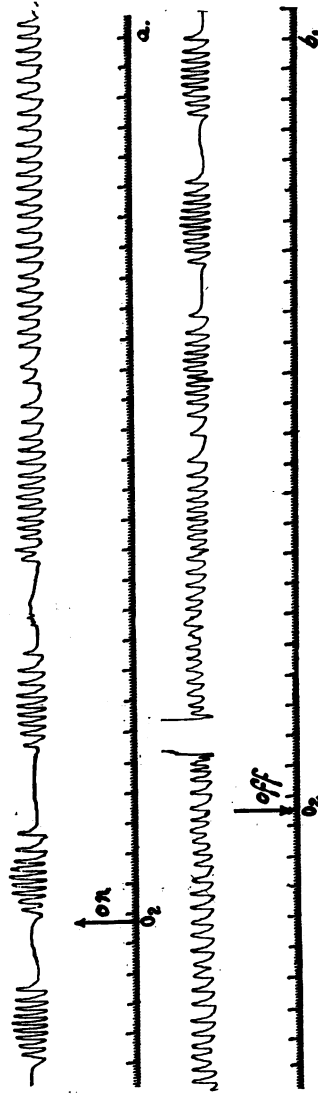


FIG. 7. THIS TRACING SHOWS THE ONLY EXAMPLE OF CONTINUOUS BREATHING OBSERVED DURING INHALATION OF OXYGEN WHICH, IN THIS INSTANCE, WAS ADMINISTERED BY A MASK.

shorter and began indeed to disappear. The length of an entire cycle did not, however, increase. When the concentration reached approximately 3 per cent (Figure 6*c* and *d*), the breathing was continuous and remained so throughout the whole period of administration lasting one and one-half hours. On discontinuing the administration of carbon dioxide, the transition to Cheyne-Stokes breathing took place. The apneic phases were at first brief, then grew longer, while the respiratory phases grew shorter (Figure 6*e*). No after effect suggesting exhaustion of the respiratory center was apparent even after this prolonged period of inhalation.

Once when oxygen was administered for a short time by mask there was a sudden transition to continuous breathing after two minutes (Figure 7). On another day, using the same technique, continuous breathing did not appear but the respiratory phase increased from 37 to 67 seconds, while the duration of apnea did not change appreciably. The whole Cheyne-Stokes cycle, therefore, increased about 50 per cent. A somewhat similar increase in another instance occurred when a mask fitted with one-way valves was used, and 80 per cent oxygen was inhaled from a large spirometer (Figure 8*a*). In this case a marked increase in

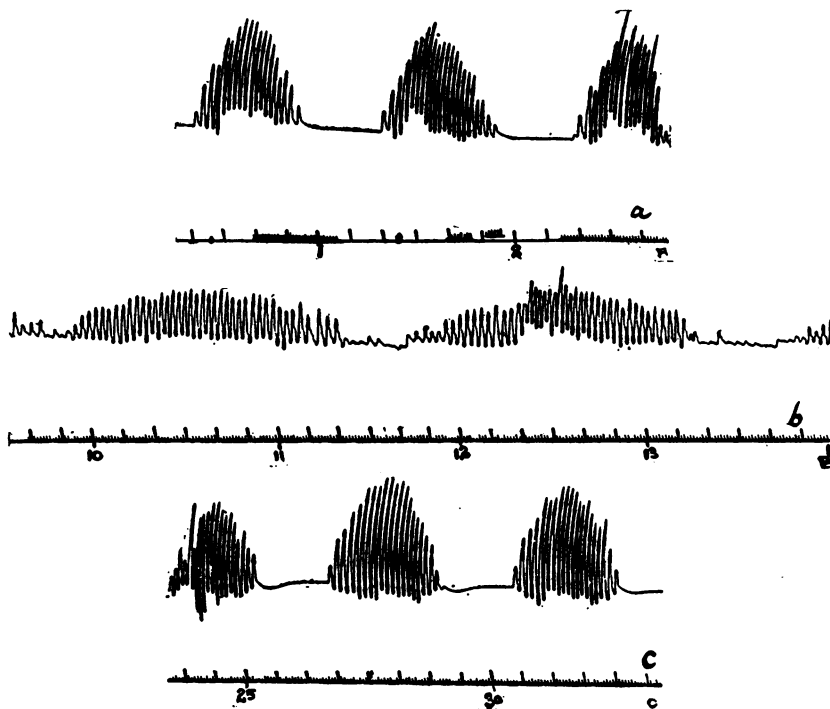


FIG. 8. TRACINGS *a* AND *c* WERE OBTAINED BEFORE AND AFTER, AND *b* DURING THE ADMINISTRATION OF 80 PER CENT OXYGEN BY MASK AND VALVE.

The increase in the length of the whole cycle is well shown in "b".



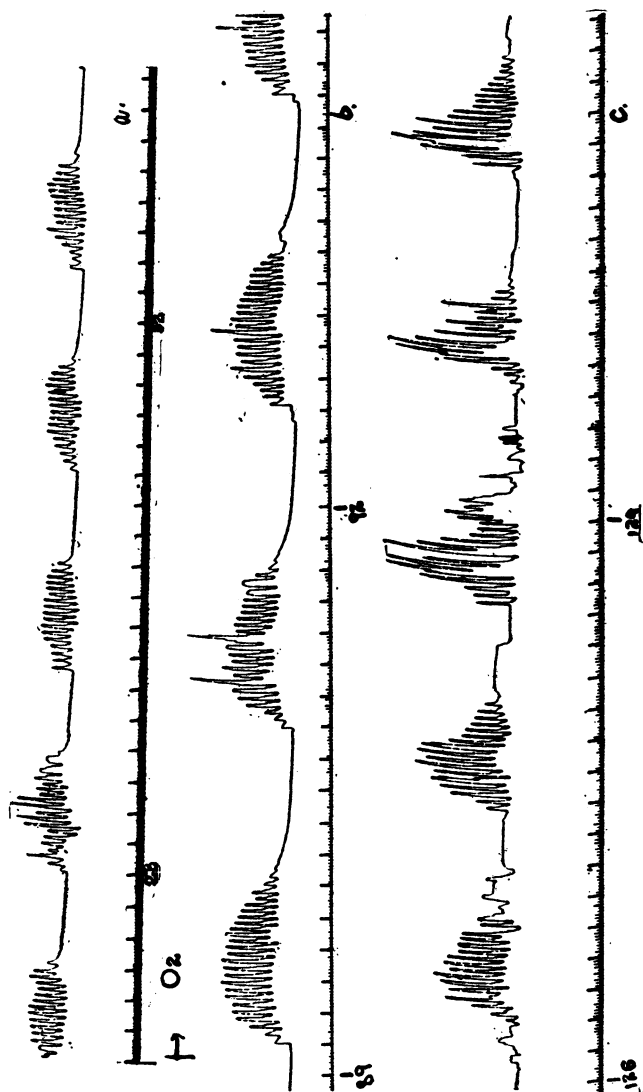


FIG. 9. TRACINGS *a*, *b* AND *c* WERE TAKEN BEFORE, DURING, AND AFTER THE ADMINISTRATION OF OXYGEN UNDER A TENT.

The whole cycle has increased as in Figure 8*b*, but the increase in this instance is mainly due to the greater duration of apnea.

the length of the respiratory phase and a decrease in the duration of apnea took place, the whole cycle increasing 75 per cent in length (Figure 8*b*). In the oxygen tent and chamber where the content of oxygen in the air breathed ranged from 40 to 55 per cent, somewhat similar results were obtained except that a decrease in the duration of apnea was never observed. When duration of apnea changed, it always increased in length. An increase in the length of the respiratory phase was always present (Figures 9, 10 and 11).

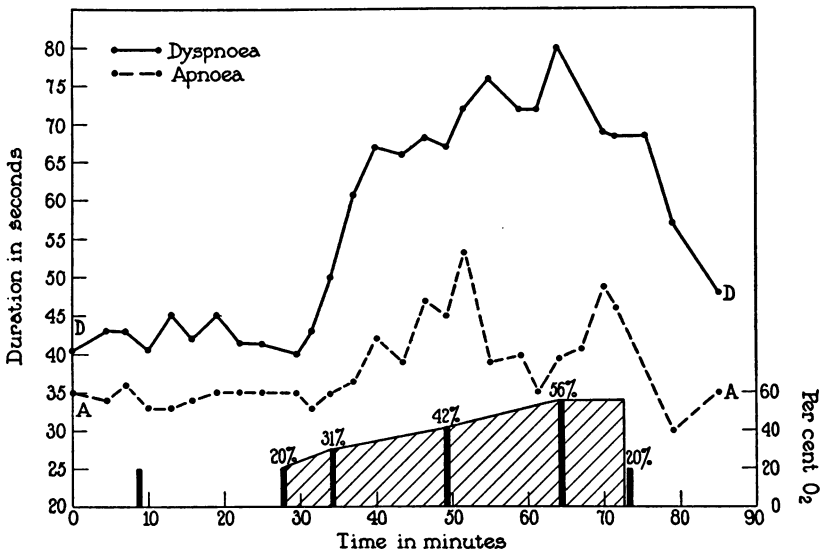


FIG. 10. CHART OF THE CHANGE IN DURATION OF APNEA AND DYSPNEA DURING INCREASE IN THE CONCENTRATION OF OXYGEN INHALED.

In one patient curves of the respiratory volume were obtained while the concentration of oxygen of the respired air was changed from 20 to 33 per cent (Figure 12). The respiratory and apneic phases both increased as usual, while the respiratory volume per minute decreased about 10 per cent, an amount just within the limit of error of measurement. The total amount of air respired during one whole cycle increased, however, about 50 per cent. This result was due to increase in length of the respiratory phase as well as to increase in the volume of each individual respiration. By modifying the cycles of his breathing a patient suffering from Cheyne-Stokes respiration may alter, without changing the volume of respired air, the composition of the gases in the blood. It is improbable therefore that measurement of the volume of the respired air would afford reliable information about the oxygen absorbed or the concentration of the gases in the blood.

## CHEYNE-STOKES RESPIRATION

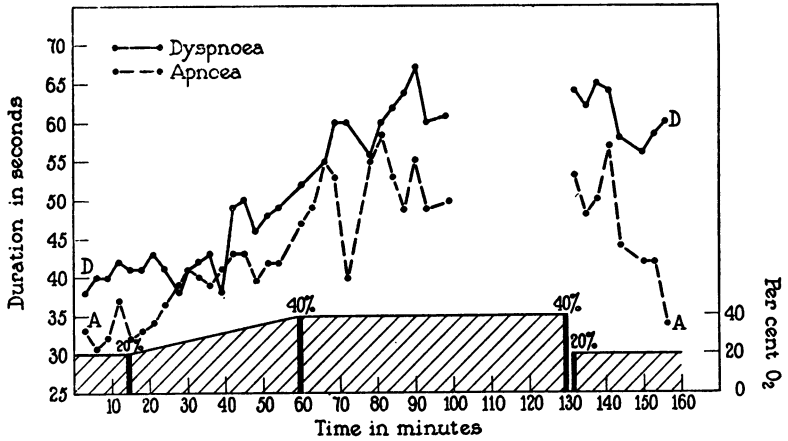


FIG. 11. CHART OF THE CHANGE IN DURATION OF APNEA AND DYSPNEA DURING INCREASE IN THE CONCENTRATION OF OXYGEN INHALED.

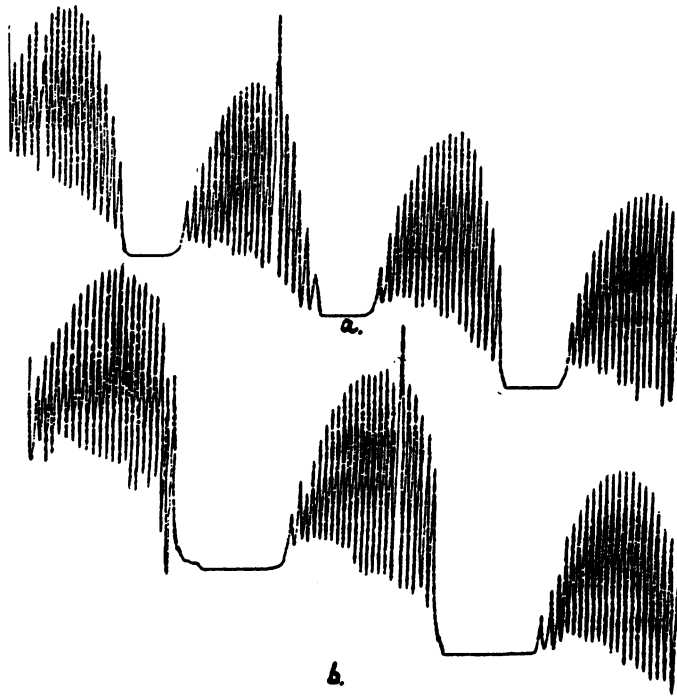


FIG. 12. VOLUMETRIC TRACING OF RESPIRATION (BENEDICT-ROTH MODIFIED) (a) BEFORE AND (b) DURING INHALATION OF INCREASED CONCENTRATION OF OXYGEN.

A series of samples of arterial blood were examined during the administration of oxygen for comparison with the results obtained when room air was respired. During its administration the variations in concentration of both oxygen and carbon dioxide in the blood were much less during a respiratory cycle. In none of the samples did the content of oxygen fall below 90 per cent even though the cyclic form of breathing did not cease.

#### DISCUSSION

In the present study increase of carbon dioxide content of the atmosphere to which patients, the subjects of Cheyne-Stokes breathing, were exposed, consistently brought about continuous respiration. A similar result was not obtained by the administration of oxygen even if the concentration was increased up to 80 per cent.

With carbon dioxide, the respiratory phase increased and the apneic phase decreased in length, so that the duration of the whole cycle remained unchanged. With oxygen, on the other hand, the length of the respiratory phase increased while that of apnea remained the same or became even longer, so that the duration of the whole cycle was greatly prolonged. That continuous breathing may follow the administration of high percentage of oxygen when given by means of a mask may be due to factors suggested earlier in the paper as objections to this method of administration. It may be due, however, to conditions inherent in the experiment which differ from those obtaining in the use of the oxygen tent or chamber, namely, the occurrence of much greater concentrations of oxygen or the abruptness of the change from atmospheric to higher concentrations of oxygen. Further investigations of the conditions of administration are necessary. These observations do not, we think, permit the inference which has been drawn by others, that inhalation of increased concentrations of oxygen stops Cheyne-Stokes breathing. It is possible, however, to confirm that part of the results of Uhlenbruck's experiences which show that the form of Cheyne-Stokes respiration can be modified by a change in concentration of the gases which are inhaled. It is impossible, therefore, to regard the periodicity of Cheyne-Stokes breathing as an expression of the peculiar rhythm of the respiratory center alone since this periodicity may be modified or even arrested by changing the composition of the inhaled air.

That inhalation of percentages of carbon dioxide higher than normal brings about continuous breathing is probably due to the fact that no matter how great the degree of dyspnea, the concentration of carbon dioxide in the alveolar air prevents the escape of carbon dioxide from the blood in sufficient quantities to allow the stimulating properties of the blood to fall below the threshold value for the respiratory center. Administration of a concentration of carbon dioxide just sufficient to occasion

continuous respiration might, therefore, constitute another measure of the irritability of the respiratory center. An analysis of the effect of breathing high percentages of oxygen is more complicated because two factors are involved. In the first place oxygen lack is generally regarded as a respiratory stimulus. When more of this gas is made available, the strength of the stimulus, therefore, decreases; but the stimulating property of the blood may, nevertheless, be increased as the result of oxygenation, since oxyhemoglobin develops stronger acid properties than hemoglobin (9, 10). The two factors act in opposite directions. For instance, by eliminating oxygen lack, one might suppose that the apneic phase would be prolonged, the respiratory phase shortened, and the depth of ventilation decreased. But by reason of the greater acid property of oxyhemoglobin, the effect of better oxygenation might be similar to that of breathing carbon dioxide in that it might result in an increase in the acidity of the blood. Analysis of the nature of the mechanism is also complicated by the fact that every change in the relations of the phases of the Cheyne-Stokes cycle occasions change in the carbon dioxide content of the blood. Further studies of the behavior of the gases in the blood are necessary in the attempt to solve this problem.

If the treatment of Cheyne-Stokes respiration has as its object the restoration to normal of the concentrations of the gases in the blood, then bringing about continuous respiration need not of itself be regarded as improvement, because continuous breathing alone does not necessarily mean that the ventilation is more nearly sufficient. For example, two patients with Cheyne-Stokes respiration were observed in whom the last stage of their disease was accompanied by an increase in cyanosis, and return to continuous breathing at one and the same time. If the object of treatment is to bring about continuous respiration, then inhalation of carbon dioxide in a chamber may be attempted, using the smallest concentration necessary to assure this result. To decrease the rhythmic recurrence of lack of oxygen, the effect of inhalation of oxygen in the chamber may also be utilized as is shown by the analysis of blood of patients while they are in the oxygen chamber.

#### SUMMARY

The influence on Cheyne-Stokes respiration of breathing varied mixtures of carbon dioxide and air has been studied in periods both of short and of long duration.

Increase in concentration of carbon dioxide in the air inhaled prolongs the respiratory phase, and decreases the apneic phase until continuous breathing appears.

Increase in the concentration of oxygen up to 80 per cent in the air inhaled prolongs the respiratory phase markedly. The duration of apnea is sometimes increased, and sometimes remains constant. Inhaling

oxygen in greater concentrations than that of air does not usually result in continuous breathing.

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